



Endometriosis Bulletin

December 2018 / Issue VIII



1 in 10 Women are Affected by Endometriosis

www.endometriosis.org

PREFACE

HELLO

Here we are with you again with the 8th issue of our bulletin. We would like to give you a preview of our bulletin and share with you important news from the world of endometriosis.

On November 22-24, 2018 in Vienna, Austria we attended the **4th European Endometriosis Congress**. Our board members gave presentations and chaired several sessions. Younger members of the society prepared five oral and 6 poster presentations. We are also proud to announce that our society's founding president **Prof. Engin Oral, MD.** was announced to be the 'President Elect' of **European Endometriosis League (EEL)** in 2019.

For the first time on December 10-11, 2018 we have organized **Endometriosis School of Turkey** in Istanbul. We discussed endometriosis with our national and international colleagues. We held interactive oral presentations and had a stimulating 'case-discussion' session. Our colleagues had a chance to watch live surgery on a patient and also and practice laparoscopic surgery on pigs at the animal laboratory. After two days of intensive and reproductive work and since we had very encouraging feedback, we are motivated to organize similar meetings in the future.

Prof. Engin Oral, MD., and **Assoc. Prof. Hale Goksever Celik, MD.,** attended **TSRM Congress** in Antalya in November and represented our society.

We are very excited to announce that we have realized one of our dream projects; seminars for high school students on reproduction and endometriosis. **Prof. Umit Inceboz, MD.,** held a seminar and discussion session in Izmir at American Collegiate Institute and Saint Joseph Highschool. We will organize similar seminars at other schools as well.

To raise awareness on endometriosis, **Prof. Banu Kumbak Aygun, MD.,** and **Prof. Umit Inceboz, MD.,** have joined to '**The Fancy Ladies Bicycle Tour**' which was held in Istanbul and in Izmir. In Samsun **Seher Sari, MD.,** pedaled for the same reason we well.

In Ankara, Antalya, Van and Samsun **Eda Ureyen, MD., Salih Yilmaz, MD.,** and **Seher Sari, MD.,** organized seminars titled as "**Endometriosis and Reproductive Health**" for endometriosis patients. The seminars were very successful and we had a lot of positive feedback.

Under the interviews section where we interview each month a different national or international colleague specializing in the field of endometriosis we would like to share with you our latest interview with **Prof. Mario Malzoni, MD.** from **Italy.** You can read a summary of the interview in this bulletin and watch the video online through our website.

For the first time in this issue we are introducing a new section called 'Endometriosis and Other Specialties'. Our first article is written by **Prof. Huseyin Nazlikul, MD.,** with the title '**Neuraltherapy in Endometriosis**'.

As in the previous issues, below we share with you a selection of international and national articles. Hoping to be with you in the next issue with more news and achievements in the field of endometriosis.

Best regards,

Board Members of Endometriosis&Adenomyosis Society

Founding President Prof. Engin Oral, MD.



Board Members of Endometriosis&Adenomyosis Society 2018



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(Member)

Endometriosis e-bulletin is prepared by Turkish Endometriosis & Adenomyosis Society. If there are any topics that you would like us to include in the bulletin or any questions that you would like to ask, you can contact us via e-mail to dr_pinaryalcin@hotmail.com or baharyl86@gmail.com.

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A SELECTED ARTICLES

1 PROGESTERONE RECEPTOR STATUS PREDICTS RESPONSE TO PROGESTIN THERAPY IN ENDOMETRIOSIS

Valerie A. Flores, Arne Vanhie, Tran Dang, and Hugh S. Taylor *The Journal of Clinical Endocrinology & Metabolism*, 103(12), 4561-4568, 2018

