

The effectiveness of osteopathic treatment in women with endometriosis-related pain

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Abstract

Background: Endometriosis, a chronic disease characterized by endometrial tissue located outside the uterus is associated with chronic pelvic pain and subfertility. An understanding of the pathophysiology and effective treatment strategies remain elusive. Osteopathic treatment is commonly used in gynaecological disorders and osteopaths are confronted with the symptoms of endometriosis. The purpose of this study was to assess the effectiveness of osteopathy as a complementary treatment for women with endometriosis-related pain.

Subjects: Twenty women aged between twenty-seven and forty-eight were recruited for this study; five women were excluded. All had been experiencing chronic pelvic pain for at least six months and had been diagnosed with endometriosis by laparoscopy.

Methods: A non-randomized, non-blinded within-subject design was used. The subjects received four osteopathic treatments after a baseline phase of eight weeks. Scores were collected twice in each phase to compare pre and post treatment results. The materials included a Visual Analogue Scale (VAS) and a validated disease specific quality of life questionnaire called EHP-5. The intervention consisted of a collection of osteopathic techniques adapted to the individual needs of the patient.

Results: A significant decrease of the primary outcome measure pelvic pain could be measured by the end of the treatment phase compared to the baseline phase ($p=0,007$). The results of the secondary outcome measure showed significant changes within five out of eleven domains of the EHP-5. A linear regression demonstrated that the osteopathic treatment showed the best results in women who reported a severe loss of control at baseline.

Conclusion: The present study shows a significant change in the perceived pain and in some domains of health-related quality of life indicating that osteopathic treatment can be an acceptable tool in the treatment of endometriosis-related pain. Nevertheless, more research to understand the connection between pain in endometriosis patients and osteopathy is needed.

Keywords: *endometriosis, chronic pelvic pain, health-related quality of life, osteopathy, osteopathic manipulative treatment*

Zusammenfassung

Hintergrund: Endometriose ist eine chronische Erkrankung bei der sich Gebärmutter-schleimhaut ausserhalb der Gebärmutter ansiedelt. Unterbauchschmerzen und Subfertilität können die Folge sein. Bis heute bestehen Lücken im Verständnis der Pathophysiologie und der medizinischen Behandlung. Osteopathie wird bei gynäkologischen Krankheitsbildern angewendet und Osteopathen/innen sind mit den Symptomen der Endometriose konfrontiert. Die vorliegende Studie untersucht die Effektivität einer osteopathischen Behandlung bei endometriose-bedingten Unterbauchschmerzen.

Stichprobe: 20 Frauen zwischen 27 und 48 Jahren wurden für diese Studie rekrutiert, 5 Frauen wurden aufgrund der Ausschlusskriterien nicht in die Studiengruppe aufgenommen. Alle Frauen hatten seit mindestens 6 Monaten Unterbauchschmerzen und sind durch eine Bauchspiegelung mit Endometriose diagnostiziert worden.

Methodologie: In dieser nicht randomisierten, nicht-blinden prospektiven Studie mit within-subject design wurden die Probandinnen nach einer achtwöchigen Wartezeit viermal osteopathisch behandelt. Die Messvariablen (VAS und der endometriose-spezifische Quality of Life Fragebogen EHP 5) wurden in beiden Studienphasen jeweils zweimal ermittelt. Die Behandlung bestand aus osteopathischen Techniken, die individuell an die Probandin adaptiert wurden.

Ergebnisse: Eine signifikante Verringerung der Messvariable chronischer Unterbauchschmerz konnte am Ende der Interventionsphase gemessen werden ($p=0,007$). Die Ergebnisse der zweiten Messvariablen zeigten signifikante Verbesserungen in 5 von 11 Bereichen des EHP-5. Eine Regressionsanalyse veranschaulicht, dass die Variable Schmerz bei Frauen, die in der behandlungsfreien Zeit einen ausgeprägten Kontrollverlust aufgrund ihrer Erkrankung angaben, besonders gut mit Osteopathie zu beeinflussen war.

Schlussfolgerung: Da die vorliegende Studie eine signifikante Verringerung des Schmerzes und ebenfalls eine Verbesserung der Lebensqualität in einigen Bereichen vorweist, kann angenommen werden, dass die Osteopathie im Bereich der Endometriose eine wirkungsvolle Behandlungsstrategie ist. Jedoch sind weitere Forschungsergebnisse nötig, um den Zusammenhang einer osteopathischen Behandlung und dem endometriose-bedingten Schmerz zu erklären.

Schlüsselwörter: *Endometriose, chronische Unterbauchschmerzen, gesundheitsbezogene Lebensqualität, Osteopathie, osteopathische Behandlung*

Table of Content

1.. Introduction.....	7
1.1.Common facts _____	7
1.2. Motivation _____	7
2.. Background	9
2.1. Anatomy and physiology of the human endometrium – an overview _____	9
2.2. Cyclic endometrial changes _____	10
2.3. Innervation of the female pelvis _____	11
2.4. Physiology of endometriosis _____	11
2.4.1. Inflammation	12
2.4.2. Adhesions.....	12
3.. Endometriosis	13
3.1. Definition _____	13
3.2. History _____	13
3.3. Prevalence and epidemiology _____	13
3.4. Theories on the causes of endometriosis _____	14
3.4.1 Metastatic theory	15
3.4.2. Metaplastic theory	15
3.4.3. Immunological theory	15
3.4.4. Archimetra concept	16
3.4.5. Heredity.....	16
3.4.6. Conclusion	16
3.5. Diagnosis _____	16
3.5.1. Physical Examination.....	17
3.5.2. Medical imaging techniques	17
3.5.3. Laboratory Testing	17
3.5.4. Endometrial Biopsy.....	18
3.5.5. Laparoscopy.....	18
3.6. Classification _____	18
3.7. Localization _____	19
3.8. Signs and Symptoms _____	19
3.8.1. Pain.....	20
3.8.2. Dysmenorrhea.....	21
3.8.3. Chronic pelvic pain	21
3.8.4. Dyspareunia	22
3.8.5. Infertility	22
3.8.6. Health related quality of life burden	23
3.9. Treatment _____	23
3.9.1. Medication	24
3.9.2. Surgery	25
3.9.3. Complementary and alternative medicine	26
4.. Endometriosis and Osteopathy	27
4.1. Research _____	27
4.2. Osteopathic treatment concept _____	28
4.3. Theoretical explanations _____	30
4.4. Existing osteopathic studies in the field of endometriosis _____	31
5.. Materials and Methods	34
5.1. The aim of the study _____	34
5.2. Subject Selection / Recruitment _____	35

Table of Content

5.3. Subjects	36
5.4. Inclusion and exclusion criteria	36
5.4.1. Inclusion criteria	36
5.4.2. Exclusion criteria	36
5.4.3. Termination Criteria	37
5.5. Measurement methods	38
5.5.1. Pain - Ratings of pelvic pain	38
5.5.2. HRQoL	39
5.5.3. The use of rescue analgesia	39
5.6. Procedure	40
5.6.1. Intervention	40
6.. Statistics	41
6.1. Descriptive statistics	42
6.1.1. Sample description	42
6.2. Inferential statistics	44
6.2.1. Primary outcome measure	44
6.2.2. Influence of other variables on the assessment of the pain	46
6.2.3. Secondary outcome Measure	49
6.2.4. Linear regression	54
7.. Discussion	56
7.1. Sources of Error	59
7.2. Suggestions for further research	61
7.3. Conclusion	63
8.. Bibliography	64
9.. List of figures, tables and diagrams	69
9.1. List of figures	69
9.2. List of tables	69
9.3. List of diagrams	70
10.. Appendix	71
10.1. Letters and Declaration of consent	71
10.2. History Taking	71
10.3. Endometriosis Health Profile Questionnaire EHP 5	71
10.4. Acknowledgements	71
10.1. Letters and declaration of consent	72
10.2. History taking	75
10.3. Endometriosis Health Profile EHP-5	76
10.4. Acknowledgements	78

1.. Introduction

1.1.Common facts

Endometriosis is a chronic disease that affects women during their reproductive years. It occurs when uterine lining tissue appears outside the uterus in the abdominal cavity and presents itself with an array of clinical symptoms, including non cyclic pain, dysmenorrhea, dyspareunia, and infertility (Lindheim, 2005). The most important characteristics of the disease from the patients perspective are according to Bitzner et al. (2008) delayed diagnosis of a chronic disorder of which the cause is not clear, onset at young age, chronic pain and infertility.

As the estimated number of undetected cases is believed to be quite high, records on the frequency of the disease vary greatly. However, Olive and Schwartz (1993) estimate that between 5% and 15% of all women suffer from the disease. Most of the women report a long delay between the onset of symptoms and diagnosis and claim that delayed diagnosis is a problem. Jones et al. (2004) have estimated, that the mean delay in the UK is 8 years and that delay in diagnosis leads to feelings of frustration and isolation. According to Husby et al. (2003) anglo-american studies have shown a delay from 3 to 11 years between the onset of pain symptoms and the final diagnosis of endometriosis.

Because the clinical symptoms of endometriosis range from severe dysmenorrhea, chronic pelvic pain to infertility, and medical treatment involves unwanted side effects (Urđl, 2006) it is apparent that the disease interferes with the patients quality of life and affects according to Jones et al. (2006) social life, sexuality, and psychological well-being. These factors have socio-economic consequences, as the women's capacity to work is limited and the costs for treatments such as medication and surgery must be partially covered by the general health system. Therefore, Simsa et. al. (2007) state that Endometriosis is an expensive disease. In 2009 the World Endometriosis Research Foundation (WERF) announced the first ever prospective study to assess the hidden cost of endometriosis to society and to women with the disease, and found out that the estimated cost to society in the United States alone at \$ 22 billion in 2002 – higher than the cost of migraine or Crohn's disease.

1.2. Motivation

The key motivation for investigating the symptoms of endometriosis and thus make it the subject of this thesis was the fact that research into this disease has brought to light numerous unknown factors and has generated uncertainties regarding diagnosis and therapy amongst both doctors and those affected. The central focus of this thesis lies on answering

the following questions: Can there be a relation between the symptoms of endometriosis and an osteopathic intervention? Are there any explanations for this? Does the affected quality of life for patients change after they have been treated with osteopathy? Can osteopathy for women with endometriosis-related pain be regarded as a useful form of therapy?

Currently, treatment of pain associated with endometriosis includes both medical treatment and surgical procedures. Unfortunately, either type of treatment has side effects and has to be repeated when symptoms return. Sinaii et al. (2007) surveyed 1276 women diagnosed with endometriosis according to their different treatment methods and summarized that women with endometriosis undergo multiple medical treatments and surgical procedures, which are not always perceived as helpful and are commonly stopped due to ineffectiveness or side effects. Due to this situation, this study aims to investigate whether osteopathy can be considered as a viable form of therapy for endometriosis-related pelvic pain and examines through a trial the effect of osteopathy on the parameters of pelvic pain and health-related quality of life using a Visual Analogue Scale (VAS) and a validated disease-specific quality of life questionnaire.

Evidence that osteopathy can be considered as a possible alternative therapy can be found for instance in some editions of "Endo-Info", the newsletter published by the German Endometriosis Association. For example, Endo-Info Nr. 21 cited an article from the Zentralblatt für Gynäkologie: *"Physical measures such as visceral Osteopathy, [...] may be a useful addition to the therapeutic approach."* (Brons 2003). Endo-Info Nr. 32 : *"Manual therapies and in particular osteopathy can be used to treat pain."* According to Sinaii et al. (2007) 66.7 % of all the women who chose osteopathy as an alternative treatment found it to be helpful for treating their symptoms. This statement is also supported by Bergquist et al. (2000), who suggest that manual therapy should be evaluated for the treatment of pelvic pain.

Since endometriosis has been clearly associated with manual therapies in general and osteopathy in particular, I wish to examine these correlations and connections in this study in more detail. In order to perform an effective osteopathic treatment for endometriosis, ideally the causes and symptoms of the disease should be understood. In the following chapters, I aim to summarize the anatomical basis and physiological correlations of endometriosis so that they constitute a reasonable starting point for the actual study design.

2.. Background

2.1. Anatomy and physiology of the human endometrium – an overview

The uterus is located in the pelvis, is pear-shaped and 7-9 cm long. According to Hebgen (2004), topographic connections exist to the peritoneum, bladder, rectum, vagina, small intestine loops, sigmoid colon, tubes, ovaries and ureter. The blood is supplied through the A. uterina originating from the A. iliaca interna. The venous draining flows through the V. uterine, which flows into the V. iliaca interna. The wall of the uterus is formed by three layers: the peritoneum builds the outer layer, in the middle lies a thick layer of smooth muscle (myometrium), and the uterine lining (endometrium) being the inner layer, whereby a distinction is made between a deeper basal layer (basalis) and a surface functional layer (funktionalis). The following picture shows how the endometrium lines the inside of the uterus.

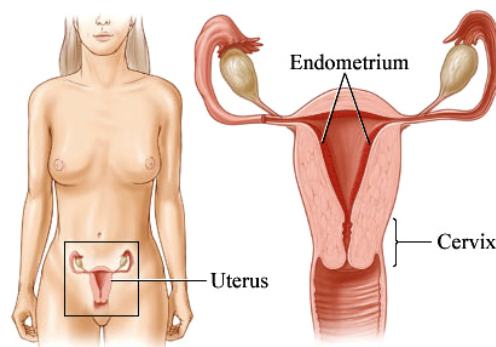


Figure 1 : endometrium and cervix

Young and Loy (2005) describe that the endometrium is composed of multiple cell types, including epithelium, stroma, resident bone-marrow-derived immunocompetent cells and blood vessel endothelium, and Zalpour (2002) explains further that stroma is connective tissue forming the supportive framework of the organ and contains the blood vessels and nerves.

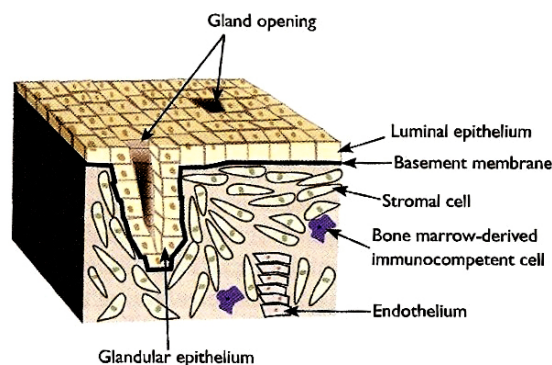


Figure 2: Structural organization of human endometrium

2.2. Cyclic endometrial changes

The inner walls of the uterus are completely covered with the endometrium, the uterine lining tissue. What particularly distinguishes it from other body mucous membranes is its ability to change. During each menstrual cycle its cells increase, it becomes thicker and prepares for its role as a breeding ground for a fertilized egg. During approximately a one-month-period the endometrium undergoes cyclical changes that are triggered by hormones.

The hypothalamus is the top centre of the hormone system. From here, the releasing hormone GnRH is secreted, which causes a release of the follicle-stimulating hormone (FSH) and the luteinizing hormone (LH) in the anterior pituitary gland (adenohypophysis). FSH causes the maturation of an egg in the ovaries as well as the secretion of oestrogen in the first half of the cycle. Oestrogen causes the reconstruction of the endometrium after menstruation. Also in the first half the corpus luteum develops from an ovarian follicle, stimulated by LH, which secretes progesterone in the second half of the cycle. Progesterone triggers the preparation of the endometrium for the reception of the oocyte. In this phase, the glands of the uterine lining grow rapidly. If after ovulation the ovum is not fertilized, the corpus luteum regresses and stops its progesterone production. This reduces the blood flow to the functionalis immediately. The feeding arteries close down, making the superficial zone ischaemic which eventually leads to decay or degeneration. After some time the constricted arteries open up again, the walls of the damaged surface vessels burst to release blood into the stroma, and ultimately patches of tissue separate from the basal layer of endometrium (Shaw, 1995). Menstruation begins. The following figure shows how the endometrium changes within one menstrual cycle due to the influence of oestrogen and progesterone.

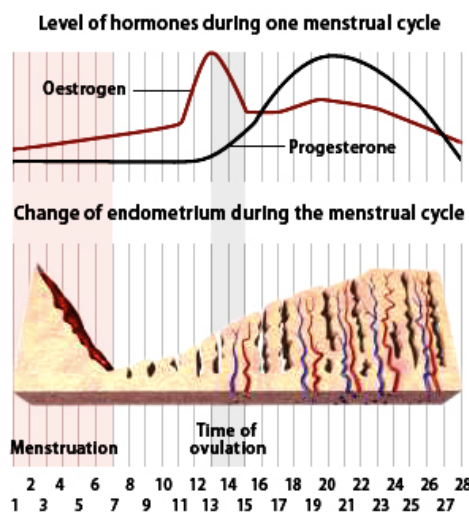


Figure 3: hormonal influence on the endometrium within the menstrual cycle

Young and Loy (2005) documented that the primary functions of the human endometrium are to allow the implantation of a normal embryo and provide mechanisms for the clearance of tissue and homeostasis at menstruation. At the same time, the endometrium must also provide a defense against invasion by potential pathogens and prevent the implantation of an abnormal embryo. In order to achieve these functions, the endometrium undergoes profound changes in structure and function during each cycle that result in defined periods of proliferation, embryo receptivity, and menstruation.

2.3. Innervation of the female pelvis

As described by Shaw (1995) all internal reproductive organs as well as the pelvic peritoneum have solely autonomic innervation with no somatic supply. The autonomic nerves carry sensory and motor fibres. Visceral branches generally arise from the spinal cord and then descent to form visceral plexuses. Sympathetic fibres arising from the tenth thoracic vertebra to the first lumbar vertebra (Th 10-L1) and parasympathic fibres coming from the roots of sacral segments S2 to S5 form the inferior hypogastric plexuses (left and right). The plexuses lie on either side of the rectal ampulla, as shown in the picture below.

