The role of diagnostic and operative laparoscopy in the treatment of infertility

The thesis of Ph.D. dissertation

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1. Introduction

The demographic data of the last few years indicate that Hungarian population may decrease to nine million people in a few decades. The reason for this fact is, on one hand, the decline of the average life expectancy, and behind it the general aging and the worsening health quality of the population. On the other hand, the birth rate has also been falling during the last decades due to unwillingness to have more than one, two or more children. It is also important that we can notice an increase in the number of sterile couples, whose proportion may reach 15-20% these days. As a result of the statistically growing number of the infertility patients, the medical research on infertility has been in the limelight all over the civilized world.

Laparoscopy, which has been widely used in the world since the 1970s, has opened new perspectives in the diagnosis and therapy of infertility. It has become a routine method in Hungary since the 1990s. The more and more frequent chronic pelvic alterations—with special regard to ones caused by endometriosis and different types of infectious diseases spreading by sexual intercourse, may play an important role in infertility. Operative laparoscopy helps not only with defining the status of the pelvic organs, but with the treatment of them, so it may give patients a chance for a spontaneous conception. In the case of irreversibly damaged oviducts the operative laparoscopy increases the success rate of the modern assisted reproductive techniques.

The author summarizes and analyses the results of his ten year work on the field of operative laparoscopy. He puts great emphasis on the role of laparoscopy in the treatment for infertility and chronic pelvic pain.
2. Objectives

I have made my research in a prospective way on the basis of my own created protocols.

My object was to identify the place and role of laparoscopy in diagnosis and therapy by infertility patients based on the following points:

1. Comparison and evaluation of the findings of HSG and laparoscopy by infertility patients.
2. The role of diagnostic and operative laparoscopy in the diagnosis and treatment for pathological changes of the pelvis by infertility patients?
3. The role of diagnostic and operative laparoscopy in the diagnosis and treatment for the possible causes of the chronic pelvic pain?
4. The prevalence of endometriosis and PID in Hungary.
5. Knowing the prevalence of endometriosis and PID what should we change in our treatment options?
6. The importance of laparoscopy in the infertility treatment in those cases when behind the infertility and/or chronic pelvic pain endometriosis can be found. Can-the combined operative-GnRH-analogue-operative treatment-increase the fertility chances of the patient?
7. The importance of laparoscopy in the treatment of chronic pelvic pain patients caused by endometriosis.
8. Examination of the effectiveness – in a long - term, non-conventionally administered, monophasic oral contraceptive treatment for infertility and/or chronic pelvic pain caused by endometriosis for the symptoms of chronic pelvic after combined operative – GnRH analog - operative treatment. A two year monitoring and follow up in comparison with a control group without this treatment.
9. Examination of the effectiveness of the non-conventionally administered, monophasic, oral contraceptive treatment to avoid radical surgical solution (hysterectomy with bilateral oophorectomy). Comparison with the control group without the treatment.
10. A successful pregnancy - in long term - has any influence on the symptoms of chronic pelvic pain caused by endometriosis?
3. Material and methods

The object of my work is the evaluation of my ten-year (01/09/1991 - 01/09/2000) experience gained by the examination and treatment of patients suffering from infertility and/or chronic pelvic pain - attending the Outpatient’s Department of Endocrinology-and Endometriosis at I. st. Department of Obstetrics and Gynaecology of Semmelweis University Budapest. The whole examination period I have divided into two parts.

3.1. First examinations period: 01/09/1991 - 31/12/1995

First, I drew up a diagnostic protocol for patients suffering from infertility and/or chronic pelvic pain. In the protocol, I included the indications for diagnostic and operative laparoscopy. In the case of infertility patients, I compared the HSG findings with the later performed LSK findings.

3.1.1. Examinations protocol by infertility couple

The registration of infertility couples consisted of a detailed anamnesis and a gynaecological examination (colposcopy, cytology, and bimanual examination). It was followed by a routine and for endocrinological laboratory examination. The partner was suggested for an andrological examination. In the middle of the following spontaneous cycle transvaginal pelvic ultrasonography was performed in order to examine the status of the pelvic organs and to make folliculometry. In possession of the findings, according to the protocol, laparoscopy was recommended to the patients in order to get more specified picture of the status of the pelvic organs.