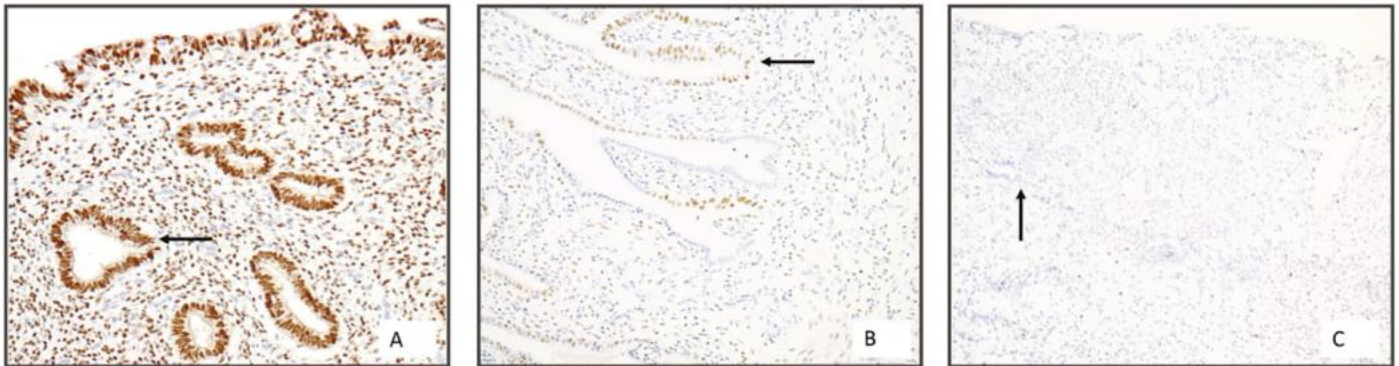


Figure 1. PR immunohistochemistry. A to C, Representative images of PR expression in endometriotic lesions. PR expression quantified using H-score: A, high PR staining; B, medium PR staining; C, low PR staining. Arrows denote glandular epithelium (magnification $\times 20$).

Abstract

Context

Progestin-based therapy is the first-line treatment for managing endometriosis-associated pain. However, response to progestins is currently variable and unpredictable. Predictive markers for response to progestin-based therapy would allow for a personalized approach to endometriosis treatment.

Objective

We hypothesize that progesterone receptor (PR) levels in endometriotic lesions determine response to progestin-based therapy.

Design

Retrospective cohort study.

Setting

Academic center.

Patients

Fifty-two subjects with histologically confirmed endometriosis and a previous documented response to hormonal therapy were included.

Interventions

Immunohistochemistry was performed on sections of endometriotic lesions using a rabbit polyclonal IgG for detection of PR-A/B.

Main Outcome Measures

The Histo (H)-score was used for quantifying PR status. Response to progestin-based therapies was determined from review of the electronic medical record.

Results

H-score was higher in responders compared with nonresponders. Subjects were categorized into three groups: high (H-score > 80 , $n = 7$), medium (H-score 6 to 80, $n = 28$), and low (H-score ≤ 5 , $n = 17$) PR status. The threshold of PR > 80 was associated with a 100% positive predictive value. The threshold of PR < 5 was associated with a 94% negative predictive value.

Conclusion

PR status is strongly associated with response to progestin-based therapy. Receptor status in endometriosis could be used to tailor hormonal-based regimens after surgery, and negate trialing progestin-based therapy to determine resistance. Ascertainment of PR status may allow for a novel, targeted, precision-based approach to treating endometriosis.

2 ANTIMÜLLERIAN HORMONE IS REDUCED IN THE PRESENCE OF OVARIAN ENDOMETRIOMAS: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Ludovico Muzii, M.D., Chiara Di Tucci, M.D., Mara Di Feliciano, M.D., Giulia Galati, M.D., Violante Di Donato, M.D., Angela Musella, M.D., Innocenza Palaia, M.D., and Pierluigi Benedetti Panici, M.D. *Fertility and sterility*, 110(5), 932-940, 2018

Abstract

OBJECTIVE: To evaluate if the presence of endometriomas impacts on the ovarian reserve as evaluated with antimüllerian hormone (AMH).

DESIGN: Systematic review and meta-analysis.

SETTING: Not applicable.

PATIENT(S): Patients with unoperated endometriomas versus controls without endometriomas.