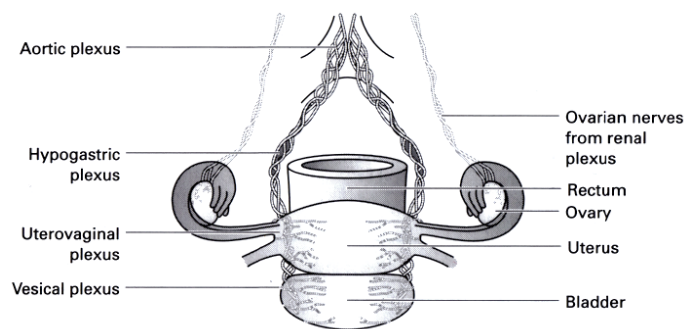


Figure 4: Innervation of the pelvis

2.4. Physiology of endometriosis

In endometriosis, endometrial cells appear outside the uterus, usually in the area of the pelvis. Figure 5 shows where endometrial growths can be found within the pelvic peritoneum.

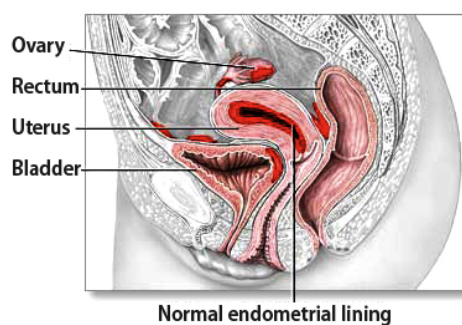


Figure 5: Common sites for endometrial growths in red

Like all other cells of the endometrium, they are subject to the monthly cycle, i.e. they build up and then bleed out. However, because the peritoneum does not have access to a body opening, the blood is unable to flow away and accumulates in endometriosis lesions of sizes ranging from less than a millimetre to several centimetres large.

This results in symptoms such as abdominal and pelvic pain and sometimes infertility. Different theories exist that try to explain how these symptoms are caused and will be discussed in the following.

2.4.1. Inflammation

Olive (2005) explains that endometrial tissue secrete various local products, such as growth factors and cytokines. Cytokines, like interleukin 1 or TNF α , to mention just a few, or growth factors, such as VEGF (vascular endothelial growth factor) are important mediators of intercellular communication within the immune system and seem to play a role in the pathogenesis of endometriosis, which is according to Shaw (1995) associated with an inflammatory peritoneal environment. Usually, levels correlate with the severity of the disease, with the highest amounts of cytokines being present in advanced stages of endometriosis. It has been found out by Iwabe et al (2002) that cytokines are produced not only by immune cells, but also by endometriotic implants themselves. Supposedly, they play a role in the development and progression of endometriosis. But the question whether the inflammation is a cause or a consequence of the disease has yet to be answered and could be one of the reasons why scientists have up to now been unable to find a cure for the disease.

2.4.2. Adhesions

„Adhesions are defined as connections between opposing serosal and/or nonserosal surfaces of the internal organs and the abdominal wall, at sites where there should be no connection (Hammoud et al. 2004) “

Lindheim (2005) estimates that the endometrial lesions form adhesions and that these adhesions can be the cause for the typical endometriosis-symptoms such as dysmenorrhea, chronic pelvic pain or infertility, as they cause anatomic distortion and nerve compression. Shaw (1995) suggests that endometrial tissue is likely to adhere to the mesothelial lining after arrival in the peritoneal cavity. This adherence may be mediated by cell adhesion molecules and soluble factors produced by peritoneal macrophages. After adherence, endometrial tissue growth seems to be promoted by hormones, growth factors and angiogenic factors. Porpora et al. (1999) conclude that the presence and extent of pelvic adhesions correlates significantly with the severity of endometriosis-related pelvic pain.

3.. Endometriosis

3.1. Definition

„Endometriosis is defined as the presence of endometrial-like tissue outside the uterus, which induces a chronic, inflammatory reaction. The condition is predominantly found in women of reproductive age, from all ethnic and social groups. The associated symptoms impact on general physical, mental and social well being.“ (ESHRE guideline, 2005)

Endometriosis is defined by Adamson (1999) as the growth of endometrial tissues composed of both glandular and stromal elements at an extrauterine site which can cause dysmenorrhea, dyspareunia, non-cyclical pain and subfertility. Schindler (2007) classifies endometriosis under the so-called benign, oestrogen-dependant diseases in women of reproductive age, because it is rare before menarche or after menopause. Shaw (1995) found several studies that suggest that endometriosis is a progressive disease. Tariverdian (2007) describes various forms of endometriosis, such as *endometriosis genitalis interna* with endometrium adjacent to the myometrium or the fallopian tubes. *Endometriosis genitalis externa* is being referred to if lesions can be adjoining ovaries, Douglas pouch, uterine ligaments, vagina or elsewhere within the pelvic cavity. *Deep infiltrating endometriosis* is according to Porpora et al. (1999) a very painful form of endometriosis and is characterized by fibrosis and smooth muscle proliferation. In the interest of clarity, a distinction between the different forms has not been made in this work and was not taken into consideration when selecting the subjects for the trial.

3.2. History

According to Schindler (2007) endometriosis was first described as a disease process more than 300 years ago. The oldest publication can be traced back to Schroen (1690) who describes his findings as peritoneal „ulcers“ occurring on the surface of the bladder, intestine, and the uterus. In 1896, from the observation of 100 cases, which he called adenomyoma, Cullen concluded that glandular inclusions found in adenomyoma derived from the mucous membrane of the uterus. In 1927 Sampson accomplished a publication that was considered the discovery of endometriosis and provided the first theory on the pathogenesis of the disease.

3.3. Prevalence and epidemiology

Despite decades of basic and clinical research, no accurate data on the prevalence are known, as this would have initially required that all women undergo a laparoscopy. Therefore, because the gold standard according to the ESHRE Endometriosis Guideline

Development Group (2005) for the definitive diagnosis of endometriosis is by laparoscopy the observed prevalence may be biased by the selection of patients for surgery. Missmer and Cramer (2005) assume that patients with more frequent utilization of the medical system, those of higher socioeconomic class, or those with the most severe / aggressive disease may be more likely to undergo investigative laparoscopy. Moreover, endometriosis is present in some women who are asymptomatic and do not have surgery. The observed prevalence may also depend on the skill and experience of the surgeon in identifying endometriosis. It is also possible that those with endometriosis whose symptoms are improved by less invasive, more generic treatments (e.g. anti-inflammatory medications or oral contraceptives) may never 'need' an invasive, albeit confirmatory, diagnosis. Therefore, estimates of the frequency of endometriosis vary widely. Based on the few reliable data, the prevalence of the condition can reasonably be assumed to be around 10% (Vigano et al., 2004; Missmer and Cramer, 2004; Schindler, 2007). According to Schindler (2007), in 50-70% of young women with severe dysmenorrhoea an endometriosis was found by laparoscopy. According to Bush (2007) it is becoming increasingly recognised that endometriosis in teenagers is extremely common. A graph by Schweppe (2003) illustrates the frequency of endometriosis in different patient groups and explains, among other things, how the number of pain patients increase in later reproductive age (between 33 and 43 years).

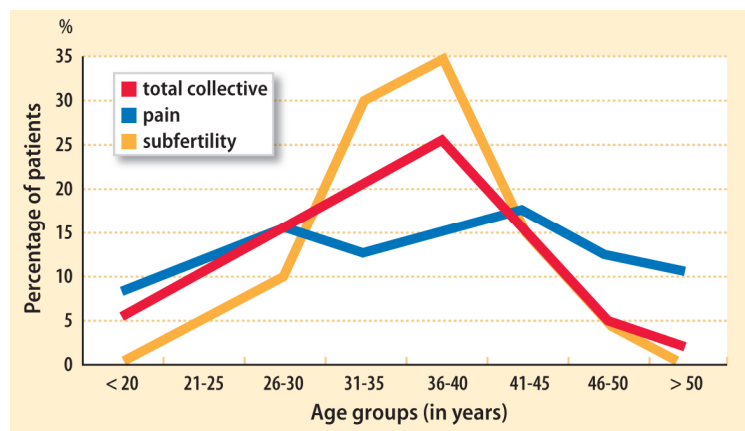


Figure 6: Frequency distribution of endometriosis in pain patients, infertility patients, and the overall number of patients at the Endometriosis Ambulanz Westerstede in 1998 (n = 865).

3.4. Theories on the causes of endometriosis

Several theories have been developed in the past years to explain the causes of endometriosis. Many articles exist that describe the different theories of the development of the disease, with some more accepted than others (Shaw, 1995; Witz, 2002; Suwandinata, 2005; Schindler, 2007). This study adopts the collection by Schindler (2007), as it appears to be the most recent. The following theories are briefly described here:

3.4.1 Metastatic theory

It is the most widely accepted theory that endometriosis results from retrograde menstruation, usually referred to as Sampson's theory, which proposes that endometrial tissue passes through the fallopian tubes during menstruation, and once there the still viable cells subsequently implant and grow. According to Simsa et al. (2007) it is the most supported theory based on studies with women and baboons. D'Hooge et Debrock (2002) suggest that the quantity and quality of retrograde menstruation could be the crucial factor in initiating the onset of the disease.

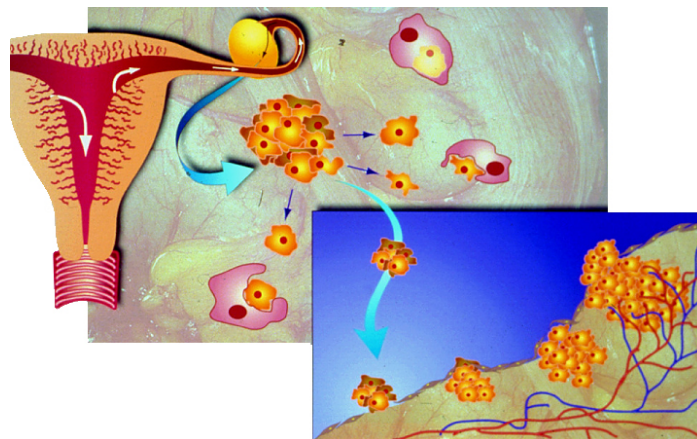


Figure 7: Retrograde transplantation

3.4.2. Metaplastic theory

The metaplastic theory stands in contradiction to the metastatic theory. The theory of metaplasia (cell type conversion) suggests the possibility of peritoneal cells differentiating into functional endometrial tissue. A prerequisite of this theory is that mesothelial cells lining the ovary and pelvic peritoneum contain cells capable of differentiating into endometrium (Witz, 2002). According to this hypothesis endometriosis arises as a result from secondary stimulation of inflammation or hormonal influences. This theory could also explain the occurrence of endometriosis anywhere that mesothelium is found.

3.4.3. Immunological theory

The ability of endometrial implants to survive in locations outside the uterus may be related to an abnormal immune response. As described by Suwandinata (2006) the theory of an altered immune system in endometriosis suggests that changes in cell-mediated immunity and humoral immunity may contribute to the development of the disease. Olive (2005) showed that endometriosis patients have increased numbers of activated macrophages compared to healthy controls. These cells secrete various products, such as growth factors and cytokines, which are associated with an inflammatory peritoneal environment.

3.4.4. Archimetra concept

According to Leyendecker et al. (1998) endometriosis is considered a disease of the archimetra, which consists of the glandular and stromal part of the endometrium. In patients with endometriosis, fundamental alterations of the archimetra can be demonstrated that involve the anatomical structure and the cellular biochemistry, as well as specific functions such as uterine peristalsis and the inflammatory defence system.

3.4.5. Heredity

Endometriosis is also very likely a genetic disease. Witz (2002) found that there is an increased prevalence of endometriosis in first-degree relatives of affected women compared with the general population and that endometriosis may be a genetically transmitted disorder which results in an altered immune surveillance that allows for the attachment and growth of endometrium outside the uterus.

3.4.6. Conclusion

As endometriosis has multiple manifestations it is likely that several mechanisms are involved in its pathogenesis. According to both Urdl (2006) and Schindler (2007) it is the so-called combination theories that are most likely responsible for the development of the disease. Olive (2005) finds the theory of retrograde menstruation the most plausible. However, given the near universality of retrograde menstruation, it is also likely that additional factors are involved in the development and maintenance of the disease. Halis et al. (2010) argue, that this hypothesis fails to explain why endometriosis does not affect all women, and see the answer supplied by the archimetra-concept. This discussion may show that no single theory can explain all cases of endometriosis.

3.5. Diagnosis

Generally, affected women seek a gynaecologist due to pain or suspicion of subfertility. This is why according to Schindler (2007) a medical history is compiled at the start of the examination, listing the various symptoms. History-taking gives the physician the opportunity to become thoroughly acquainted with the patient and her complaints and to correlate the symptoms with the physical findings. Halis (2010) suggests that a physician should pay close attention to the dynamics and temporal course of the patients's symptoms. According to a verbal survey of a few local gynaecologists, (Windelen, Dewitt, Kuhn) initially a palpation is conducted and an ultrasound image is created before, in the case of substantiated evidence, the patient is advised to undergo a laparoscopy. There are no non-invasive tests that can reliably diagnose an endometriosis. This explains why for a lot of women a long time elapses between the onset of symptoms and an established diagnosis. Ballweg (2004) has

summarized that the delay in the diagnosis of endometriosis from over 7000 confirmed cases is on average more than 9 years. According to Husby et al. (2003) women reporting infertility in addition to pain did not have a significantly shorter delay. Moreover, it seems, according to Schindler (2007), that the younger the affected woman at the time of symptom onset, the longer the time interval to diagnosis. According to Hummelshoy et al. (2006), this long time delay in diagnosis results in severe symptoms and more drastic forms of treatment, which is additionally stressful for the women concerned.

3.5.1. Physical Examination

Finding pelvic tenderness, a fixed retroverted uterus, tender utero-sacral ligaments or enlarged ovaries on examination is suggestive of endometriosis (ESHRE guidelines, 2007). Ideally, the examination should be performed while the patient experiences at least some symptoms, preferably during menstruation. Koninckx et al. (1996) describe that careful palpation during menstruation increases the detection rate of deep endometriosis whereas Spaczynski et al. (2003) have arrived to the conclusion that, when compared with surgical evaluation, pelvic examination showed poor sensitivity, specificity, and predictive values.

3.5.2. Medical imaging techniques

Imaging studies may be a useful adjunct in the identification endometriosis in patients. Among the various techniques available, ultrasonography and magnetic resonance imaging (MRI) seem to be the most useful (Kim und Adamson, 2008). Techniques such as standard radiography and computer tomography are, according to the author's knowledge, not used in the diagnosis of endometriosis.

3.5.3. Laboratory Testing

Since endometriosis is a frequently unrecognized disease, research today is increasingly concerned with developing new blood tests for diagnosis in order to facilitate the detection of the disease. Dogan et al. (2008) published that the diagnosis of endometriosis with the determination for the tumour marker CA-125 is possible. This tumour marker is typically elevated in ovarian cancer but it appears that patients with endometriosis as well show significantly higher values in the blood serum. However, Simsa et al. (2007) documented that tumour markers such as Ca-125, Ca19-9, and serum protein PP14 lack sensitivity and specificity when used to screen for endometriosis. Nevertheless, according to Dogan et al. (2008), research continues on the development of blood tests for the diagnosis of endometriosis, even if they are yet to be available for routine use in clinical practice.

3.5.4. Endometrial Biopsy

It has been documented by Al-Jefout et al. (2009) that endometrial biopsy, with detection of nerve fibres, provides a reliability of diagnosis of endometriosis which is close to the accuracy of laparoscopic assessment. Should this diagnostic method find its way into daily clinical use, it would probably reduce the time to diagnosis significantly, thereby helping many women to find the right treatment for themselves. The same study showed that women with endometriosis and pain symptoms had significantly higher nerve fibre density in the functional layer of the endometrium compared to women with infertility but no pain, which could explain the frequent occurrence of endometriosis-related pain.

3.5.5. Laparoscopy

The 'gold standard' investigation for women with symptoms of endometriosis is, according to the ESHRE guideline (2007), a visual inspection of the pelvis at laparoscopy. That means that a definitive diagnosis of most forms of endometriosis requires an invasive operation. This is based on the presumption that laparoscopy allows the visualization of the pelvis, and if pathology is encountered the procedure affords the opportunity to treat any disease surgically. Schweppe (2007) suggests that it is reasonable to complete surgical removal of the disease and the adhesions during the same operation.

3.6. Classification

Disease severity is assessed by simply describing the findings at surgery, or quantitatively using a classification system such as the one developed by the American Society for Reproductive Medicine (ASRM) in 1997. It has been proposed to allow clear communication among those who study and treat this disease. Here, the severity of the disease is divided into different stages, classifying Stage I as minimal, Stage II as mild, Stage III as moderate and Stage IV as severe. The ideal classification system should enable accurate assessment of the extent and location of disease, be useful in predicting outcome based on the stage of disease, and provide guidance in selecting the appropriate treatment. However, Kim und Anderson (2008) indicate that all attempts to develop a classification scheme for endometriosis that fulfill these criteria have failed, because studies comparing stage-specific treatment outcomes are hindered by the limited ability of the ASRM classification system to correlate the anatomic abnormalities with the degree of infertility and pelvic pain. Vercellini et al. (2006) studied the association between lesion type, disease stage and severity of pain in a large group of women with endometriosis to verify whether endometrial implants at different sites determine specific complaints and evaluated the validity of the current classification system in women with symptomatic disease and found out that the association was marginal and inconsistent.