If it was justified by the laboratory and/or palpation findings the patients initially received a wide-spectrum antibiotic treatment (doxycyclinum 200mg/day or clindamycinum hydrocloricum 1200mg/day and metronidazol 1000mg/day) for at least 12 days. If the palpation findings or the complaints remained unchanged in a month, laparoscopy was recommended. In those cases when the bimanual examination and the ultrasonography were suggestive for benign adnexal process, laparoscopy or laparotomy was considered. In possession of negative laboratory and palpation findings a HSG was performed. If HSG verified any kind of pathological change after the same antibiotic
treatment - mentioned above - LSK was performed. In the case of a patient who in spite of a negative HSG and satisfactory andrological findings of the partner was not able to get pregnant within six verified ovulatory cycles, LSK was performed. During the laparoscopy the alterations were specified and the necessary surgical interventions were performed (cystectomy, ovarian resection, endometriosis endocoagulation, adhaesiolysis). Histology was performed on the basis by laparoscopy or by laparotomy taken samples, and in the case of the verified pathological changes the patients received special medical treatment (antibiotics, NSAID, GnRH analog, etc.). In justified cases second-look laparoscopy was considered in order to control the efficiency of the medication and to clarify the functional status of the pelvic organs especially of the oviducts. If the oviduct was irreversibly damaged (hydrosalpinx) or functionally damaged, after the surgical solution (salpingectomy) I suggested special assisted reproductive technics (ART). In possession of the endocrinological findings the patients got a personally established ovulation-inducti on treatment. In the case of unfavorable andrological findings I decided on the suitable ART (IUI, IVF-ET). I evaluate the success of the performed laparoscopic interventions by the results of the conceptions within the 12 month check-up period.

3.1.1.1. Hysterosalpingography and later performed laparoscopy comparisons method

In 124 cases (out of 186 infertility patients) HSG and later on a LSK was performed. I compare the data of the alterations found by HSG and LSK.

3.1.1.2. First line laparoscopy method

According to the protocol, in 62 cases I omitted HSG and I decided on performing LSK at first. I publish the data of the alterations found.

3.1.1.3. Summarized data of hysterosalpingography and later performed laparoscopy and first line laparoscopy groups

The evaluation of all laparoscopic findings by the 186 infertility couples.
3.1.1.4. Summarized pregnancy rate after all laparoscopic interventions by the 186 infertility couples

I evaluate the success of the performed laparoscopic interventions by the results of the conceptions within the 12 month check-up period.

3.1.2. Examination protocol for patients suffering from chronic pelvic pain

3.1.2.1. Laparoscopic examinations methods by chronic pelvic pain patients

The registration of the patients suffering from CPP consisted of detailed anamnesis and a gynaecological examination (colposcopy, cytology, bimanual examination). After the routine laboratory transvaginal ultrasonography was performed. In possession of the findings I decided on laparoscopy in order to clarify the status of the pelvic organs and to find out the causes of CPP.

If the laboratory and/or the palpation findings justified it, the patient initially got wide-spectrum antibiotic treatment (doxycyclinum 200mg/day, or clindamycinum hydrocloricum 1200mg/day and metronidazol 1000 mg/day) for at least 12 days. If the palpation findings and the complaints remained unchanged, or if the complaints recurred within 3 month after the therapy, laparoscopy was performed. In those cases when the bimanual examination and the ultrasonography were suggestive for endometriosis, laparoscopy or laparotomy was decided on. In the case of more than 6-month long CPP complaints with negative laboratory, palpation and ultrasonographical findings I suggested LSK.

3.2. Second examinations period: 01/01/1996-01/09/2000

In the Outpatient’s Department of Endocrinology-Endometriosis of our clinic 511 patients were treated with histological verified endometriosis of different position and stadium between 01/01/ 1996-01/09/2000. Among the patient there were cases of, peritoneal, urinary bladder, intestinal and lung endometriosis cases.