INTERVENTION(S): Electronic databases searched up to June 2017 to identify articles evaluating AMH levels in patients with unoperated endometriomas versus controls without endometriomas.

MAIN OUTCOME MEASURE(S): The primary analysis was aimed at evaluation of AMH levels (mean and SD) in patients with and without endometriomas. Secondary analyses were aimed at evaluating AMH levels in patients with ovarian endometriomas compared to patients with either non-endometriosis benign ovarian cysts or healthy ovaries.

RESULT(S): Of the 39 studies evaluated in detail, 17 were



included, for a total of 968 patients with endometriomas and 1874 without endometriomas. AMH was significantly lower in patients with unoperated endometriomas compared to patients with no endometriomas (mean difference -0.84, with 95% confidence interval [CI] -1.16 to -0.52). At secondary analyses, AMH in patients with endometriomas was significantly lower both versus non-endometriosis benign ovarian cysts (mean difference -0.85, 95% CI -1.37 to -0.32, and versus women with healthy ovaries (mean difference -0.61, 95% CI -0.99 to -0.24).

CONCLUSION(S): Ovarian reserve evaluated with AMH is reduced in patients with ovarian endometriomas compared both to patients with other benign ovarian cysts, and to patients with healthy ovaries.

KEYWORDS: Antimüllerian hormone; endometrioma; endometriosis; ovarian reserve

3 EFFICACY OF LEVONORGESTREL RELEASING INTRAUTERINE SYSTEM AS A POSTOPERATIVE MAINTENANCE THERAPY OF ENDOMETRIOSIS: A META-ANALYSIS

Soo Youn Song, Mia Park, Geon Woo Lee, Ki Hwan Lee, Ha Kyun Chang, Sang Mi Kwak, HeonJong Yoo *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 231, 85-92, 2018

Abstract

Objective

To compare the efficacy of levonorgestrel releasing intrauterine system (LNG-IUS) with other treatments as a postoperative maintenance therapy for endometriosis in terms of pain reduction, recurrence prevention, side effects and patients' satisfaction.

Study design

We searched MEDLINE, EMBASE, and the Cochrane Library from January 1986 until February 2018. Two evaluators independently extracted and reviewed prospective and retrospective articles based on pre-determined selection criteria. Outcomes were expressed as mean difference (MD), risk ratios (RR) or odds ratios (OR) in a meta-analysis model, using Revman software.

Results

Among the 962 studies, 7 studies were selected: 7 studies included 4 randomized controlled trials with 212 patients, 1 prospective cohort study with 88 patients, and 2 retrospective studies with 191 patients. A meta-analysis showed that LNG-IUS was significantly effective in reducing pain after surgery (MD = 12.97, 95% confidence interval (CI): 5.55–20.39), with a comparable effect to gonadotropin-releasing hormone analogues (MD = -0.16, 95% CI:

-2.02 to 1.70). LNG-IUS was also effective in decreasing the recurrence rate (RR = 0.40, 95% CI: 0.26–0.64), with an effect comparable to OC (OR = 1.00, 95% CI: 0.25–4.02) and danazol (RR = 0.30, 95% CI: 0.03–2.81). Furthermore, patients' satisfaction with LNG-IUS was significantly higher than that with OC (OR = 8.60, 95% CI: 1.03–71.86). However, vaginal bleeding was significantly higher in the LNG-IUS group than in the gonadotropin-releasing hormone analogue group (RR = 27.0, 95% CI: 1.71–425.36).

Conclusion

Our meta-analysis found a positive effect of LNG-IUS as a postoperative maintenance therapy for endometriosis on pain relief, prevention of dysmenorrhea recurrence, and patients' satisfaction.



4 NLRC5 AND AUTOPHAGY COMBINED AS POSSIBLE PREDICTORS IN PATIENTS WITH ENDOMETRIOSIS

Lei Zhan, M.D., Shun Yao, M.D., Shiyang Sun, M.D., Qian Su, M.D., Jun Li, Ph.D., and Bing Wei, M.D. *Fertility and sterility*, 110(5), 949-956, 2018

Objective:

To investigate the levels of NLRC5 and autophagy in women with leiomyoma and endometriosis and the correlation between NLRC5 level and autophagy level.