Basically, a reasonable classification is only possible within the framework of a laparoscopy or an abdominal incision. The division in stages is based on the description of the number, size and location of the lesions. It also includes the adhesions that have incurred as a result of endometriosis. The ASRM classification system however does not take into account these deeply infiltrating types of the disease that can also occur in the intestine, the bladder and other organs. For this purpose, the **ENZIAN** Score was developed that, according to ESHRE (2005), should be used for deeply infiltrating endometriosis.

However, these classifications reflect neither the activity level of the endometriosis nor the symptoms of the patient, so that the severity of the stress due to the symptoms does not always clearly correlate with the stage. Some women with severe endometriosis suffer no or very little symptoms, whilst other women with minimal endometriosis suffer severe pain. For these reasons, this classification was not addressed when selecting the subjects for this trial.

3.7. Localization

According to Schindler (2007) endometriosis lesions are most commonly found on the ligamentum sacrouterinum (60%) followed by the ovaries (52%) and the Douglas pouch (28%). Approximately 10 % of the lesions can be found on the bladder, the ligamentum latum (broad ligament of the uterus), the rectum and the mesosalpinx. Red, white, yellow, and black lesions have been found simultaneously present in the same woman. In osteopathy, techniques have been described that can specifically treat the above-mentioned areas. Therefore, in this trial, particular attention was given to these areas during the osteopathic examination.

3.8. Signs and Symptoms

Clinical presentation of endometriosis is associated with a wide variety of symptoms, although in some patients it is asymptomatic. Common symptoms that can occur together or alone are: dysmenorrhea, dyspareunia, pelvic pain and infertility (Lindheim, 2005; Suwandinata, 2006; Kim und Anderson, 2008). Although dysmenorrhea is not predictive of endometriosis, it is recognized, among others, by Porpora et al. (1999); Fauconnier and Chapron (2005); and Vercellini et al. (2007) to be the most commonly reported symptom. As the aim of the present study is to examine and investigate pelvic pain with and without dysmenorrhea, it will be described below in detail and several theories on the cause will be discussed, whereas the other symptoms will be discussed briefly for the sake of completeness. Firstly, however, the attempt is to offer a basic definition and a physiological explanation of pain.

3.8.1. Pain

“Pain: an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.” (IASP, 1979)

Pain is perhaps the cardinal symptom of endometriosis. Shaw (1995) explains that various types of pain are associated with the disease : dysmenorrhea, deep dyspareunia as well as pelvic pain which can be unrelated to intercourse or menstruation. However pain perception is subjective. On the one hand, tissue damage may not necessarily trigger the pain that would be expected from a specific injury. On the other hand, pain can also occur without the stimulation of pain receptors. Maurischat (1995) describes every pain reaction as an expression of social context (education, cultural background, personality traits) as well as the present condition, which depends, among other factors, on the time of day and the state of the endocrine or central nervous system. Pain as suffered in endometriosis is primarily chronic. According to Zalpour (2002), chronic pain occurs either as a constant pain or as a frequently recurring pain and is very difficult to localise and treat. According to Flor (1991) accompanying feelings may include helplessness, depressive mood swings, general irritability and loss of control. Lederman (2007) also points out that pain perception strongly depends on the patient’s mental condition. Thus mental factors such as anxiety, depression, low self-esteem and irritation increase the sensitivity to pain.

3.8.1.1. Neurophysiology and biochemistry of pain

Nociception refers to the central nervous system’s reception, transmission and processing of tissue damaging stimuli, so-called noxious stimuli. Pain is mostly attributable to inflammation or reduced blood flow to a tissue (Maurischat, 1995). Due to local physiological changes, various pain-transmitting nerve fibres are stimulated. According to Meyer et al. (1994), three different mechanisms are responsible for this stimulation:

- Mechanical stimulation occurs due to the pressure increase in the tissue resulting from swelling, which in turn activates the pain receptors.
- Chemical stimulation occurs when in the affected area cells secrete substances such as bradykinin, histamine and prostaglandin, which activate the pain receptors.
- Thermal stimulation occurs when the temperature increases in the damaged area and activates the pain receptors.

This follows that also in the case of the pain in endometriosis, the mechanical stimulus of a pressure increase in the tissue as well as an inflammation with its chemical and thermal processes may be responsible for causing the pain.

A recent study (Al-Jefout et al., 2009) documented, that women with endometriosis and pain symptoms had significantly higher nerve fibre density in comparison with women with infertility but no pain. On the one hand, this result indicates that in the future it will be

possible to diagnose endometriosis using endometrial biopsy and, on the other hand, it can also show why pain is such a leading symptom in women with this disease.

3.8.2. Dysmenorrhea

Dysmenorrhea refers to the occurrence of painful menstrual cramps of uterine origin and is a common gynaecological condition. Dysmenorrhea comes in two forms, primary (functional) and secondary (acquired). It occurs due to spasms of unstriated musculature, lack of blood flow and inflammation. Kokjohn et al. (1992) define primary dysmenorrhea as abdominal and/or back pain associated with the ovarian cycle in the absence of an organic pelvic pathology such as endometriosis or polyps. When there is a presence of a pelvic pathology such as endometriosis or polyps it is referred to as secondary dysmenorrhea. Kim and Anderson (2004) describe that the onset of symptoms generally occurs before the onset of menstruation and gradually improves over several days after initiation of flow. The pain is often localized in the lower abdomen and deep pelvis. It is bilateral, sometimes radiating to the back and thighs. It is described as dull and aching and may be associated with rectal pressure, nausea and episodes of diarrhoea.

It is assumed by Lindheim (2005) that in dysmenorrhoea the pain is caused, among other things, by myometrical contractions induced by prostaglandins.

There appears to be several possible explanations: Firstly, Lindheim expands that in human and experimental animals, endometriotic tissue contains and produces prostaglandins. Moreover, clinical trials demonstrate that prostaglandin synthetase inhibitors such as ibuprofen substantially reduce dysmenorrhea symptoms in the treatment of endometriosis-associated pain. (Kauppila et al., 1979)

3.8.3. Chronic pelvic pain

„Chronic pelvic pain is defined as the presence of non-menstrual pain below the navel for more than three months, or menstrual pain of at least 6 months in duration causing functional disability.“ (Lindheim, 2005)

Pelvic pain is the second most commonly presenting symptom in women with endometriosis and occurs in 30-50% of patients (Porpora et. al., 1999). The patient usually describes the pain as aching, constant, dull and deep and rubs a general area when asked to indicate the site of their pain. Shaw (1995) has been suggested that these characteristics of poor localization and the aching, dull, deep nature of the pain are typical of visceral pain. One explanation for this behaviour is supported by two studies that examine the relationship between endometriosis and pelvic pain. Porpora et al. (1999) write that the severity of pain significantly correlates with the presence and extent of pelvic adhesions ($p=0.004$). The pain may be in relation with compression or infiltration of nerves in the sub-peritoneal pelvic space

by the implants. This theory is also supported by Al-Jefout et al. (2009), who found a higher nerve fibre density in women with endometriosis. Fauconnier and Chapron (2005) write that the association between severe pelvic pain and endometriosis is independent of the macroscopic type of the lesion or their anatomical locations and may be related to recurrent cyclic microbleeding in the implants. Endometriosis-related adhesions may also cause severe pelvic pain. Mechanisms of causation may generally be divided whether the pain is caused directly by endometriotic deposits (early) or consequent of scarring and ensuing fibrotic reaction (late).

3.8.4. Dyspareunia

Dyspareunia occurs in 25-40% in endometriosis patients (Shaw, 1995) and is according to Spaczynski et al. (2003) usually positional and most intense during deep penetration. Suwandinata (2006) documented that it was found mostly in the rectovaginal form of the disease. Dyspareunia seems to be most intense prior to menstruation, but in severe cases it may preclude intercourse throughout the month. This can cause anxiety and avoidance and seems to cause a lot of misery amongst endometriosis sufferers. According to Lindheim (2005) it may be related to the stimulation of pain fibers by traction or stretching of scarred elastic tissues and / or by pressure on nodules of endometriosis embedded in fibrotic tissues. This theory is also supported by Vercellini et al. (2006) who found that the stretching of inelastic scar tissue and the mechanical pressure on the endometrisis lesions accounted for the presence of dyspareunia .

3.8.5. Infertility

Infertility is another symptom in patients with endometriosis, and viewed by Spaczynski and Duleba (2008) the most important risk factor in endometriosis. According to Kim and Anderson (2008) the incidence of endometriosis in infertile women ranges between 4,5 to 33%, whereas Lindheim (2005) reports that the rate of endometriosis in the infertile patient undergoing surgical evaluation has ranged from 20% to 68%. In the presence of adhesions infertility may be reasonably explained by mechanical interference, but in the absence of anatomic distortions the mechanism of subfertility associated with endometriosis is poorly understood. However, Garrido et al. (2002) point out that results from egg donation programs show that egg cell development and early embryonic development in women with endometriosis can be disturbed. Endometriosis-related infertility can be adressed with surgery. In general, within 1–2 years after surgical therapy for endometriosis, a pregnancy rate of approximately 65% can be expected (Kim and Adamson, 2008). The chance of conceiving from in-vitro-fertilization was significantly lower for endometriosis patients than for a control group, as described by Barnhart et. al. (2002). These authors also reported that

endometriosis patients experienced significantly lower fertilization and implantation rates as well as number of oocytes obtained.

3.8.6. Health related quality of life burden

Colwell et al. (1998) describe health-related quality of life as a multi-dimensional concept encompassing physical, social and psychological aspects associated with a particular disease. Endometriosis impairs health related quality of life (HRQL), especially in the domains of pain, psychological and social functioning (Gao et al. 2006). According to Lemaire (2004) symptoms caused by endometriosis may alter the ability to perform particular tasks and impair a persons perceived health as well as an overall sense of well-being. Psychologically, endometriosis-related symptoms like pain and infertility seem to encourage depression, anxiety and feelings of uncertainty, which in turn can interfere with a woman's perceived sense of control, handling of adverse situations and resourcefulness. In this study health related quality of life burden is regarded as a consequence of the above mentioned symptoms and will therefore be further analysed in an experimental situation.

3.9. Treatment

„Treatment must be individualised, taking the clinical problem in its entirety into account, including the impact of the disease and the effect of its treatment on quality of life. Pain symptoms may persist despite seemingly adequate medical and/or surgical treatment of the disease. In such circumstances, a multi-disciplinary approach involving a pain clinic and counselling should be considered early in the treatment plan.“ (ESHRE guideline)

The efficacy of medical and surgical treatment of endometriosis is a source of questions and controversies. A complete resolution of endometriosis is not yet possible. Therefore Donnez et al. (2003) have come to the conclusion that therapy should be directed to three essential outcomes: reduction of pain, increasing of the pregnancy rate and delay of recurrence as long as possible. The treatment effects on health related quality of life for patients with endometriosis have been evaluated by Gao et al. (2006) and showed that pharmacologic interventions as well as surgical interventions have been shown to improve physical and psychological functioning. The choice of the primary therapeutic approach is determined by the patient's living conditions (e.g. the wish to have children), the psychological strain, the side effect profile, and the costs of medication. The figure below shows the overall utilization of treatments for endometriosis of 1160 women (Sinaii et al., 2007).

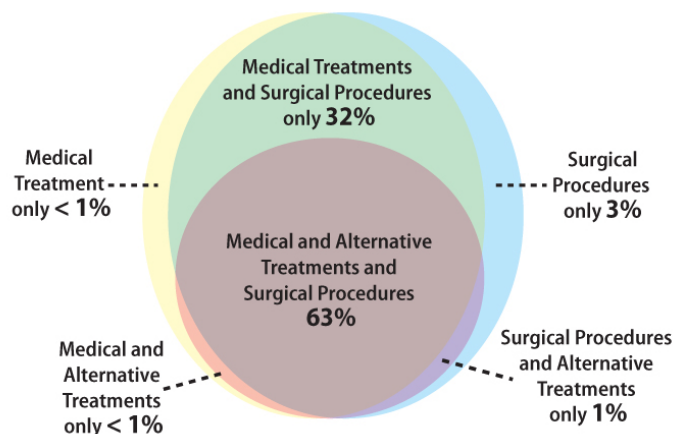


Figure 8: Overall utilization of treatments for endometriosis

3.9.1. Medication

The use of medical therapy in the treatment of endometriosis has a long history, with a wide variety of medications having been utilized. Today, the treatment of endometriosis and the associated pain consists predominantly in the administration of various non-steroidal anti-inflammatory drugs (antiphlogistics) and oral contraceptives. Sinaii et al. (2007) confirm that 74.2 % of all the examined women (n= 1160) took non-steroidal anti-inflammatory drugs for the pain symptoms, 71.9 % of the women had taken contraceptives at some point, followed by 51.3 % who had taken gonadotropin-releasing hormone agonists (GnRH agonists) during the course of their illness.

3.9.1.1. Non-steroidal anti-inflammatory drugs (NSAIDs)

Nonsteroidal antiinflammatory drugs (NSAID's) are among the most frequently prescribed drugs in western countries. But Allen at al. (2009) found only limited evidence to show whether NSAIDs are effective for the treatment of pain caused by endometriosis. One of the main adverse drug-reactions is a high incidence of adverse gastrointestinal effects (Köhler et al., 1997).

According to Halis et al. (2008), the most commonly used drugs in gynaecological practice are Ibuprofen and Diclofenac, which are comparable in their effect as cyclooxygenase inhibitors. Selective Cyclooxygenase-2 (COX-2) inhibitors have been on the market since 1999. Compared to non-specific COX inhibitors, COX-2 inhibitors are said to reduce the adverse gastrointestinal effects by more than half. On the other hand, Mukherjee et al. (2001) have shown that selective COX-2 inhibitors increase the incidence of cardiovascular complication. Interestingly, Chishima et al. (2002) described that in the uterus, COX-2 was localized in the endometrial epithelium. They also observed more frequent and denser

Cyclooxygenase-2 staining in the ectopic (occurring in an abnormal place) endometriosis implants when compared with eutopic (situated normally) endometrium. Levels of COX-2 in endometriosis were increased up to five times than of eutopic endometria. Therefore, selective COX-2 inhibitors could also pose a causal therapeutic approach in the future.

3.9.1.2. Endocrine Therapies

The action mechanism of endocrine therapies is based mostly in the anti-oestrogenic effect on the endometrium. Endometriosis implants are capable of responding to hormones. Hormonal therapy interrupts the cycle of stimulation and bleeding of endometrial tissue and induces atrophy of the implants, thereby decreasing the pain and the inflammatory response that may cause adhesions. According to Halis et al. (2008), the currently used endocrine drug treatment approaches such as the administration of progestogens (gestagens) or oral contraceptives were found to be equivalent in meta-analyses. In cases of extensive endometriosis (rASRM III or IV) the primary administration of GnRH analogues is useful. Hummelshoj et al. (2006) documented that it can be injected monthly or taken daily by a nasal spray. A downregulation of pituitary gonadotropin secretion will appear. The end result is a lack of ovarian stimulation followed by a temporal medical menopause. Generally an amenorrhoea is achieved. Arndt et al. (2006) recommend the use of concomitant medication (substitution for the reduced endogenous oestrogens) when administering GnRH analogues to eliminate the hypo-oestrogenic side effects such as hot flashes, insomnia, headaches or bone demineralization. The duration of treatment with GnRH analogues for pain patients is six months. Even though a three-month treatment would be, according to Schindler (2003), just as effective, however, the recurrence-free interval would be shorter. Unfortunately, current medical therapy is not definitive in the treatment of endometriosis because existing adhesions cannot be removed and recurrence of endometriosis may occur after cessation of treatment. Just as the endometrium resumes its function after discontinuation of hormone therapy, this obviously also occurs in the ectopic lesions.

3.9.2. Surgery

Usually endometriosis is diagnosed by invasive laparoscopy. According to Schweppe (2009) it is reasonable to complete surgical removal of the disease and the adhesions during the same operation. Different types of endometriosis and different therapeutic goals such as pain relief or pregnancy require different individual therapeutic strategies. With regards to pain relief the aim is to achieve satisfactory relapse-free intervals after complete surgical removal of the endometriosis lesions. According to Schweppe (2003), the principle of conservative, organ-preserving surgery for endometriosis is based on an as complete as possible removal of the implants while preserving fertility. The surgical approach to endometriosis may be

accomplished by laparotomy or laparoscopy. With improvements in equipment and operative technique laparoscopy is probably the most common choice for surgery. Kim and Anderson (2008) describe that laparoscopy provides better visualization compared with laparotomy, less tissue trauma and exposure to foreign bodies, possibly less adhesion formation, and lower complication rates. Laparoscopic incisions seem to be smaller and less painful, allowing faster recovery times. Other possible surgical procedures include uterine nerve ablation (UNA) or Presacral neurectomy (PSN), both involve surgical interruption of the sensory nerve fibres near the cervix to block the pain pathways. Proctor et al. (2005) found there was only little evidence for its use in women with endometriosis. This statement is also supported by Halis et al. (2008), who consider bilateral oophorectomy (surgical removal of the ovaries) with or without hysterectomy as the most effective form of therapy for a recurrent endometriosis and a completed family planning. However this only seems justifiable in the case of substantiated extensive recurrence after medical and surgical therapies, as the women go straight into their menopause with all its side effects. Sinaii et al. (2007) describe that in 18 % of the 1160 examined women, a hysterectomy was conducted because of endometriosis. After extensive surgery, there is often need for rehabilitation. Here Arndt et al. (2006) recommend that the focus of the rehabilitation should be on the recovery of physical, psychological and social well-being and that the main emphasis should lie on the patient's quality of life.

3.9.3. Complementary and alternative medicine

Because of the above mentioned unwanted side effects of medical treatment, women may use alternative treatments to relieve symptoms and doctors may recommend alternative treatments. Sinaii et al. (2007) describe that women with endometriosis turn to whole medical systems and energy medicine such as acupuncture or homeopathy, mind-body medicine including counseling or meditation, biologically based therapies like diets or herbs and body-based therapies such as physical therapy or osteopathic treatment, in order to get the help that conventional traditional medicine does not seem to offer. Therefore the following will attempt to show whether an osteopathic treatment could possibly display the results the affected women are looking for when they turn towards complementary medicine.