Laparoscopy or laparotomy was performed and the patients suffering from histological verified endometriosis received a 6 month GnRH analog treatment. In 8-10 weeks after the medical treatment a second–look laparoscopy was suggested. The
necessary surgical interventions (cystectomy, ovarian resection, endocoagulation, adhaesiolysis) were made during both operations.

The extension of the endometriosis was determined on the basis of the R-AFS scoring system (revised in 1986) of the American Fertility Society (AFS).

Operative laparoscopies were performed with Karl Storz (Tuttlingen) video-laparoscope. To evaluate the CPP caused by endometriosis I used the short-form of McGill pain questionnaire suggested by Melzack. The questionnaire evaluates separately the pain scores of CPP caused by endometriosis, dyspareunia (DP) and dysmenorrhoea (DM). The patients evaluate the different kinds of pain separately from 0 to 3 scores.

The patients received a long-term, non-conventionally administered, oral, monophasic contraceptive treatment consisting of third-generation gestagen for at least 3-6 month. If spotting longer than 5 days appeared during the continuous administration, after a 7 day break the patient was administered to take oral contraceptive in the way mentioned above. I evaluate the McGill pain scores of the patients without contraceptive treatment for any reason as a control group.

I have done my research in two groups:
1. patients of infertility and CPP
2. patients of CPP only.

3.2.1. Examinations methods by 165 patients suffering of infertility and chronic pelvic pain caused by endometriosis

3.2.1.1. The method of pain evaluation by infertility patients after combined surgical - GnRH analog medical - surgical treatment

3.2.1.2. Conception rates after combined surgical - GnRH analog medical - surgical treatment by infertility patients caused by endometriosis

I evaluate the data of 165 patients, in the cases of whom the cause of the treatment was primarily infertility caused by endometriosis and CPP of secondary importance. In the case of infertility patients I judged the functional state of the oviducts with the help of chromopertubation after the surgical correction made during the second-look laparoscopy.
I publish the data of spontaneous or ART conceptions within 12 month of the infertility patients getting individualized ovulation-induction treatment.

3.2.1.3. The method of pain evaluation by infertility patients after successful gestation and lactation using a non conventionally ordered oral contraceptive pill treatment

After the surgical- GnRH analog medical - surgical treatment, successful pregnancy, delivery and the lactation period the infertility patients – if they did not want to be pregnant again - were treated with non-conventionally administered, monophasic, oral contraceptive treatment containing third generation gestagen.

I have evaluated the McGill pelvic pain scores given by the patients before the first surgical intervention, those of given before the second-look laparoscopy after the medication, and those of given at the end of the 6th, 12th, 18th and the 24th months after the lactation period. I have evaluated the data of the patients without medication for any reason as a control group.

3.2.2. Examinations methods by 181 patients suffering from chronic pelvic pain caused by endometriosis

3.2.2.1. The method of pain evaluation after combined surgical - GnRH analog medical - and surgical treatment by chronic pelvic pain patients caused by endometriosis

I have worked up the McGill pelvic pain scores of the patients treated for CPP caused by endometriosis after the surgical - GnRH analog medical - surgical treatment.

3.2.2.2. The method of pain evaluation by chronic pelvic pain patients caused by endometriosis with a non conventionally ordered oral contraceptive pill treatment

I evaluate the data of 181 patients. Due to CPP caused by endometriosis the patients received surgical - GnRH analog medical - surgical treatment, after which similarly to infertility patients they got non-conventionally administered, monophasic, oral contraceptive treatment containing third generation gestagen. I have worked up the
McGill pelvic pain scores given by the patients before the first surgical intervention, those of given before the second–look laparoscopy after the medication, and those of given at the end of the 6th, 12th, 18th, and the 24th month after the control intervention.

3.2.2.3. Comparison method of the cases needing radical surgical solution (hysterectomy at adn. l.u.) due to recurrence of pain complains caused by endometriosis by infertility and chronic pelvic pain patients using or not using non-conventionally ordered oral contraceptive treatment

I compare the data of needed radical interventions (hysterectomy + adn. lu.) because of intolerable pain despite the used operative and medical treatment.