Design: Case-control study.

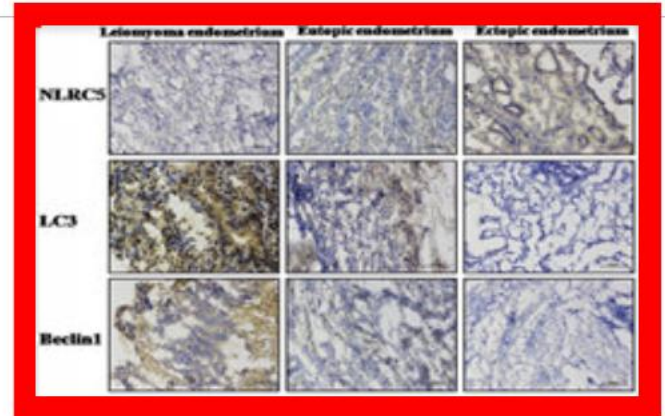
Setting: Clinics.

Patient(s): Sixty-five patients were recruited: 30 women with endometriosis were compared with 35 women with leiomyoma.

Intervention(s): Endometriosis was definitively diagnosed during surgery by laparoscopy or laparotomy and was confirmed by histopathological evaluation (n=30). Secretory phase ectopic endometrium tissues and eutopic endometrium tissues were obtained from 30 women with endometriosis. Control endometrium tissues were collected at hysterectomy from 35 women with leiomyoma. Immunohistochemical staining of NLRC5, LC3, Beclin1 and P62 were performed.

Main Outcome Measure(s): A semiquantitative analysis was performed. Correlations between NLRC5 level and LC3, Beclin1, P62 levels were compared.

Result(s): The expressions of NLRC5 and P62 in the ectopic and eutopic endometrium of endometriosis groups were significantly higher than that in the endometrium of leiomyoma group. And their expressions in ectopic endometrium were significantly upregulated compared to the eutopic endometrium. The expressions of LC3 and Beclin1 were down-



regulated in the ectopic and eutopic endometrium of endometriosis groups compared to the leiomyoma group. LC3 and Beclin1 levels were lower in ectopic endometrium than in the eutopic endometrium. There is a negative correlation between NLRC5 level and LC3, Beclin1 levels. There is a positive correlation between NLRC5 level and P62 level.

Conclusion(s): There is a negative correlation between NLRC5 level and autophagy level. NLRC5 and autophagy combined may be promising predictors in patients with endometriosis. (*Fertil Steril* 2018;110:949-56. 2018 by American Society for Reproductive Medicine.)

KeyWords: Endometriosis, NLRC5, autophagy, correlation, predictors

5 RISK OF PRETERM BIRTH, LOW BIRTHWEIGHT AND SMALL-FOR-GESTATIONAL-AGE INFANTS IN PREGNANCIES WITH ADENOMYOSIS: A COHORT STUDY OF THE JAPAN ENVIRONMENT AND CHILDREN'S STUDY

Akiko Yamaguchi, Hyo Kyozyuka, Keiya Fujimori, Mitsuaki Hosoya, Seiji Yasumura, Tadahiko Yokoyama, Akiko Sato, Koichi Hashimoto *The Japan Environment and Children's Study Group Acta Obstet Gynecol Scand.* 00:1-6, 2018

Introduction

This study evaluated the risk of preterm birth, low birthweight and small-for-gestational-age neonates born to mothers with adenomyosis during pregnancy.

Material and methods

We used the results of a Japanese nationwide prospective birth cohort study, identifying 93 668 singleton deliveries from 2011 to 2014. We identified 314 pregnancies with adenomyosis using self-reported questionnaires. Multiple logistic regression analyses were conducted to examine whether adenomyosis was associated with adverse pregnancy outcome. Maternal age, smoking status, method of conception, history of parity, fibroids, endometriosis and body mass index before pregnancy were analyzed as confounding factors.