4.. Endometriosis and Osteopathy

„I have never found enlargements or tumefactions of the uterus or ovaries with a perfectly normal articulation of the hip, sacrum, coccyx, lumbar and lower dorsal vertebrae.[...] We reason that a dislocated or strained hip, coccyx, sacrum, innominate, lumbar vertebra or rib will produce an abnormal irritation, stagnation, secondary growth of the uterus, kidney, bladder or other organs. When consulted on such diseases it is wisdom to withhold your opinion until you have found the cause and known that you are right, then your advice will be good and to the point. To the mechanic all abnormalities are effects.“ (Still, 1910)

4.1. Research

The amount of literature on endometriosis is extensive in medical databases. Medline for example lists 17,416 articles for the term „Endometriosis“. Oral et al. described already in 1996 that endometriosis stands as one of the most investigated disorders of gynaecology, with more than 4500 articles published in the past 25 years. In order to obtain sound results the literature research for this thesis was done using both German and English search terms. Keywords were “endometriosis”, combined with the words “dysmenorrhea”, “pain”, “adhesions”, “quality of life”, “chronic pelvic pain” or “alternative treatment”, as well as the combination with the words “osteopathy”, “osteopathic medicine” or “manual therapy”. Searches have been conducted in the Pubmed databases for any relevant articles and the Cochrane Collaboration for systematic reviews, as well as in two osteopathic evidence databases (WSO and AFO) and the library of the European School of Osteopathy. The literature study was completed with a search for scientific trials in the various national and international endometriosis associations. Relevant articles were searched for also in the Journal of the American Osteopathic Association and the two german osteopathic journals (not listed in pubmed): DO, Thieme, Stuttgart; and Osteopathische Medizin, Elsevier, Munich/Jena.

In the Journal of the American Osteopathic Association 28 articles appeared for the search term “endometriosis”, one of which directly addressed the correlation between osteopathic techniques and chronic pelvic pain (Tettambel, 2005). In the german journals, no articles were found on endometriosis. After reviewing all the abstracts, articles and reviews relevant to the study were selected for the establishment of the background and in turn their bibliographies were searched for significant source references.

In addition, osteopathic textbooks as well as personal course materials were included in order to incorporate current theories for a workable treatment plan.

4.2. Osteopathic treatment concept

„An osteopathic treatment is always individual because no patient is like the other and even the same patient presents differently in his tissue tension and energy potential from one day to the other“ (Liem, 2001)

The following aims to explain the concept of osteopathic treatment on which the intervention of this study is based on. Only a small part of these techniques are based on scientifically proven facts, the larger part consists mainly of traditional knowledge and osteopathic hypotheses, which have not been investigated in a scientific trial until this day. In the eyes of Andrew Taylor Still (1910) it is essential for an osteopath to possess excellent anatomical knowledge in the fields of gynecology and obstetrics. Still (1910) recommends that the first step should always consist of a thorough examination of the patient. He advised: “Lead a thorough examination before you are convinced that an abnormal growth exists on or near the uterus.” According to Still (1910) the idea of an osteopathic treatment is the elimination of dysfunctions diagnosed through osteopathic methods in order to support the body’s own repair and adjustment processes. Thus the choice of techniques are accordingly of a parietal, visceral or craniosacral kind.

To select an appropriate treatment concept for endometriosis-related pain, the author collected techniques from osteopathic literature and textbooks. The disease has been discussed by Barral (2004), Liem et al. (2002) and Hebgen (2004) among others. In addition, the textbooks by Riedl and Schleupen (2010), Lederman (2007) and Meert (2006) have been also considered in order to gain the largest range of treatment techniques possible from which to select.

The choice of timing for the beginning of the treatment period was based on Barral’s (2004) concept, which states that the visceral manipulative treatment is most effective during the week following the end of the menstrual period. Barral’s advice to work more on a lymphatic basis during the second half of the cycle was also taken into consideration. Barral grounds his reasons for the selected techniques to treat endometriosis as follows: *„ Since the uterine lining bleeds chronically, one should avoid administering direct or stronger treatment techniques as this could otherwise increase the bleeding. On the other hand, a functional treatment according to the Ecoute Test is recommended, as this releases local tension and improves the venous blood and lymph flow.“* However, even though the author followed this guideline in this trial, it is relevant to acknowledge Barral’s concept as an assumption which has no specific scientific proof.

Tettambel (2006) stated that chronic pelvic pain relates to endometriosis and recommends: *„the stabilization of anterior and lateral pelvic curves through exercise or osteopathic*

manipulative treatment utilizing techniques of muscle energy, balanced ligamentous tension, myofascial release and counterstrain to assist muscles to keep the spine upright and sufficiently flexible to support good posture.“ This quote hints to the close relationship between the mechanics of the spine and pelvis and the organs of the pelvic cavity which are most affected in endometriosis.

Since one of the principles of a general osteopathic treatment (GOT) is rhythm, routine and rotation, Eyal Lederman's book (2007) was helpful, as harmonious techniques seem to be especially effective in the area of pain relief and moving body fluids. Other techniques considered relevant for the osteopathic treatment of women with endometriosis-related pain were found at Liem et al. (2010) who recommend a mobilization of the ligamentum latum as well as a treatment of the liver combined with a light drainage of the pelvis to increase and balance vasculature. Meert (2006) suggest a technique for adhesions of the excavatio rectouterina, which is often affected by deep infiltrating endometriosis.

Nevertheless, an osteopathic treatment does not only consist of applying a series of techniques. Cherkin et al. (2003) find that osteopathic manipulation is not a single monotherapy, but rather a collection of interventions that are tailored to the needs of individual patients and that reflect the specific practitioners training and preference. The osteopathic principles do not intend to give detailed instructions as to which intervention is to be used with which disease. According to Liem et Dobler (2002) it always should be based on Still's basic principle to find the osteopathic lesion, provide treatment and then leave it alone (find it, fix it and leave it alone).

I have decided against using vaginal and rectal techniques in this trial for two reasons: On the one hand, these techniques may only be administered by doctors and natural health professionals in Germany (Meert, 2006), on the other hand all the subjects had a long history of pain as well as a generally increased tissue tension of the abdominal cavity, the tendency here should be to work very mindfully with direct visceral mobilizations. Barral (2004) also warns against routinely selecting a rectal or vaginal approach and advises to clearly access the advantages and disadvantages.

4.3. Theoretical explanations

It is assumed that there are several possible causes for pelvic pain that can be differently addressed in osteopathy, which will be discussed in the following:

- Inflammation: Implantation on to peritoneum seems to cause an inflammatory reaction, with release of painmediators such as prostaglandins, histamine and kinins.
- Adhesions.
- Increased pressure of the endo-lesions on the surrounding nerve tissue during cyclical microbleeding.
- Spasms of the smooth musculature.

Within the framework of an osteopathic treatment we have to distinguish between the different types of techniques : those that improve loss of mobility in relevant parts of the body, those that influence the hormonal balance and those that affect the autonomic nervous system to improve the blood circulation. Some authors have tried to find theoretical explanations for the effectiveness of osteopathic techniques on the above-mentioned causes. Proctor et al. (2006) substantiate the question of why structural techniques applied to the spine for menstrual problems might work as follows: *„Mechanical dysfunction in certain vertebrae causes decreased spinal mobility. This could affect the sympathetic nerve supply to the blood vessels supplying the pelvic viscera, leading to dysmenorrhoea as a result of vasoconstriction. Manipulation of this vertebrae increases spinal mobility and may improve pelvic blood supply.“* Licciardone et al. (2010) suggest that some of the benefits of osteopathic manipulative treatment may be mediated by analgesic effects and Wright (1995) discovered that pain relief through osteopathic treatment depends on the possible inhibitory effect of higher brain centres on incoming pain signals. So for example a direct stimulation of the sensorimotor cortex can suppress the sensory activities of the spinal level.

Hebgen (2003) describes that the uterus and its environment can be influenced through its circulation. This includes the arterial, venous and lymphatic supply as well as the sympathetic and parasympathetic innervation. Known osteopathic techniques such as the Rib-raising Technique for vegetative balance or the Grand Manoeuvre to promote hemodynamics are related to these subject area. Riedl and Schleupen (2010) describe that the venous supply can be improved through an osteopathic intervention, whereby local irritants such as prostaglandin or bradykinin can be discharged and cleared from the liver faster. As a result, the contractility of the uterus, and thereby the pain, is reduced.

The treatment of the endocrine organs should also be considered. According to Akerlund (1994), vasopressin and oxytocin, both secreted by the neurohypophysis, play a pathophysiological role in dysmenorrhea and chronic pelvic pain. It is also said by Akerlund

(1994) that oestrogen can be increasingly induced by local inflammatory substances in the uterine tissue, which cause an increase to the contractility of the uterine myometrium and can be held responsible for pelvic pain. Thus Riedl and Schleupen (2010) recommend that an osteopathic treatment should also take place at the level of the cranium, as here the hypothalamus and the pituitary gland are located, which are responsible for the release of vasopressin, oxytocin and oestrogen.

It has to be emphasized once more that most of this explanatory models have not yet been tested for their effectiveness in a scientific study with reference to the symptoms of endometriosis-related pelvic pain and urgently require scientific trials in the field of fundamental research. Nevertheless, some small studies already exist and will be discussed in the following.

4.4. Existing osteopathic studies in the field of endometriosis

„Evidence-based medicine aims to apply the best available evidence gained from the scientific method to clinical decision making. It seeks to assess the strength of evidence of the risks and benefits of treatments. Evidence quality can range from meta-analyses and systematic reviews of double-blind, placebo-controlled clinical trials at the top end, down to conventional wisdom at the bottom.“ (Wikipedia)

Osteopathy has traditionally been based on the opinions of experts and underpinned by biomechanical and physiological models that appeared plausible in light of the evidence that was available at the time of initial development (Fryer, 2008). The manual medicine world has changed over the last few decades and today health professionals are expected to be well-informed of current evidence as it relates to their discipline.

In order to verify existing knowledge, possibly avoid making the mistakes that have already been made and compare my thought processes with those who have explored the subject before me. I searched for already existing studies that have addressed the subject of endometriosis in osteopathy. Only a few studies that assess the potential of influencing endometriosis-associated pain with a non-drug and non-operative therapy have been found. Three trials were identified that included osteopathic treatment for endometriosis, which cannot be compared, considering the heterogeneity of the studies, for example the in- and exclusion criteria, the number of treatments, the presence of control groups or the selection of the outcome parameter. However, the results of these studies show a trend that encouraged me to write another research on the subject in order to confirm what earlier studies have measured.

In addition to a master's thesis by Ferreira (2005) written at the European School of Osteopathy (ESO) and the bachelor thesis by Dominique Antiglio (2001) of the same school, another study conducted by Dick und Koop (2009) has been found on the subject of osteopathy and endometriosis, which is probably the most important study regarding the

osteopathic treatment of women with endometriosis-related pain, because it had the largest patient sample with 27 participants.

1. "Can osteopathy help endometriosis?" by Dominique Antiglio, European School of Osteopathy, 2000-2001

The study in this Bachelor's thesis involved questionnaires that were sent out to 29 affected women, who had undergone osteopathic treatment with the aim of investigating whether there is a correlation between the presentation of symptoms of endometriosis before and after the treatment. The result of the Spearman's test indicated that there is no correlation. As this involves a questionnaire that has not been validated, I cannot say anything about the reliability or responsiveness of the questionnaire.

2. „The effectiveness of osteopathic treatment in patients diagnosed with endometriosis and complaining of abdominal, lumbo-pelvic pain and discomfort“ by Valeria Alves Ferreira, European School of Osteopathy, February 2006.

This is a pilot study with the same subject design, involving seven women, as part requirement for MSc Osteopathy. This study is devised as a comparative, qualitative, same subject design, with two conditions (before and after treatment) and no control group.

Ferreira used the Revised Oswestry Pain Questionnaire and the outcome of the trial has demonstrated an overall reduction of symptoms such as pain intensity and changing degree of pain. The experimental hypothesis could therefore be accepted as a significance level ($p = 0.05$) for a reduction in the severity of abdominal, lumbo-pelvic pain and discomfort in women with endometriosis. Ferreira admitted that there were limitations in comparing and challenging the findings and results with other relevant osteopathic studies due to the lack of other research projects.

3. "Do osteopathic treatments have a positive effect on the symptoms of women suffering from endometriosis?" by Susanne Dick and Jan Koop, Schule für klassische Osteopathie SKOM, 2009.

A randomized, controlled clinical trial, conducted with 27 participants, which appears to be the most significant due to the size of the trial and its methodological implementation. Pain sensation was set as the primary outcome measure, recorded through the SES pain scale. The second outcome measure was quality of life, assessed using an SF-36 Questionnaire as well as pain frequency and analgesic consumption. The result shows no statically significant improvement in the primary outcome measure. The greatest improvements were seen in the mental total score of the SF-36, which remained constant up to the follow-up after 5 months and therefore shows that an osteopathic treatment has a lasting effect on some domains that influence the quality of life in women with endometriosis-related pain.

As discussed in this chapter the osteopathic school of thought offers an explanatory model how an osteopathic intervention can have an impact on endometriosis-related pain and the

results of past studies seem to support that. The next section of the thesis will set out to examine the following hypothesis: It is possible through an osteopathic intervention to decrease pelvic pain in women with endometriosis and increase their health related quality of life.

5.. Materials and Methods

5.1. The aim of the study

The present study aims to investigate the effectiveness of osteopathic treatment in participants with endometriosis-related symptoms. Specific interest lies in the question whether osteopathic treatment decreases chronic pelvic pain and increases the health related quality of life.

Because randomized controlled trials (RCT's) are considered by the scientific community to provide the "gold standard" in terms of evidence my concept was based on a RCT in which two groups of 25 subjects would have received an osteopathic or physiotherapeutic treatment. It was designed as a randomized single-blinded, controlled trial to evaluate the efficacy of osteopathic medicine in women with endometriosis-related pelvic pain. But according to Proctor et al. (2006) a difficult issue in all randomized controlled trials of physical therapies is what to use as a control- or placebo-treatment. The issue of control group treatment took up long consideration also for this study. In the case of so-called sham treatments, one must surely pose the question of whether the applied treatment is in the interest of the participants. In the end, also in the light of ethical considerations, a physiotherapeutic treatment in the form of standardized pelvic exercises was considered as a control. The decisive factor for this was that a training program is currently running at the Hannover Medical School that includes pelvic floor exercises for women with endometriosis to reduce the pain and achieve an improvement in quality of life.

After a recruitment period of nine months in which the search for participants proved to be more difficult than initially expected the study type was changed into a within-subject design, because Hicks (1988) recommends no less than 12 subjects per group otherwise some statistical tests would be difficult to apply. That meant that also the idea of a randomization had to be abandoned.

In a within-subject design, the changes in the parameters in a phase without treatment are compared to those during a phase with treatment. According to www.davidmlane.com (2011) every single participant is subjected to every single treatment, including the control. It is also referred to as repeated-measures design by www.experiment-resources.com (2011) because within-subjects variables always involve taking repeated measurements from each subject. Thus, in this study design, the patients form their own control group. Advantages are, according to Hall (1998) that the conditions are always exactly equivalent with respect to individual difference variables, because the participants are the same. According to Sommerfeld (2006) the effect of an intervention can thus become more clearly apparent. One

of the weaknesses of this design would be a carryover-effect such as practice or fatigue, but are unlikely to happen in this case because the waiting period consists only of an observation. Furthermore a lower dropout rate can be expected, as it is a non-blinded study due to recruitment reasons, compliance of the osteopathic group will most probably be higher. In a pilot experiment involving three participants, it became evident how difficult it is to maintain the women's motivation over a period of four months, even if they received their treatments free-of-charge and they were actually feeling better than before the treatment began. As this trial involves a chronic disease, it is not to be expected that the symptoms will improve on their own, but that they will most probably only vary depending on known and unknown factors.

5.2. Subject Selection / Recruitment

Various sources estimate that 4-12 % of all women in their reproductive phase develop endometriosis (Olive and Schwartz, 1993; Schweppe, 2003). Most often, endometriosis is diagnosed after the age of 30 (Schweppe, 2003). Another source estimates that the average age at diagnosis is 28 years (Oehmke et al., 2007). Furthermore, according to a study of the Endometriosis-Ambulanz Westerstede, where the average age of 865 endometriosis patients with various symptoms were compared, it can be safely estimated that both young women under the age of 20 years and older women above the age of 45 years, each account for 5-10 % of the total population. For this reason, a wide-ranging recruitment was considered interesting, which took place over a period of 9 months. The search was for women aged between 18 and 48 years with a history of endometriosis-associated pain and surgical confirmation of the disease. Five local gynaecologists were contacted both verbally and in written form. Moreover, two clinics that perform laparoscopies were contacted in writing. The endometriosis association expressly recommended both clinics. Despite this effort, the overall response was very low, a total of six patients from two gynaecological practices were informed of the study. The author made efforts to contact endometriosis self-help groups that even after several inquiries did not respond. In addition, the author twice ran a call for applicants in a Cologne monthly magazine, to which seven patients responded and three of which fulfilled the inclusion criteria. A call for applicants in the author's own practice proved to be the most successful. Here seven more patients and/or their acquaintances applied, all of whom could be included in the trial. Even though, as described in chapter 3.6, there is an outline of the stages, this was not considered in the selection of the patients as, according to Halis et. al (2006), there is no correlation between the pain symptoms and the stage of the disease because the patient's subjective sensation of pain seems to vary too greatly.