Statistics

I have collected the data of my research from surgical records and patients’ examination files. The data have been worked up and evaluated with the help of a program.

The frequency of alterations found in laparoscopies is given in percentage. The change of McGill pelvic pain scores depending on time is indicated in percentage of patients. The following statistical evaluation was done by student t-test and the $\chi^2$ test.

4. RESULTS

4.1. First examinations period: 01/09/1991-31/12/1995

4.1.1. Results by infertility couple

4.1.1.1. Hysterosalpingography and later performed laparoscopy results

From comparison of HSG and LSK findings of 124 patients I have drawn the following conclusion. On the basis of the results the operative laparoscopy in every respect has given better chance to evaluate the tubes. During LSK I found 180% more (p<0,0001) periaidnexal adhesions (76/42 case) and 165% more (p<0,000001) patent tubes (208/126 case) than it had been presumed by HSG. Similar significant alteration
can be found in the case of fimbrial ampullary stop - 240% (p<0,000001) (24/10 case). However, I found half the number of intramural stops during LSK than during HSG - 55,8% (38/68 case) (p<0,0001). But the difference is also significant here.

4.1.1.2. First line laparoscopy result

Due to lack of the conditions of HSG I performed only LSK and I found 90 permeable tubes, 26 intramural stops and 98 periadnexal adhesions.

4.1.1.3. Summarized data of hysterosalpingography and later performed laparoscopy and first line laparoscopy groups

In 21,5% out of the examined 186 infertile patients I found traces of passed off chronic pelvic inflammation, and in 23,7% endometriosis could be seen. Endometriosis was more frequent in the case of primary sterile patients (28,57%), while PID was more frequent in the case of secondary sterile patients. I found subtle periadnexal adhesions in 72,5 % of PID, and in 59,09% of endometriosis. I want to put emphasis on the fact, that I found adhesions after appendectomy in 64,3% and after previous gynaecological operations in 78,6% of the patients.

4.1.1.4. Summarized pregnancy rate after all laparoscopic interventions by the 186 infertility couples

After the LSK I monitored the patients for a year. Within this 12 month period 98 spontaneous pregnancies (52,6%), 27 IUI conceptions (14,51%), and 52 IVF-ET conceptions (27,99%) happened, which means that the 95,16% of the patients got pregnant. We had first or second trimester pregnancy loss in 12,3% (11-6-6) of the cases.
4.1.2. Examinations results of patients suffering from chronic pelvic pain

4.1.2.1. Laparoscopic findings done by chronic pelvic pain patients

In the case of LSK performed due to CPP I found endometriosis in 51.9%, traces of PID in 12.38% and adhesion due to previous surgical interventions in 22.8%. In 3.81% varicosity of the latum ligament, could be verified. In 9.05% I was not able to find objective explanation for CPP.

4.2. Second examinations period: 01/01/1996-01/09/2000

4.2.1. Examination results by 165 patients suffering of infertility and chronic pelvic pain

I evaluate the data of 165 infertile patients, who were treated primarily for infertility secondary for CPP caused by endometriosis.

4.2.1.1. The results of pain evaluation scores after combined surgical – GnRH analog medical - surgical treatment

The “0” score for pelvic pain changed from 7.27% to 73.33% (12/121 patents), that for dysmenorrhoea from 20.61% to 67.88% (34/112 patents) and that for dyspareunia from 59.40% to 84.85% (98/140 patents). The McGill score “1” for pelvic pain decreased from 43.03% to 25.45% (71/42 patents), that for dysmenorrhoea from 48.49% to 32.12% (80/53 patents) and that for dyspareunia from 21.82% to 15.15% (36/25 patents). Patients in groups “0” and “1” of the McGill score changed their total percentage from 50.3% to 98.78% (83/163 patents) for pelvic pain, from 69.1% to 100% (114/165 patents) for dysmenorrhoea and from 81.22% to 100% for dyspareunia (134/165 patents).

If I classify pelvic pain depending on McGill-score and on the basis of R-AFS staging, I should say, that the extension of endometriosis and the pelvic pain caused by it are not in direct correlation. The change after the surgical-medical therapy shows the pain scores of the enduring complaints due to the irreversible alterations caused by
endometriosis. However, the light shift of the curve to the left proves the efficiency of the medication.

The results are similar for dysmenorrhea and dyspareunia - there is no linear relationship between extension of endometriosis and McGill score.

4.2.1.2. Conception rates after combined surgical - GnRH analog medical - surgical treatment by infertility patients caused by endometriosis

Among the 165 patients there were 134 primer and 31 secondary infertile. The number of primer sterile patients is strikingly high (81,2%), however, in the average age there is not much difference (31,81 – 34,82 years).

With the help of the adequate ovulation induction treatment 83 patients got pregnant spontaneously (50,3%) within a one year period after the second-look surgical intervention. If the andrological or tubal factors justified it, homolog intrauterine insemination or various ART techniques (IVE-ET, ICSI etc.) were applied. As a result, other 48 pregnancies (29,0%) were achieved by intrauterine insemination and 29 (17,5%) by IVF. In 24 (15%) cases we had first or second trimester pregnancy loss. From the 136 remaining pregnancies premature or mature infants were born. In 12 cases (7,5%), twins and in one case (0,62%) triplets were born.

4.2.1.3. The results of pain evaluation by infertility patients after successful gestation and lactation using a non conventionally ordered oral contraceptive pill treatment

During the 24 month check-up period the deterioration of McGill scores for PP, DM and DP was slower in the group medicated with non-conventionally administered, monophasic contraceptives than that in the control group. In 24 month, the number of the patients with any kind of complaints was doubled in the control group than in the group of contraceptive takers.

In one case from each group - contraceptive pill users and non-users - we had no other choice to solve the severe CPP problems just in a radical surgical way (hysterectomy+adn.l.u.).
4.2.2. Examination results by 181 patients suffering from chronic pelvic pain caused by endometriosis

I evaluate the data of 181 patients treated for CPP caused by endometriosis.

4.2.2.1. The results of pain evaluation scores after combined surgical – GnRH analog medical- and surgical treatment by chronic pelvic pain patients

The best results of the combined surgical - GnRH analog medical - surgical therapy in the McGill scores I have found in the evaluation of pelvic pain. The “0” score for pelvic pain has changed from 8,83% to 75,69% (16/137 patients), that for dysmenorrhea from 25,41% to 65,19% (46/118 patients) and that for dyspareunia from 58,01% to 85,63% (105/155 patients). The McGill score “1” for pelvic pain decreased from 30,38% to 22,65% (55/41 patients), that for dysmenorrhea from 46,96% to 34,8% (85/63 patients) and that for dyspareunia from 18,78% to 13,25% (34/24 patients). Patients in groups “0” and “1” of the McGill score changed their total percentage from 39,21% to 98,34% (71/178 patients) for pelvic pain, from 72,37% to 100% (131/181 patients) for dysmenorrhea and from 76,79% to 98,88% (139/179 patents) for dyspareunia.

If we summarize the correlation of pelvic pain caused by endometriosis on the basis of R-AFS staging with the McGill scoring system before the treatment, the graph shows a bell-shaped form, i.e. the extension of the endometriosis and the pelvic pain caused by it are not in direct correlation. However, after the surgical and medical intervention the graphs do not show it indicating the efficiency of the surgical and medical intervention.

The results are similar for dysmenorrhea and dyspareunia- there is no linear relationship between the extension of endometriosis and McGill score. However, in the case of DM the bell - shaped graph is flatter. It can be explained by the fact, that the pain evaluation after the surgical intervention depends not on the severity of the endometriosis but on the severity of the adenomyotic alteration of the uterus. In the case of dyspareunia, which is in connection with deep endometriosis, there is a light shift of the graph to the left. It means that dyspareunia is less influenced by loosening of the pelvic adhesions. Nevertheless, the medication results in positive pain evaluation thanks to the decrease of the retro cervical endometriosis.
4.2.2.2. The results of pain evaluation by chronic pelvic pain patients using a non conventionally ordered oral contraceptive pill treatment