5.3. Subjects

Fifteen (N=15) women aged between 27 and 48 with endometriosis diagnosed by laparoscopy participated in the study. For the study itself, no invasive examination methods were included and no therapy pauses were required. Twenty women were recruited, however four women were excluded from the study. One participant had never had a diagnosis confirming laparoscopy, one woman did not show any or only some symptoms of pelvic pain after laparoscopy, one already reported symptoms of menopause such as irregular bleeding due to the intake of GnRH-analogues and another woman had a intrauterine device (IUD). During the baseline phase one participant became pregnant and was excluded from the trial without taking her obtained data into the statistical analysis.

Before beginning the study, the participants completed and signed a consent form. Once consent had been granted, I compiled a full medical, gynecological and menstrual history. This was to determine that the source of pain was most likely due to endometriosis and to ensure that it was safe to perform any relevant treatment on the participant.

5.4. Inclusion and exclusion criteria

The selected inclusion and exclusion criteria are considering the current state of research according to Vincent et al. (2008).

5.4.1. Inclusion criteria

- Because the condition is predominantly found in women of reproductive age premenopausal women aged 18- 48 were chosen for this study.
- Endometriosis had to be documented by laparoscopic assessment, which is considered the gold standard according to the ESHRE guideline for the diagnosis and treatment of endometriosis (2007). To avoid postoperative influence, laparoscopy should have been performed at least twelve weeks ago.
- Symptoms of pelvic pain due to endometriosis for at least the last 6 months with a minimum rating of four on a visual analogue scale (VAS) at baseline.
- Had to be grown up in Western Europe, because Lock (1994) specified that measuring instruments such as questionnaires that have been developed in one cultural environment need not necessarily be valid in a different environment.

5.4.2. Exclusion criteria

- Pregnancy
- Intra Uterine Device (because some osteopathic techniques should not be performed on women with IUD's)
- GnRH analogues — Since according to Halis et al. (2008) these induce menopause which

may lead to a significant decrease in bone density (contraindication for some osteopathic techniques such as spinal manipulations)

- No other complementary alternative medicine treatments during the time of the trial to avoid possible influences
- Other relevant diseases
- Does not speak sufficient German to understand the questionnaire

5.4.3. Termination Criteria

- Severe worsening of the symptoms
- Emergence of an additional disease
- Termination at the subject's own request.

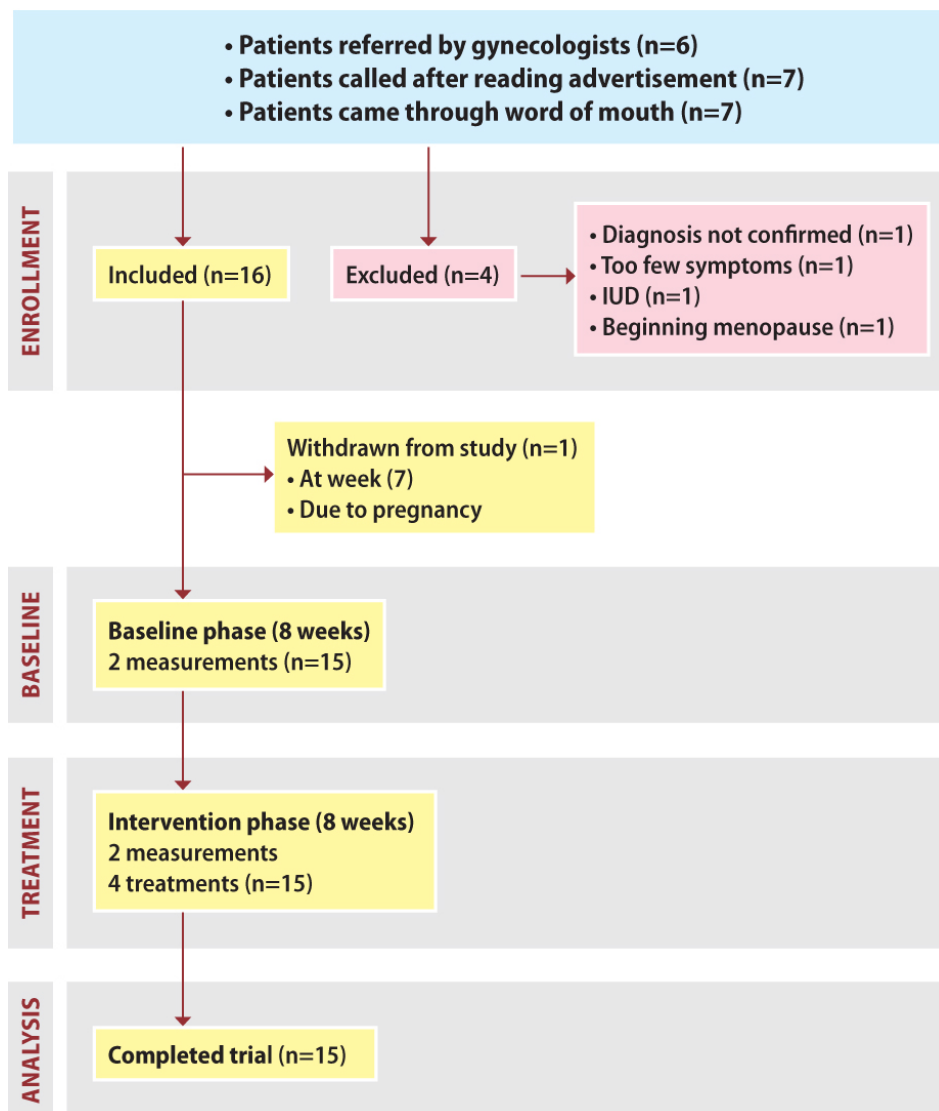


Figure 9: Flowchart of the progression of the trial

5.5. Measurement methods

As demonstrated in chapter 4.3. every former osteopathic trial in endometriosis-related pain used a different instrument to measure the outcome. But according to Vincent et. al. (2008) standardized entry criteria and outcome measures for clinical trials in endometriosis-related pain would facilitate the comparison of results, improving evidence-based practice in this area. A outcome measure should demonstrate validity and reliability and be sensitive to changes.

5.5.1. Pain - Ratings of pelvic pain

Vincent et al. (2008) suggest that dysmenorrhea and pelvic pain should remain the two primary endpoints in every clinical trial dealing with endometriosis. Because dysmenorrhea is more difficult to measure in women with endometriosis due to possible hormon medication that can cause irregular bleeding this study concentrates on measuring the chronic pelvic pain, as defined in chapter 3.8.3. by Lindheim (2005) .

As agreed by consensus groups in other chronic pain conditions it is recommended by Vincent et al. (2008) to use one of the rating scales as the baseline pain measurement. The three most commonly used instruments to assess pain intensity are verbal rating, numerical rating and visual analog scales. A Verbal Rating Scale (VRS) consists of a list of adjectives describing a component of pain. Disadvantages include forcing the patient to choose only one word which may not adequately reflect his pain experience. A Numerical Rating Scale (NRS) is similar to a VRS but the patient is required to rank components of her pain with a numerical value. This may be between 0 and 10 (11 point scale) or 0 and 100 (101 point scale) with endpoints representing the extremes of pain.

In this study, a Visual Analog Scale (VAS) was used to measure the perceived pain intensity, because they provide an unlimited number of possible responses, which is seen as an important advantage of VAS compared with NRS by Price et al. (1993). A VAS is a 10 cm=100 mm long straight line that is only verbally anchored at the end points with e.g. 0 = no pain and 10 = maximum pain. The patient is asked to express her perception of pain by placing a mark on the scale. The distance on the scale marked by the patient is then converted into millimetres to establish the measurement reading. Story et al. (2005) documented that this instrument for measuring subject pain intensity is an established method in clinical pain diagnosis and is easily comprehensible for the patient. In this study, the patients were asked to specify the maximum pain during the past month; other options would have been to assess the minimum or average pain intensity. However all of these scales are unidimensional, which means they can only address one component of pain at a time and this is considered to be a disadvantage. The way that pain affects a patient's life

can also be assessed in a more global way, both quantitatively in terms, for example of the amount of painkillers taken, or qualitatively by assessing the effect of pain of daily activities measuring the so called health-related quality of life (HRQoL).

5.5.2. HRQoL

The measurement of HRQoL, once the remit of the social sciences, is gradually being adopted in clinical medicine because it is being increasingly recognized that traditional outcome measures, such as pain levels, may not adequately assess the patient's experience of health. It is considered a multidimensional concept incorporating general health, emotional state, subjective wellbeing, life satisfaction and social support.

Vincent et al. (2008) emphasized the importance of measuring Quality of Life, as well as the value of using a patient oriented, disease specific measure with multiple domains such as the Endometriosis Health Profile Questionnaire EH-30 and its short form Endometriosis Health Profile Questionnaire EHP-5.

To measure health-related quality of life in this trial I chose the EHP-5, a shorter version of the EHP-30 which seemed to be the first disease-specific questionnaire to measure the health status of women with endometriosis. Developed at the University of Oxford by Jones et al. in 2003, the questionnaires include HRQoL concepts that are particularly relevant to endometriosis (work, sexual intercourse, relationship with the medical profession, infertility, relationship with children, treatment). The authors reported that the EHP-30 demonstrated high reliability and validity, but because it has been found that the data quality may be affected when instruments which collect large amounts of information are used, a short form has been developed as well, to be used in clinical settings where a short and economical health status measure is required. Two studies were carried out to develop the EHP-5. The results showed that the short form measure were very similar to those obtained from the long form, which suggests that it can be used without substantial loss of information in the measurement of health status in women with endometriosis.

Because I could not find a German translation of the questionnaire, which ideally would have to undergo a full linguistic validation methodology, I translated the EHP-5 myself.

5.5.3 The use of rescue analgesia

Vincent et al. (2008) also recommend that data on the use of rescue analgesia and complementary alternative medicine (CAM) should be captured in a clinical trial. For the descriptive statistics in this study the number of patients and the type of drug therapy they took was recorded. Patients undergoing menopause-inducing therapy (GnRH analogues) were excluded from this trial, because the treatment could induce amenorrhoea and reduce bone-density (ESHRE 2005).

5.6. Procedure

A baseline score was collected from each of the participants to compare pre-and post-treatment results. In the baseline phase participants rated their pain and health related quality of life burden using a Visual Analogue Scala (VAS) and the EHP 5 at the time at which they had maximal endometriosis-related pain during their last month. This procedure was repeated within the next four weeks one more time, again during a time of pelvic pain. A certain repeatability of the dependent variable of endometriosis-related pain is expected when using more than one measurement and should improve internal validity. Because the monthly cycle of the women differed widely, the day of the second measurement varied individually. When the first eight weeks with no treatment except what the woman had done previously (e.g. medication etc) was completed, the treatment period began and went on for another eight weeks. Every participant received her first treatment around the 8th day of her menstrual cycle. The next treatment took place in the second half of their menstrual cycle. This routine continued for the next cycle. In total the patients received four treatments and rated their pain each month. Altogether the trial took four months.

5.6.1. Intervention

This study deliberately did not provide a set treatment program for women with endometriosis-related pain because this would contradict some basic osteopathic principles. Before I began administering treatment, I collected, as described in detail in chapter four, references for osteopathic tests and techniques relevant to this study. The first osteopathic examination consisted of a complete full-body check-up with special focus on the pelvis. Every region was examined globally and in the case of existing anomalies was then further tested locally. During each treatment thereafter, the detected dysfunctions were treated and documented. Treated dysfunctions were retested and where necessary given further or complementary treatment.

The following flow chart illustrates the sequence of the trial with the different measurement and treatment times.

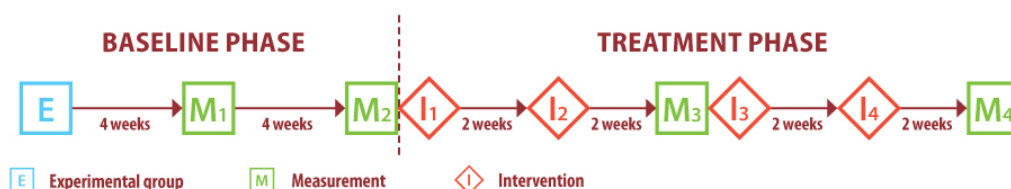


Figure 10: Flowchart of measurement and treatment times

6.. Statistics

The present study examines whether it is possible to influence pelvic pain and health-related quality of life through osteopathy. The treatments were carried out between April and December 2010. A total of 16 patients participated, one patient had to be excluded and was not considered in the statistical analysis. Because there were no further drop-outs, an intention-to-treat-analysis was not considered necessary.

During this trial the dependent variables were measured four times with a visual analogue scale and a questionnaire. The obtained patient data was gathered from these scales and questionnaires. The computer programs Excel and PASW 18 were used for the collection, analysis and graphical presentation. The collected data was presented on the basis of mean, standard deviation, minimum and maximum, and was tested for normal distribution using the Kolmogorov Smirnov Test. For measurements in which no significant deviation from a normal distribution was detected, differences in processes (within-subject factors) were tested using repeated measures analysis of variances (ANOVA). For measurements that showed significant deviation from a normal distribution, the difference tests were conducted between the measurement points T1 and T4 using the non-parametric Friedman Test. Both tests take into account the correction of the significance levels for repeated measurements.

For the investigation of correlations between the different measurements (looking for a degree of association) in the descriptive statistics, the non-parametric Spearman's Rank Correlation test was applied, as it does not require normal distribution of the analysed measurements, to determine the significance of correlation between ordinal scores and treatment numbers. According to Hicks (1988) all that can be concluded from this test is whether or not there is a degree of similarity in the scores for each of the two variables.

In order to describe the correlation between the two outcome measures, a regression analysis was applied. The prediction of a change in pelvic pain from T1 to T4 on the basis of the statements made in the questionnaire was carried out using a linear regression with a gradual integration of the individual predictors. The inclusion criteria was set at $p=0.05$ for the F-value, the exclusion criteria was set at $p=0.10$ for the F-value.

Comparisons, trends etc. are generally regarded as „statistically significant“ if the results cannot be attributed to mere coincidence. Usually, the variable p is used to indicate the level of significance and is mostly expressed as a decimal (e.g. 0.01). If the level is small enough, the result can be taken as significant and is interpreted as important (Hicks, 1988). For this study a significance level of $p = 0.05$ was chosen. The decision about the size of the

significance level is based on the effects of the error. If the p value in this trial is equal or smaller than the significance level of 5 % or 0.05 it means that the null (no relationship) hypothesis can be rejected and that the experimental hypothesis has been supported. As usual the p -values are marked with star-symbols: $p < 0,05$ with *, $p < 0,01$ with **, and $p < 0,001$ with ***.

6.1. Descriptive statistics

In descriptive statistic, the collected data is sorted, structured and graphically illustrated. The aim is to show how the group is composed in relation to the different variables. The average age of the study samples is almost 40 years. The diagnosis has been known for an average of 6.8 years, whereby the women have previously experienced endometriosis-related symptoms for an average of 7.8 years. These figures correlate with those of larger medical studies from Ballweg (2004), Husby (2003) and Schindler (2007) among others and may offer certain conclusions about the population, that can be made concerning the study sample. 60 % of the subjects have no children, 33 % had more than one laparoscopy, and 86.7 % of the women took medication due to the pain.

6.1.1. Sample description

Table 1 shows data on the age, the time since diagnosis and the duration of symptoms of the sample (n=15). The following diagrams illustrate the number of children, the number of laparoscopies, and the type of medication taken using circle graphs.

Parameter	N	Mean	Standard-deviation	Minimum	Maximum	Median
Age	15	39,80	5,37	27,00	48,00	41,00
Time since diagnosis	15	6,80	5,06	1,00	17,00	5,00
Duration of symptoms	15	14,60	7,10	5,00	27,00	14,00

Table 1: Data on age, time since diagnosis, and duration of symptoms in years

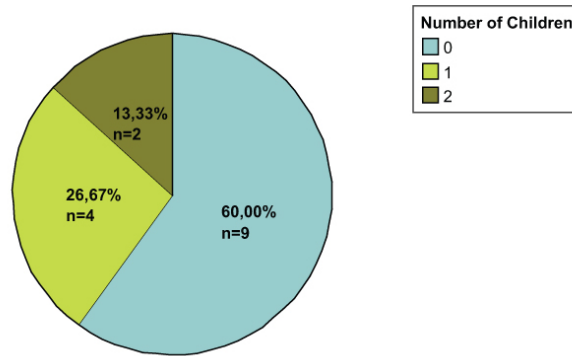


Diagram 1: Number of children

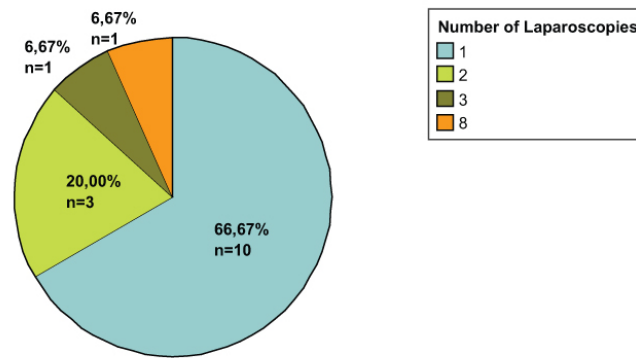


Diagram 2: Number of laparoscopies

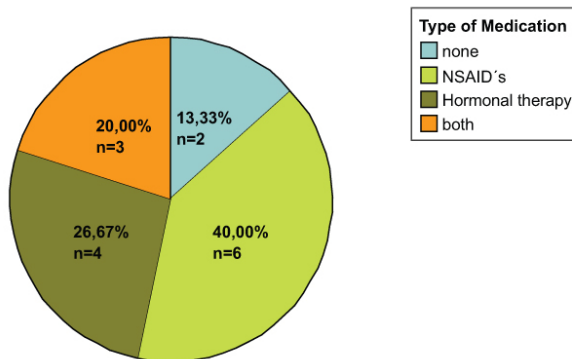


Diagram 3: Type of medication

6.2. Inferential statistics

Inferential statistics are used in testing hypotheses. Methods of inductive statistics are used to try and obtain general statements that apply to the entire population. If the statements can be generalized, this is called significance (Weiß, 2002).