The deterioration of McGill scores for PP, DM and DP is slower in the case of contraceptive takers than in the control group. In the case of PP the “0” score decreased from 87,2% (103/118 patients) to 84,7% (100/118 patients) in the medicated group, while in the control group it decreased from 87,3% (55/63 patients) to 74,6 (47/63 patients). Similar change can be observed in “0” score for DM: it decreased from 87,2% (101/118 patients) to 80,5% (95/118 patients) in the contraceptive - taker group and from 82,5% (52/63 patients) to 63,4% (40/63 patients) in the control group. In the case of DP the “0” score of the patients with medication decreased from 76,2% (93/118 patients) to 64,4% (76/118 patients), while from 73,0% (46/63 patients) to 41,0% (26/63 patients) in the control group. In other words, in 24 month the number of recidivistic patients of different scores is almost double in the control group than that in the medicated group. To sum up, with the help of the non-conventionally administered contraceptive treatment the recidivism causing complaints can be decreased into half. In other words the number of patients with PP has increased from 15,3% to 25,4%, that with DM has increased from 19,5% to 36,7% and that with DP increased from 35,6% to 58,8%.

4.2.2.3. Summarized data of the cases needing radical surgical solution (hysterectomy at adn. l.u.) due to recurrence of pain complains caused by endometriosis by infertility and chronic pelvic pain patients using or not using non conventionally ordered oral contraceptive treatment

According to the data the cases needing radical surgical solution due to the worsening complaints can be decreased into third with the help of non-conventionally administered OAC of minor dose. Within 24 month I recommended radical surgical solution in 7 cases (5,93%) of the contraceptive takers’ group and in 11 (17,4%) cases in the control group. Using the \( \chi^2 \) test the difference is significant ((p<0,02; RR 1,14 / 95%; CI 1,01-1,29). In the case of infertile patients we had to decide on the radical solution in one case of each group.
5. CONCLUSION

1. Comparing HSG and LSK findings it can be stated that LSK gives significantly more reliable information about the permeability of the oviducts, the place of the block, i.e. about the functional status of the inner sexual organs, and it provides a surgical opportunity at the same time.

2. By infertility patients the diagnostic and operative laparoscopy plays outstanding role in the differential diagnosis of the disorders of the internal genital organs. The diagnosis and minimal invasive surgical intervention, if necessary, of the endometriosis, PID and previous abdominal operations and its consequences in order to restore the fertility can be reached only with the help of LSK. This fact stresses the need to push LSK forward to HSG because it gives a therapeutic opportunity to restore fertility at the same time.

3. By CPP patients, LSK is an effective possibility in the differential diagnosis of the possible disorders causing CPP. It helps also in the long term potent medication of CPP.

4. The prevalence of endometriosis and PID by infertility patients was 23,6% for endometriosis and 21,5% for PID. While LSK performed by CPP patients verified endometriosis in 51,9% and PID and its consequences in 12,3% of the cases.

5. The high prevalence of PID and endometriosis cases in the reproductive age is a warning for the National Health care to take it in account as a general health problem. The early diagnosis is the key point of the effective therapy.

6. The combined surgical – GnRH analog medical treatment is proved to be effective in the case of infertility and CPP caused by endometriosis. The second-look laparoscopy is an important step forward in prediction of the later fertility chances.

7. The combined surgical - GnRH analog medical treatment is proved to be effective in the case of CPP caused by endometriosis. The quality of life of the patients has improved as a result of on diagnosis based therapy.

8. The recurrence of CPP complaints decreased by ordering the non-conventionally administered, monophasic oral contraceptive therapy. The results of the 24 month check-up period show that with the help of this therapy the recurrence of PP and DM decreases into half, and that of DP decreases by third.
9. The radical surgical solution became inevitable in 5.93% (7 patents) of the cases in the group of contraceptive takers, while it was 17.4% (11 patents) in the control group. The difference between the two groups is significant.

10. The number of the cases needing radical surgical solution (hysterectomy+adn.lu.) by infertility patients was 1-1 patient by OAC users and non-users. The result makes able a possible immunmodulatory effect of pregnancy on the progression of endometriosis.
6. Literature of my publications used in this thesis

Publications


Books


**Other publications**


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