6.2.1. Primary outcome measure

The first inquiry of this study: Is it possible to influence endometriosis-related pelvic pain using osteopathic intervention? Table 1 shows the data on pelvic pain at four measurement points, whereby the first two measurement points are in the baseline phase, and the following two measurement points are in the treatment phase. By using the non-parametric Kolmogorov Smirnov Test (with correction according to Lilliefors), it becomes clear that a normal distribution can be expected ($p > 0.05$).

Endometriosis-related pelvic-pain	N	Mean	Standarddeviation	Minimum	Maximum	KS*-Test p-Value
VAS T1	15	7,05	2,01	4,20	10,00	0,200
VAS T2	15	7,21	1,92	4,30	10,00	0,200
VAS T3	15	5,65	2,41	0,70	9,30	0,200
VAS T4	15	4,86	2,25	1,70	9,10	0,200

*KS-Test: Kolmogorov Smirnov Test (with correction according to Lilliefors)

Table 2: Data on endometriosis-related pelvic pain at the 4 measurement points (VAS)

The following chart gives, using box and whiskers plots, an impression of the area in which the statistics data are and how they are distributed. The box represents the area in which the mid 50% of the data lie. The median is illustrated using a continuous line in the box. The whiskers show the so-called outliers.

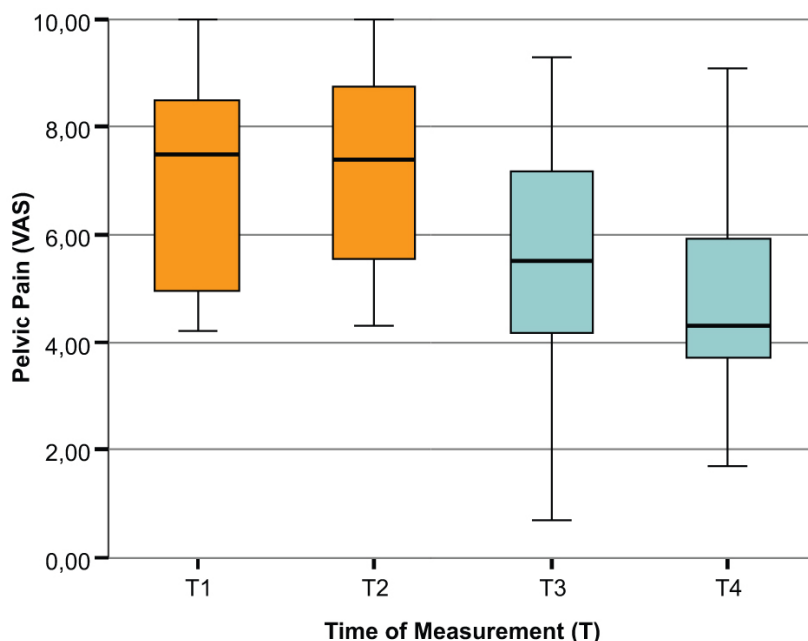


Diagram 4: Pelvic pain (VAS) over 4 measurement points (group comparison)

The test for significant differences in the progress of the reported pelvic pain using repeated-measures analysis of variances (ANOVA) results in a significant change throughout the entire progress $p = 0.007$.

The Difference from Control Test (testing for contrasts) shows no difference between the first and second measurement points. The third (T3) and the fourth measurements (T4) differ from the first measurements (T1); in comparison to the initial measurements (T1) significantly less pelvic pain is reported. This result shows that during the treatment-free interval, no measurable change in the intensity of the endometriosis-related pelvic pain could be detected, whereas during the treatment phase a significant change in terms of pain reduction could be demonstrated.

Differences between measurements	Signifikante
T2 vs. T1	0,428
T3 vs. T1	0,003**
T4 vs. T1	0,001**

Table 3: Results of the test for differences between the single measurements of pelvic pain (VAS)

6.2.2. Influence of other variables on the assessment of the pain

The following section illustrates the influence of the variables “number of children” and “number of laparoscopies” on the assessment of pain.

6.2.2.1. Children

For the statistical validation of the possible influence of children, two groups were formed: patients without and patients with children. 60% of the women (n=9) have no children, 40 % (n=6) have one or two children. The investigation of the possible influence of children on the pelvic pain measured using VAS was carried out using a repeated-measures analysis of variances, in which the existence of children was included as a variable for the investigation of between-subjects effects. According to Hicks (1988), the repeated-measures analysis of variances is a parametric test for whether there are overall differences between conditions. In addition, possible interactions between the child variable and the progress were also investigated.

Endometriosis-related pelvic pain	Children	Valid N	Mean	Standarddeviation	Minimum	Maximum	KS*-Test p-Value
VAS T1	no	9	8,20	1,57	4,80	10,00	0,200
	yes	6	5,32	1,18	4,20	7,20	0,200
VAS T2	no	9	8,37	1,15	6,80	10,00	0,200
	yes	6	5,48	1,50	4,30	8,20	0,027
VAS T3	no	9	7,00	1,72	4,20	9,30	0,200
	yes	6	3,62	1,82	0,70	5,50	0,200
VAS T4	no	9	5,66	2,38	2,40	9,10	0,200
	yes	6	3,67	1,51	1,70	5,30	0,200

*KS-Test: Kolmogorov Smirnov Test (mit Korrektur nach Lilliefors)

Table 4: Data on endometriosis-related pelvic pain for the 4 measurement points (VAS) for patients with and without children

For the variable “child”, a significant between-subject effect could be found ($p=0.020$). Patients with children demonstrate significantly less pelvic pain, regardless of the measurement point. No significant interaction between the progress of the pelvic pain and variable “child” could be detected ($p=0.314$). Patients with children demonstrate significantly less pelvic pain, regardless of the measurement point than patients without children.

This is graphically illustrated as follows:

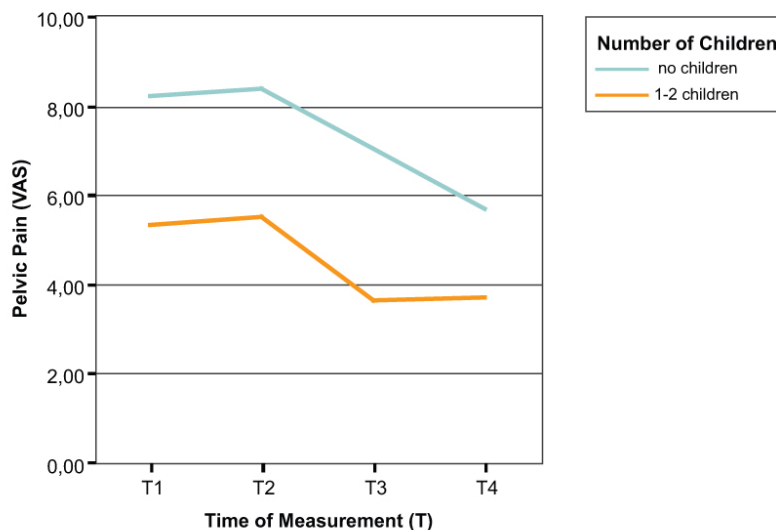


Diagram 5: Pelvic pain in patients with or without children

6.2.2.2. Number of laparoscopies

For the statistical investigation of the possible influence of the number of laparoscopies, again two groups were formed: patients with maximum one laparoscopy and patients with more than one laparoscopy. The investigation of the influence of the number of laparoscopies on the measured pelvic pain was also carried out using a repeated-measures analysis of variances, in which the number of laparoscopies was included as a variable for the investigation of between-subjects effects.

Endometriosis-related pelvic pain	Number of Laparoscopies	Valid N	Mean	Standard-deviation	Minimum	Maximum	KS*-Test p-Value
VAS T1	1	10	7,04	1,89	4,50	10,00	0,200
	more than 1	5	7,06	2,48	4,20	9,50	0,200
VAS T2	1	10	7,18	1,68	4,60	10,00	0,200
	more than 1	5	7,28	2,57	4,30	9,70	0,174
VAS T3	1	10	6,07	2,00	3,40	9,30	0,200
	more than 1	5	4,80	3,16	0,70	8,60	0,200
VAS T4	1	10	5,27	1,82	2,40	8,30	0,200
	more than 1	5	4,04	3,00	1,70	9,10	0,189

*KS-Test: Kolmogorov Smirnov Test (with correction according to Lilliefors)

Table 5: Data on endometriosis-related pelvic pain for the 4 measurement points (VAS) for patients with one and with more than one laparoscopy

For the variable “number of laparoscopies”, no significant between-subject effect could be found ($p=0.592$). No significant difference could be detected in the degree of pelvic pain between patients with one laparoscopy and patients with more than one laparoscopy. However, patients with more than one laparoscopy reported significantly less pelvic pain during the treatment phase. This is graphically illustrated as follows:

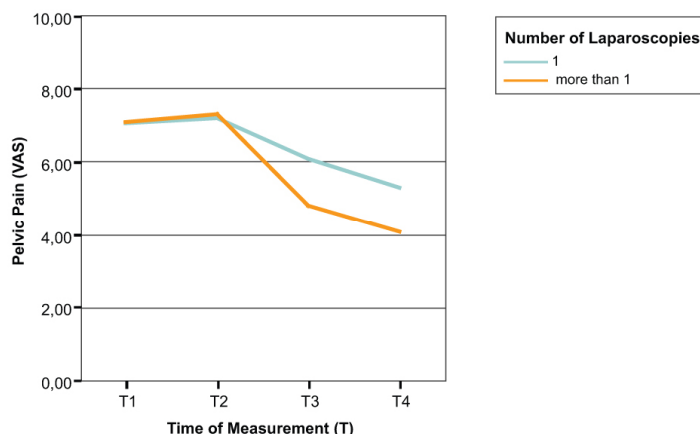


Diagram 6: Pelvic pain in patients with different numbers of laparoscopies

6.2.2.3. Time since the diagnosis, duration of symptoms and pelvic pain

A correlation analysis was conducted to examine whether there are correlations between the age of the diagnosis and the duration of the symptoms and the reported pelvic pain. This was carried out using the Spearman non-parametric correlation coefficient. No significant correlations were found between the age of the diagnosis and the duration of symptoms and the reported pelvic pain (VAS) as shown in the next table.

		Pelvic PainT1	Pelvic PainT2	Pelvic PainT3	Pelvic PainT4
Time since Diagnosis	Correlation-coefficient	0,055	0,106	-0,067	-0,366
	Sig. (2-seitig)*	0,846	0,707	0,811	0,180
	N	15	15	15	15
Duration of Symptoms	Correlation-coefficient	0,406	0,428	0,278	-0,076
	Sig. (2-seitig)*	0,134	0,112	0,315	0,788
	N	15	15	15	15

* After corrections for multiple measurements, a significant result starts from a p-value of ≤ 0.0125

Table 6: Correlations between age of diagnosis and duration of symptoms and the reported pelvic pain (VAS)

6.2.3. Secondary outcome Measure

The second investigation of this study is: Does the affected women’s quality of life improve after an osteopathic intervention with 4 treatments? Which areas are affected the most? Which areas are affected the least? Here the validated Endometriosis Health Profile-5 was used, which consists of 11 questions. The following line diagram offers an overview of all the questions at all the measurement points and shows for one that there is a significant difference between the waiting period group and the treatment group. In addition, it is evident that, apart from questions 1 and 11, the average values of the third and fourth measurements (treatment phase) are always below those of the first and second measurements (waiting period). Further analysis of the results showed that some of the domains in the questionnaire were not influenced by osteopathy. In particular questions concerning how the women felt about their outer appearance (question 5) and the sadness about not having had children (question 11) could not be influenced by osteopathic treatment.

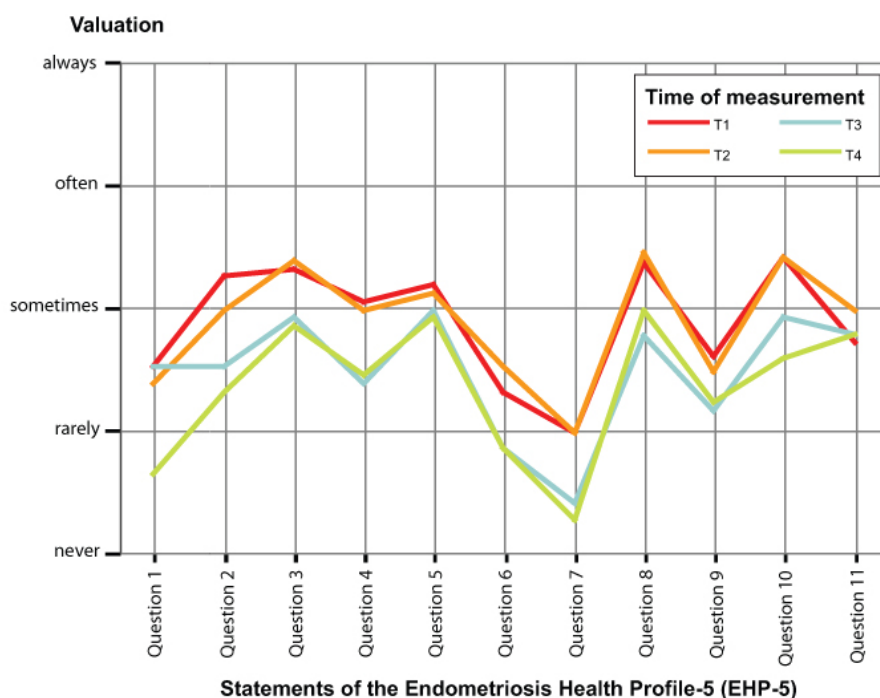
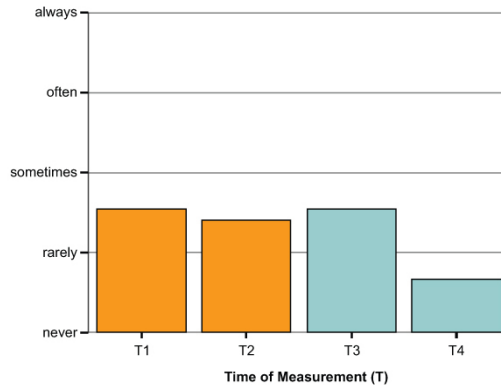


Diagram 7: Linechart including the statements at all times of measurement

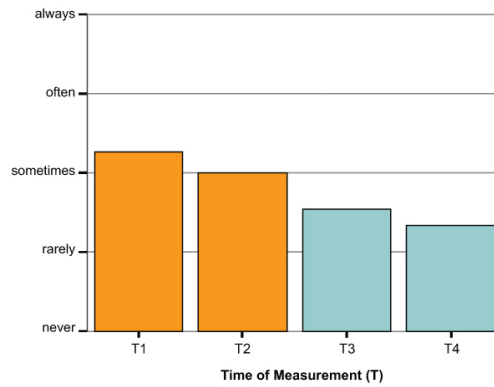
The following graphically illustrates the assessment of the single questions of the Endometriosis Health Profile questionnaire EHP-5. In the interests of clarity, the illustrations were not made using a box-plot diagram, and bar charts were created to illustrate the mean value. In the second part of the questionnaire, the questions should be answered only if it was relevant to the present life situation of the participant.

During the last four weeks, how often because of your endometriosis have you.....

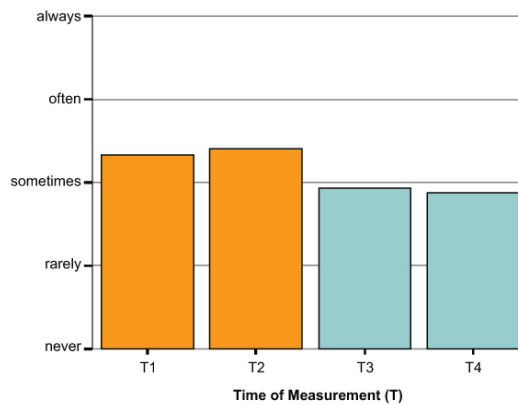
1. Found it difficult to walk because of the pain



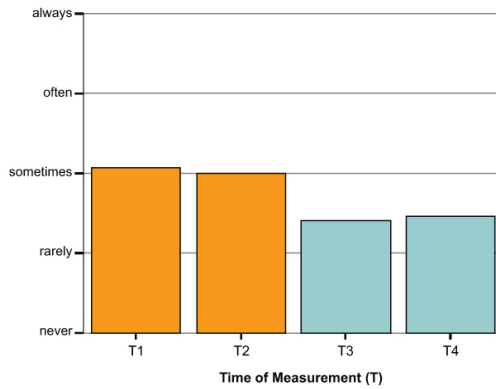
2. Felt as though symptoms are ruling your life?



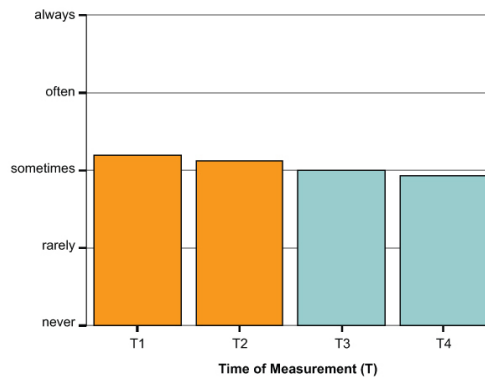
3. Had mood swings?



4. Felt others do not understand what you are going through?

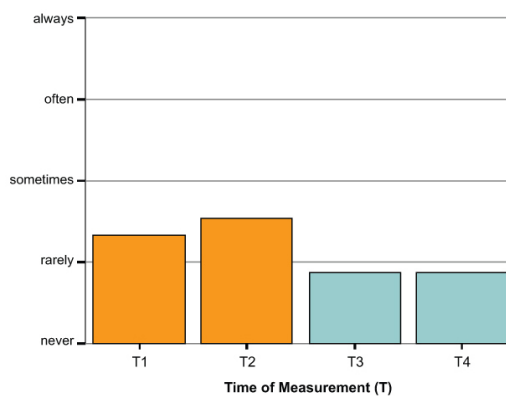


5. Felt your appearance has been affected?

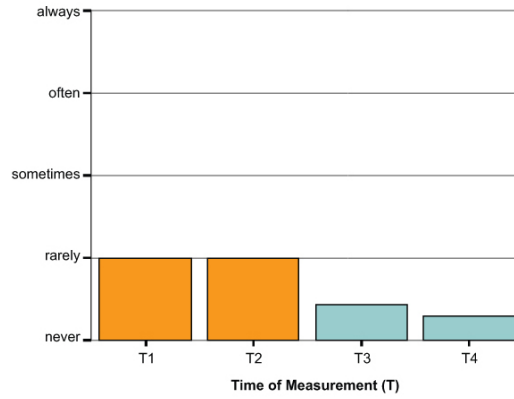


During the last 4 weeks, how often because of your endometriosis have you...

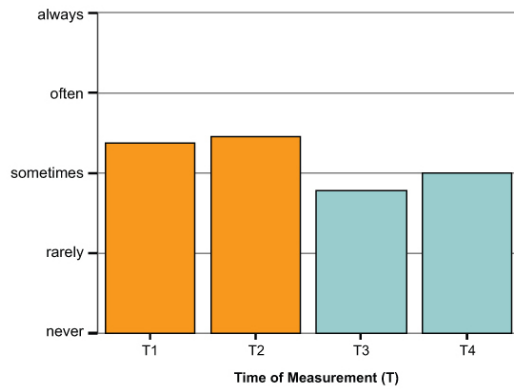
6. Been unable to carry out duties at work because of the pain?



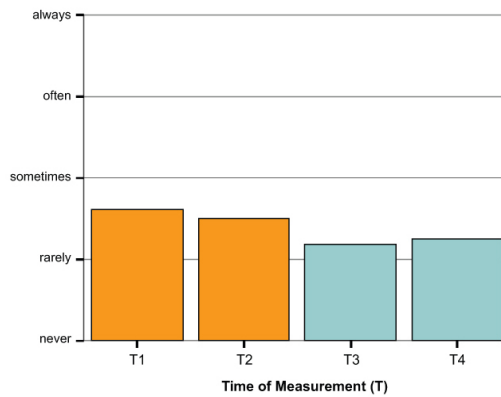
7. Found it difficult to look after your child/children?



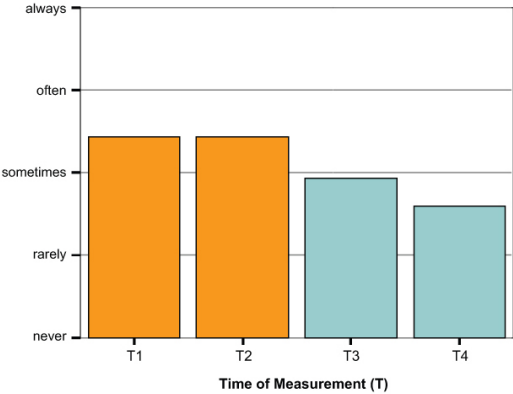
8. Felt worried about having intercourse because of the pain?



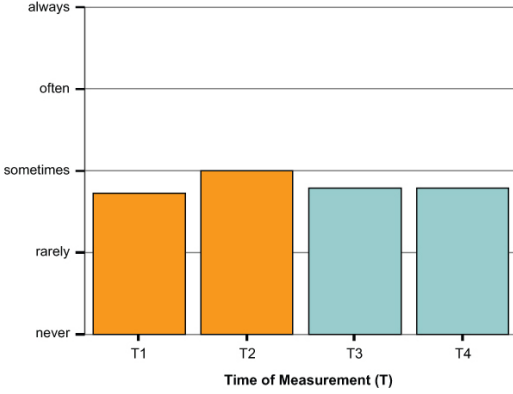
9. Felt doctor(s) think it is all in the mind?



10. Felt frustrated because treatment is not working?



11. Felt depressed at the possibility of not having children/more children?



To identify differences between the assessments of the single questions during the study period, a difference test was applied. As the scale of the EHP-5 questionnaire predominantly showed no normal distribution, in the following table the results are compared for differences with the non-parametric Friedman Test. The results shows significant changes for questionnaire question 1 (Found it difficult to walk because of the pain), question 2 (Felt as though symptoms are ruling your life), question 4 (Felt others do not understand what you are going through), question 6 (Been unable to carry out duties at work because of the pain) and question 10 (Felt frustrated because treatment is not working). Question 11 (Felt depressed at the possibility of not having children / more children) showed the least change.

Questions of EHP-5	p-Value of the within-subject factor (Friedman-Test)
1	0,002**
2	0,000***
3	0,060
4	0,019*
5	0,261
6	0,043*
7	0,078
8	0,160
9	0,060
10	0,000***
11	0,415

Table 7: Results of the Friedman Test for the within-subject factor in the evaluation of the EHP-5

6.2.4. Linear regression

To find out how the two dependent variables are associated with each other a linear regression technique was applied. A model of prediction was used to find out which of the statements of the Endometriosis Health Profile at the measurement point T1 enables a prediction of the changes in pain intensity between measurement points T1 and T4. The analysis was carried out through a gradual integration of the single questions of the questionnaire. Due to the large number of missing values, question 7 (Found it difficult to look after your child/children) was excluded from the analysis. Single missing values were replaced with the mean value. The table below shows the beta value of the increase on the level of regression for each variable that has been previously tested for their significance. If it is negative, this means that the high value of the EHP-5 variable (predictor) is linked to the lower values in the VAS (dependant variables) and vice versa. A significant contribution to the prediction of change in pain was evident for question 2 (Felt as though symptoms are ruling your life) and question 9 (Felt doctors think is all in your mind). For question 9, a high expression at measurement point T1 is linked with a small change in the perception of pain

during the study period, which in view of the low number of participants only allows a cautious interpretation. For question 2, a high initial value at measurement point T1 indicates a high reduction of pain at measurement point T4.

Variables in Model	Beta (standardised)	Signifikance	R-Quadrat (standardised)
Question 9 EHP-5	-0,916	0,002	0,506
Question 2 EHP-5	0,638	0,017	

Table 8: Linear regression to predict the changes in pelvic pain intensity (VAS) from T1 to T4 using the expression of statements of the EHP-5 at T1

7.. Discussion

The first part of the study attempted to elucidate a clear picture of the disease endometriosis with its complexity and problems. For the affected women the problems are related to several uncertainties concerning the origin of the disease, the invasive therapies and their undesirable side effects, and the sometimes very strong limitations in the different areas of daily life such as dealing with self-image, work or social life.

The second part of the study is concerned with showing possible connections between the disease and osteopathy because there has been increasing evidence of links between osteopathic treatment and endometriosis-related symptoms. Theoretical effect mechanisms in the area of osteopathy are mainly speculative and require further scientific research to explain the effect of an osteopathic treatment in the area of endometriosis-associated pain. Theories that could account for the present results were discussed in chapter four.

Three studies were discussed that have already examined the subject in recent years. However, these were conducted under different requirements and using different measuring tools and methods implemented in a heterogeneous manner and are as such not comparable. Two studies used a finding-related treatment as an osteopathic intervention. Only the study conducted by Dick and Koop (2009) corresponded to the requirements of a randomized-controlled trial with regard the randomization and controls. The difference to the present study lies in the choice of outcome parameters and in the different method of control. Although the present study shows methodological limitations, that can be partially explained by the fact that the study could only be conducted by one person in a limited period with limited resources, the current guidelines of endometriosis research were successfully met in the area of the inclusion and exclusion criteria as well as the methods of measurement.

The objective of this trial was to measure any effect of osteopathic treatment in women with endometriosis-related pain. The primary outcome measure was the rating of pelvic pain on a Visual Analogue Scale and a significant improvement during the treatment phase compared to the baseline phase could be observed. The statistical evaluation of the data shows that the experimental hypothesis could be accepted because the treatments achieved significant improvement of the perceived pain compared with the control. The measurements of the primary outcome measure can be regarded as representative because the data was normally distributed. As the measurements after the fourth and last osteopathic intervention were again lower than the first two treatments, one can assume that the number of osteopathic intervention plays a role in the success of the treatment.

The results of the present experiment indicate that the endometriosis-related pain decreased

significantly after four osteopathic treatments, thereby supporting the experimental hypothesis. These results accord with those of Ferreira (2005) who found a significant decrease in severity of symptoms of pain intensity and changing degree of pain throughout the complete course of the trial. However, the thesis of Dick and Koop (2009) provided partly contradictory findings. Their results indicated that there is no significant change of the symptoms in women with endometriosis, but the authors have themselves already argued that the measuring instruments they had selected may not have been suitable to measure changes in the patients.

To see whether additional factors other than osteopathic treatment played a role in the change of symptoms, a repeated-measures analysis of variances was applied. This showed that when the variable 'children' was considered, subjects with children showed fewer symptoms than subjects without children, independent of the time of measurement. However, possible interpretations of this statement seemed speculative.

For the variable 'number of laparoscopies' no such between-subject effect could be detected. Moreover, at no point in time could a significant correlation be made between the time of diagnosis and the reported pelvic pain. The same applies to the correlation between the duration of symptoms and pelvic pain.

The second measured variable was health-related quality of life in form of a validated questionnaire. The evaluation of the subjective perception of the patients' state of health was considered of central importance. The scales of the Endometriosis Health Profile-5 show, in contrast to the VAS readings, predominantly no normal distribution and for this reason the differences during the study were tested with a non-parametric test.

The results of the secondary outcome measure indicate that there are some significant changes within some domains during the treatment period, whereas other domains remained unchangeable. Significant change could be observed in relation to pain (question 1), sense of control (question 2) and social support (question 4) as well as the items related to work and treatment (questions 6 and 10). The improvements in the questions control, treatment and social support can be on the one hand explained by an unspecific treatment effect of care, on the other hand the significant improvement in question 10 (felt frustrated, because treatment is not working) demonstrates that the fact of having received some kind of treatment should not be undervalued in the area of health-related quality of life. The feeling of being able to do something should not be discredited and should play a role in the future of endometriosis therapies. The increase in the capacity to work after the treatment phase (question 6) can be directly linked to the measured reduction in pain.

The statements made for questions 11 (infertility), which is perhaps not surprising as osteopathic intervention can have no direct influence on the condition of an unintended infertility, 5 (self image) and 8 (sex life) were either not or only slightly influenced by the treatment.

In the evaluation of the Regression analysis for the predication of change in pain from T1 to T4 based on the statement of the EHP-5, a significant contribution could be seen in questions 2 (control) and 9 (relation to medical profession). In view of the small number of participants, this can only be cautiously interpreted and must be verified in studies with a larger population. Question 2 can be interpreted that women who experience a high loss of control due to the disease in particular may benefit greatly from an osteopathic treatment whereby in question 9, one can only assume the contrary: the pain value in women who initially demonstrate very little trust in the medical profession only slightly improves after one osteopathic intervention. Unspecific factors such as negative expectations certainly play more than just a minor role.

The overall positive outcome of this trial can be explained by several unspecific factors such as the regularity of the treatments, the utilisation of a variety of techniques to address the diversity of tissues affected by the symptoms of endometriosis and the time allocated for patients. Without doubt it is positive when there is a predominately normal distribution in the assessment of the VAS data and the experimental hypothesis can thus be confirmed, nevertheless the small number of test persons included in this study only allows a limited statistically relevant result. Nevertheless, this study has several strengths such as the differential inclusion and exclusion criteria that are based on the gold standard as well as the validity and reliability of the selected variables that correspond to the recommendations of the European Special Interest Group on Endometriosis to maintain potential systematic errors at a minimum. In addition, the criteria for the clinical suitability of this study have in my opinion been fulfilled through the transferability of the study conditions on the requirements of daily clinical conditions as well as the technical and financial implementation. Most aspects of the experimental situation such as room temperature, time of the treatment etc. have been standardised to avoid possible sources of error. Because this study was restricted in its size, several aspects have been partly described but not evaluated. These aspects are:

Severity of the disease: The severity of the disease can only be divided in stages through a laparoscopy, however this says nothing about the severity of the symptoms. In the descriptive statistics, an attempt was undertaken to identify a certain severity of the symptoms by the number of laparoscopies, however this could not be demonstrated.

Duration of the illness: As discussed in the first part it seems to be difficult to identify how long an endometriosis has been present, as this requires a laparoscopy. For this reason, for the descriptive statistics the subjects were only asked about the duration of the symptoms, which began on average 7.8 years before the disease was diagnosed.

Amount of painkillers (analgesics): For reasons of compliance and because the medications that the patients took varied widely, I decided against compiling a medication logbook. For this reason, for the descriptive statistics data on whether and which medication was taken was collected but not on the amount. Restricting the use of rescue medication during the time of the trial would have been both unethical and likely to increase the dropouts from the trial.

Social variables (marital status, employment, social status): Were not collected and statistically evaluated, even though every pain reaction is an expression of social context as well as the present mental condition. (See chapter 3.8.1.)

Osteopathic dysfunctions: The data of the findings of the osteopathic investigation in this study were not collected for the descriptive statistics because, among other reasons, according to Sommerfeld (2006) osteopathic test and diagnosis procedures are extremely controversial with respect to their validity and reliability. That is why this study, compared to the study by Dick and Koop, makes no statements regarding which osteopathic dysfunctions were present in the group and how often.

In the following, the design and the implementation of the present study are critically evaluated and possible sources of error are listed in detail.

7.1. Sources of Error

Study designs with a treated control-group effectively control for any influence associated with the osteopath-patient interaction as then procedures can be performed through use of an identical protocol, in the same clinical setting, and by the same practitioner. However, as it was not possible to recruit sufficient subjects in the set time frame of a masterthesis, the design of an RCT was changed into a within-subject design. Therefore, the first question to pose is of course which restrictions arise regarding the interpretability of the results due to the absence of an external control group. This can only be partially replaced by a within-subject design. In this way it is possible to make a statement on the effectiveness of the treatment but not whether this effect is specific. The initial values and the tendencies of the values in the waiting period only serve to demonstrate that no intervention also has no effect. Whether the osteopathic treatment has a specific effect that is superior to other measures cannot be concluded from this study.

Despite some study strengths, the validity of the study was cut down in several ways. The reasons that have been identified to account for this study's limited statements are the following:

Selection: As it was not possible to put together a representative study sample, the available population became also the sample (convenience sampling). It was unfortunate that it was not possible to attract younger women to the study even though here the estimated number of unknown cases seems to be especially high. The author is aware that a systematic error occurs when the patients select themselves for the group through contact, and so it cannot be assumed here that the group represents the basic population. This means that the external validity is not present here.

Randomization: Randomization was not applied due to the small number of participants. Although Perleth and Antes (2002) could show that the results of non-randomized studies do not consistently differ from the results of randomized studies, the results of randomized, controlled trials are considered to be evidence of the highest grade in the hierarchy of research design.

Time limits: The time factor was a limitation. Baseline scores were obtained for only two cycles and although the participants stated that their pain levels did not alter much from cycle to cycle, more measurements may have made the results more credible. Obtaining post treatment scores after the cessation of the treatment for further cycles may have indicated whether there is a longer lasting effect of treatment.

Study size: Another limitation was the small number of subjects that was recruited, which made it necessary to change the study design into a within-subject design in order to ensure some control over a waiting period despite the small number of subjects.

Blinding: An open study whereby both the practitioner and the patient know which therapy form is being used should - whenever possible - be avoided (Weiß, 2002). Because the study was not blinded, according to Beck and Unverricht (2005) there always remains a bias or prejudice of the examiner who has a personal interest in the outcome of the trial. Sommerfeld (2006) suggests that a certain increase in methodological quality can already be achieved when the head of the study does not personally perform the treatments and examinations, and in order to reduce this risk it may have been preferable to operate a single blind procedure where both the examiner and the subject would be blinded to the experimental hypothesis.

Unspecific influences: Unspecific influences such as positive expectations, as the practice is known and familiar to the patient etc., could not be prevented in this study due to its small size.

Documentation of variables : All the patients varied widely in their age, case history, treatments, operations, social situation etc., some of those factors were not documented separately.

Within-subject design: Within-subject design, as Sommerfeld (2006) emphasizes, belongs for some authors to the quasi-experimental field, since neither randomization nor controls in the classical-methodical sense are performed. Although by comparing to a treatment-free interval a certain statement can be made about the efficacy, however no statement can be made about whether an osteopathic intervention in comparison to another form of therapy demonstrates better results in the area of endometriosis-related pain.

Examiner bias: It was not possible at all times to standardise and therefore control all aspects of the experimental situation. Furthermore, as no blinding took place and I performed the treatments myself, influence factors such as positive expectations, credibility of the therapist etc. could not be avoided, so that, provided both factors were present, the fact of therapeutic care as such already has an effect on the subjects.

7.2. Suggestions for further research

Surprisingly, given the frequency and the socioeconomic implications of endometriosis, there are few clinical studies that investigate alternative forms of treatment. One reason for this could be that, according to Simsa et al. (2007), the climate for research funding in the area of endometriosis has yet to be increased because it is seen as a benign (i.e. non-fatal) condition. Another reason could be that these trials are not in the primary interest of the pharmaceutical industry and thus lack financial support.

The goal of this experimental study was to investigate an alternative form of treatment for patients with endometriosis-related pelvic pain, through which the women's pain can be reduced and thereby cutting down the amount of medication they have to take, increasing their capacity to work and, possibly delaying a surgery. While this study has demonstrated that an osteopathic intervention reduces endometriosis-related pain and therefore increases some domains of health-related quality of life, it lacks a certain methodological quality on the one hand and highlights some questions on the other. First of all it shows that there is a need to carry out further studies in the field of endometriosis. To increase the level of evidence, osteopathic studies with a larger patient sample, a randomization, a control group and a single blind design would be desirable. Standardised entry criteria and outcome measures

for clinical trials in endometriosis-related pain would facilitate the comparison of results, improving evidence-based practice in this area.

A larger population in principal increases the validity of a study as it ensures statistical significances and thus provides the highest possible generalization.

A randomization could, according to Sommerfeld (2006), ensure that differences in the values measured are not due to differences in the group but in fact due to the treatment.

A placebo or another treatment group could specify whether or not the osteopathic treatment is having an effect. Another treatment could be a physiotherapeutic measure in the form of active pelvic exercises, the effect of which is currently being studied on endometriosis patents at the medical university of Hanover.

A simple blinding would counteract a concealment bias. To avoid single operator bias, it would be ideal for future studies to have several experienced examiners.

The form of one-dimensional pain measurement using a VAS was recommended by Vincent et. al. (2008), however in a future study, in addition to measuring the intensity of pain, a pain logbook could be introduced in order to investigate the multidimensionality of pain. In order to achieve a reliable statement on the progress of the pain during the entire study, it would also be desirable to have more measurement points, for example once a week. To standardize the measurement it should always take place at the same time of the day, which would require a good compliance of the participants and could be difficult to put into practice.

In a follow-up study, consideration should also be given to conducting a follow-up over several months after the end of the treatment, in order to obtain a statement about the duration of the effect of an osteopathic treatment on endometriosis-related pain.

It could be of interest to investigate how the inner workings of the treatments can be explained. This could form the basis of some future research projects in the area of basic research in order to understand the influence of a specific osteopathic technique on physiological processes such as inflammation, adhesion, hormonal regulation, improvement of circulation, etc. Up to the present moment, theoretical effect mechanisms are mainly speculative. As discussed in chapter four there are explanatory models in the literature of how a spinal dysfunction can lead to increased pelvic pain or how a hormonal imbalance can partly be responsible for the development of endometriosis-related pain. These models could be of further interest in coming research projects. Since osteopathic diagnosis is very subjective and controversial regarding its validity and reliability, a methodical study could be interesting that compares the inter-rater and the intrarater reliability of a visceral test for example on adhesions in the abdominal cavity.

It is hoped that some of these suggestions will be considered in future trials so that scientific evidence can be increased in the area of osteopathy and endometriosis.

7.3. Conclusion

To conclude, it should be noted that many factors stand in the way of the present study and thus it cannot constitute a universal statement. Nevertheless the findings can be important to the osteopathic profession in the field of endometriosis with its multidimensional implementations as well as to the affected women. Osteopaths are confronted with the symptoms of endometriosis and the present trial implies that there is a possibility that the symptom of chronic pelvic pain can be relieved. Overall significant improvements could be demonstrated in the area of pain reduction, which led directly to an increase in the capacity to work and a reduction of absence from work. These factors could have socioeconomic implications and therefore can be relevant for the general public.

Because osteopathy needs to develop a more evidence-based practice, a carefully thought-out and conducted research project on the benefits of the osteopathic approach can be a step in the right direction. An osteopathic treatment protocol could address the symptoms of women who are affected by endometriosis and be a helpful tool for new osteopaths to help with their treatment strategy. Whereas it has to be said that osteopathy does not offer an aetiological explanation or a cure for endometriosis, an osteopathic treatment could nevertheless be considered a tool outside the field of medical and/or surgical treatment that could make the pain more manageable for women with endometriosis and thereby stimulate an increase in the areas of health-related quality of life such as the sense of control, the perception of well-being and a general life satisfaction.

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9.. List of figures, tables and diagrams

9.1. List of figures

Figure 1: Endometrium and cervix. (www.health.com/health/library/mdp/0,,tp12652,00.html)

Figure 2: Structural organisation of human endometrium. (*Endometriosis in clinical practice* edited by Olive L, Taylor and Francis. London)

Figure 3: Hormonal influence on the endometrium within the menstrual cycle. (www.gesundheitsinformation.de/wie-funktioniert-der-weibliche-zyklus.562.de.html, modified)

Figure 4: Innervation of the pelvis. (*Endometriosis: current understanding and management.* edited by Shaw R, Blackwell Science Ltd. London)

Figure 5: Common sites for endometrial growths in red. (www.health.nytimes.com/health/guides/disease/endometriosis/overview.html, modified)

Figure 6: Frequency distribution of endometriosis in pain patients, infertility patients and the overall number of patients at the Endometriosis Ambulanz Westerstede in 1998. (Schweppe, K-W (2003) *Endometriose: Was tun - und wann?* Frauenarzt 44 Nr 7, modified)

Figure 7: Retrograde transplantation. (www.eshre.eu/binarydata.aspx?type=doc&sessionId=bslzbcir3kellq45pmatfoeb/bordeaux_2007_syllabus.pdf)

Figure 8: Overall utilization of treatments for endometriosis. (Sinaii N, Cleary S, Younes N, Ballweg ML, Stratton P *Treatment utilization for endometriosis symptoms: a cross-sectional survey study of lifetime experience.* Fertility and Sterility, Vol 87, No 6, June 2007, modified)

Figure 9: Flowchart of the progression of the trial.

Figure 10: Flowchart of measurement and treatment times.

9.2. List of tables

Table 1: Data on age, time since diagnosis and duration of symptoms in years.

Table 2: Data on endometriosis-related pelvic-pain at the 4 measurement points.

Table 3: Results of the test for differences between the single measurements of pelvic pain (VAS).

Table 4: Data on endometriosis-related pelvic pain for the 4 measurement points (VAS) for patients with and without children.

Table 5: Data on endometriosis-related pelvic pain for the 4 measurement points (VAS) for patients with one and with more than one laparoscopy.

Table 6: Correlations between age of diagnosis and duration of symptoms and the reported pelvic pain (VAS).

Table 7: Results of the Friedman-Test for the within-subject factor in the evaluation of the EHP-5.

Table 8: Linear regression to predict the changes in pelvic pain intensity (VAS) from T1 to T4 using the expression of statements of the EHP-5 at T1.

9.3. List of diagrams

Diagram 1: Number of children.

Diagram 2: Number of laparoscopies.

Diagram 3: Type of medication.

Diagram 4: Pelvic pain (VAS) over 4 measurement points (group comparison).

Diagram 5: Pelvic pain in patients with or without children.

Diagram 6: Pelvic pain in patients with different numbers of laparoscopies.

Diagram 7: Linechart including the statements at all times of measurement.

10.. Appendix

10.1. Letters and Declaration of consent

10.2. History Taking

10.3. Endometriosis Health Profile Questionnaire EHP 5

10.4. Acknowledgements

10.1. Letters and declaration of consent

Wissenschaftlich-klinische Verlaufsstudie im Rahmen der Osteopathie

bei endometriosebedingten Schmerzen

Sehr geehrter,

Ich plane im Zusammenhang meines Masterstudienganges in Osteopathie eine Studie, in deren Rahmen untersucht werden soll, ob sich mit Hilfe von Osteopathie endometriosebedingte Schmerzen lindern lassen, so dass die Patientinnen eine Verbesserung ihrer Lebensqualität feststellen können.

Innerhalb der kontrollierten Studie wird ein Fragebogen (Endometriosis Health Profile Questionnaire) sowie eine visuelle Schmerzskala als Zielparameter dienen.

Für diese Studie suche ich geeignete Teilnehmerinnen und möchte Sie in diesem Zusammenhang um Ihre Mithilfe bitten. Ich suche Teilnehmer, die folgende Voraussetzungen erfüllen:

1. Frauen zwischen 18-und 45 Jahre alt, nicht schwanger, keine Spirale, müssen Deutsch sprechen können
2. Seit mindestens einem Jahr endometriosebedingte Schmerzen, Diagnose mit Laparoskopie bestätigt
3. Zeit, um ca. 4 Mal in den nächsten Wochen zur Behandlung in meine Praxis in der Kölner Südstadt zu kommen

Die Studie dauert insgesamt etwa vier Monate und umfasst eine Erst- und Schlussbefragung sowie vier kostenlose Behandlungen in meiner Praxis in Köln.

Natürlich werden alle Informationen streng vertraulich behandelt und nur anonym ausgewertet.

Ihre Unterstützung bei der Suche nach Teilnehmern würde mir sehr weiterhelfen.

Ich würde mich freuen wenn Sie meinen Aufruf in Ihrem Wartezimmer aushängen könnten oder Sie Ihre Patientinnen direkt auf meine Studie aufmerksam machen könnten.

Hiermit bedanke ich mich schon einmal für Ihre Hilfe.

Mit freundlichen Grüßen

Studienverlauf

Die Studie dauert insgesamt etwa 10 Wochen und umfasst eine Erst - bzw. Schlussbefragung sowie vier kostenlose jeweils ca. 45-minütige osteopathische Behandlungen in Köln.

Die Behandlungen finden im Abstand von ungefähr zwei Wochen statt.

Jeweils vor und nach dem Behandlungszyklus sind vom Patienten validierte Fragebögen auszufüllen, die dann statistisch ausgewertet werden. Mit welcher osteopathischen Methode Sie behandelt werden, entscheidet die Therapeutin ganz individuell. Für Sie besteht kein Risiko – weder durch die angewendeten Tests noch durch die Therapie an sich. Es ist jedoch möglich, dass Sie auf die Behandlungen vorerst mit Muskelkater, Müdigkeit oder leichter Verschlimmerung Ihrer Beschwerden reagieren (Erstverschlimmerung). Während der Studie brauchen Sie eventuell ärztlich verordnete Medikamente nicht abzusetzen. Sie haben natürlich jederzeit das Recht, die Teilnahme an der Studie abubrechen, werden aber gebeten, mich rechtzeitig zu informieren. Hintergrund der Studie ist es, zu untersuchen ob sich mit Hilfe von verschiedenen osteopathischen Techniken die Schmerzen bei Endometriose wirksam behandeln lassen. Sollte das Untersuchungsergebnis positiv sein, kann den Frauen, deren Lebensqualität aufgrund der Endometriose eingeschränkt ist, zukünftig gezielt eine effektive Behandlungsmethode angeboten werden.

Was ist Osteopathie?

Osteopathie ist ein ganzheitliches Diagnose- und Therapieverfahren, mit dessen unterschiedlichen Methoden sich das Muskel-Skelett-System, die inneren Organe sowie das Zentralnervensystem behandeln lassen. Werden einzelne Körperstrukturen in ihrer Bewegung eingeschränkt, wie z. B. bei Endometriose durch Entzündungen und Verklebungen im Bauchraum, beeinträchtigt das deren Funktion und kann so die Ursache von Schmerzen sein. Ziel einer osteopathischen Behandlung ist es, die ursprüngliche Bewegungsfreiheit wieder herzustellen, um die gestörte Struktur in seiner Funktion zu normalisieren und damit die Selbstheilungskräfte des Patienten zu unterstützen.

Ein Wort zum Datenschutz

Im Hinblick auf die wissenschaftliche Auswertung sind für mich lediglich die klinischen Daten von Interesse – die Anonymität Ihrer Person ist gewährleistet.

Patienteneinwilligung zur Endometriose – Studie

Name: _____

Vorname: _____

Geburtsdatum: _____

Hiermit erkläre ich mich einverstanden, an der Endometriose–Studie teilzunehmen. In der Studie wird eine osteopathische Therapie am Patienten getestet. Ich wurde über den Hintergrund und Zweck der Studie sowie mögliche Risiken beider Therapie umfassend informiert. Ein diesbezügliches Informationsblatt (Patienteninformation) habe ich ebenfalls erhalten. Mir ist bekannt, dass ich mein Einverständnis jederzeit widerrufen kann und mir hieraus keine Nachteile entstehen. Die Studie kann auch von Seiten der verantwortlichen Therapeutin abgebrochen werden. Ich bin mit den im Rahmen dieser Studie erfolgten Aufzeichnungen meiner Krankheitsdaten einverstanden, sowie mit der Weitergabe dieser Krankheitsdaten zur wissenschaftlichen Auswertung. Schließlich erkläre ich auch mein Einverständnis zur wissenschaftlichen Veröffentlichung der Forschungsergebnisse unter Beachtung der datenschutzrechtlichen Bestimmungen.

Unterschrift des Studienteilnehmers

Ort

Datum

Verantwortliche und Ansprechpartnerin:

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10.2. History taking

When was the first menstrual period?

Was the first period already painful?

Did the patient have to miss school because of painful menstruation?

Did painful menstruation lead to excessive use of analgesics or to the administration of oral contraceptives? –

How long have the symptoms been present?

Have they changed over time, and if so, how? –

Children?

What previous operations have been performed, by whom, when, where, and with what result? Can operative notes from the previous operations be obtained? –

What endocrine treatments have been carried out to date, from when until when, and with what result? –

From when until when were other forms of treatment tried (acupuncture, TCM, naturopathy, homeopathy), and with what result? –

Dysmenorrhea: primary? Secondary? –

Dyspareunia: position-dependent? Position-independent? Loss of libido? Conjugal problems? Psychogenic dyspareunia? –

Abnormal bleeding: abnormalities of menstrual rhythm? Abnormalities of the type of menstrual bleeding? Hypermenorrhea? Additional bleeding? –

Pelvic pain: cycle-dependent? Cycle-independent? Chronic? Perimenstrual back pain? –

Urogenital symptoms: Dysuria? Polyuria? "Irritable bladder"? Frequent bouts of cystitis?

Gastrointestinal symptoms: constipation, pseudodiarrhea, postprandial cramps, hematochezia, dyschezia, "irritable bowel," painful bloating, perimenstrual change of stool consistency?

Psychosomatic and psychiatric abnormalities: fatigue? Depressive symptoms/disturbances? Anxiety disturbances? Medication abuse?

Social status? Social problems?

Previous surgery: adnexal surgery? Endometriosis surgery? Other? –

Previous illnesses: Diabetes? Hypertension? Depression? Thyroid? Other? –

Previous treatments: infertility treatment? Psychiatric treatment? Treatment of thyroid disorders? Other? –

Medication use: oral contraceptives? GnRH analogues? Gestagens? Other (e.g., antidiabetic agents, antidepressants?)

10.3. Endometriosis Health Profile EHP-5

Dieser Fragebogen wurde entwickelt, um zu untersuchen, welchen Einfluss die Krankheit Endometriose auf die Lebensqualität der betroffenen Frauen hat.

Bitte beantworten Sie die Fragen im Hinblick auf die Beziehung zwischen Endometriose und Ihrer Lebensqualität in den letzten vier Wochen.

Es gibt keine richtigen und falschen Antworten, also kreuzen Sie bitte die Antworten an, die am ehesten ihrer Wahrnehmung entsprechen.

Wie oft traf in den letzten 4 Wochen aufgrund Ihrer Endometriose folgende Aussage auf Sie zu:

1. Aufgrund der Schmerzen fiel es mir schwer, zu gehen.

<i>Nie</i>	<i>Selten</i>	<i>Manchmal</i>	<i>Oft</i>	<i>Immer</i>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

2. Es fühlte sich an, als ob die Symptome mein Leben bestimmen.

<i>Nie</i>	<i>Selten</i>	<i>Manchmal</i>	<i>Oft</i>	<i>Immer</i>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

3. Ich hatte Stimmungsschwankungen.

<i>Nie</i>	<i>Selten</i>	<i>Manchmal</i>	<i>Oft</i>	<i>Immer</i>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

4. Ich hatte das Gefühl als verstehe niemand, was ich durchmache

<i>Nie</i>	<i>Selten</i>	<i>Manchmal</i>	<i>Oft</i>	<i>Immer</i>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

5. Es fühlte sich an, als sei mein ganzes Erscheinungsbild davon betroffen.

<i>Nie</i>	<i>Selten</i>	<i>Manchmal</i>	<i>Oft</i>	<i>Immer</i>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Die nächsten Fragen bitte nur beantworten, wenn sie auf Ihre Lebenssituation zutreffen:

6. Aufgrund der Schmerzen konnte ich nicht meiner normalen Arbeit nachgehen.

<i>Nie</i>	<i>Selten</i>	<i>Manchmal</i>	<i>Oft</i>	<i>Immer</i>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

7. Es war schwierig für mich, mein Kind/meine Kinder zu versorgen.

<i>Nie</i>	<i>Selten</i>	<i>Manchmal</i>	<i>Oft</i>	<i>Immer</i>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

8. Aufgrund der Schmerzen wollte ich lieber auf Geschlechtsverkehr verzichten.

<i>Nie</i>	<i>Selten</i>	<i>Manchmal</i>	<i>Oft</i>	<i>Immer</i>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

9. Ich hatte das Gefühl, als glaubte mein Arzt, ich bilde mir das alles nur ein.

<i>Nie</i>	<i>Selten</i>	<i>Manchmal</i>	<i>Oft</i>	<i>Immer</i>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

10. Ich war enttäuscht, dass die medizinische Behandlung nicht wirkt.

<i>Nie</i>	<i>Selten</i>	<i>Manchmal</i>	<i>Oft</i>	<i>Immer</i>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

11. Ich war traurig bei dem Gedanken, keine Kinder (mehr) zu bekommen.

<i>Nie</i>	<i>Selten</i>	<i>Manchmal</i>	<i>Oft</i>	<i>Immer</i>
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

10.4. Acknowledgements

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Abschliessend möchte ich mich bei allen Studienteilnehmerinnen bedanken, die ihre Geschichte mit mir teilten und sich vertrauensvoll in meine Hände begaben.

May your life in this world be a happy one!