Results Multiple logistic regression analysis showed that pregnancy with adenomyosis was a risk factor for preterm birth at less than 37 weeks (adjusted odds ratio [aOR]: 2.49, 95% confidence interval [CI] 1.89-3.41), preterm birth at less than 34 weeks (aOR 1.91, 95% CI 1.02-3.55), low birthweight <2500 g (aOR 1.83, 95% CI 1.36-2.45), low birthweight <1500 g (aOR 2.39, 95% CI 1.20-4.77) and small-for-gestational-age neonates (aOR 1.68, 95% CI 1.13-2.51).

Conclusions

This study found that pregnancy with adenomyosis was associated with preterm birth, low birthweight and small-for-gestational-age neonates.



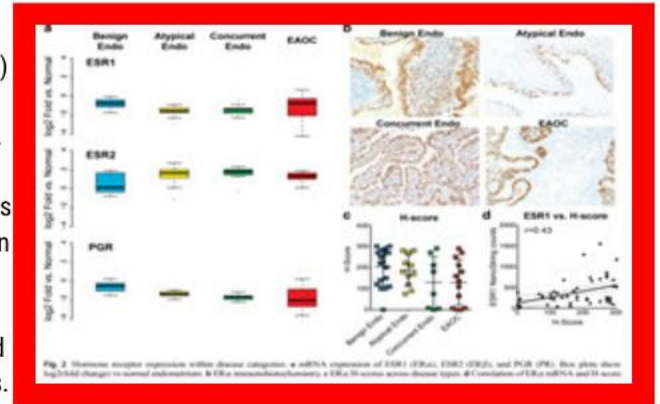
6 THE EVOLUTION OF ESTROGEN RECEPTOR SIGNALING IN THE PROGRESSION OF ENDOMETRIOSIS TO ENDOMETRIOSIS-ASSOCIATED OVARIAN CANCER.

Andersen CL, Boisen MM, Sikora MJ, Ma T, Tseng G, Suryawanshi S, Vlad A, Elishaev E, Edwards RP, Oesterreich S. *Hormones and Cancer*, 9(6), 399-407,2018

Abstract

To investigate changes in estrogen receptor alpha (ER α) signaling during progression of endometriosis to endometriosis-associated ovarian cancer (EAOC) as a driver of malignant transformation. We procured tissue samples of normal endometrium, endometriosis (benign, atypical, concurrent with EAOC), and EAOC. We evaluated expression of a 236-gene signature of estrogen signaling. ANOVA and unsupervised clustering were used to identify gene expression profiles across disease states. These profiles were compared to profiles of estrogen regulation in cancer models from the Gene Expression Omnibus (GEO). Gene Set Enrichment Analysis (GSEA) was performed to determine whether gene expression in EAOC was consistent with ER α activity. ANOVA revealed 158 differentially expressed genes ($q < 0.05$) and unsupervised clustering identified five distinct gene clusters. The estrogen signaling profile of EAOC was not consistent with activated ER α in pre-clinical models. Gene set enrichment analysis did not identify signatures of activated ER α in EAOC but instead identified expression patterns consistent with loss of ER α function and development of endocrine resistance. Gene expression data suggest that ER α signaling becomes inactivated throughout the progression of endometriosis to EAOC. The gene expression pattern in EAOC is more consistent with profiles of endocrine resistance.

KEYWORDS: Endometriosis; Estrogen receptor alpha; Estrogens; Human; Ovarian neoplasms; Transcriptome



7 OLIGO-ANOVULATION IS NOT A RARER FEATURE IN WOMEN WITH DOCUMENTED ENDOMETRIOSIS

Pietro Santulli, M.D., Ph.D., Chloe Tran, M.D., Vanessa Gayet, M.D., Mathilde Bourdon, M.D., Chloe Maignien, M.D., Louis Marcellin, M.D., Khaled Pocate-Cheriet, M.D., Charles Chapron, M.D., and Dominique de Ziegler, M.D. *Fertility and sterility*, 110(5), 941-948,2018

Objective:

To study the prevalence of oligo-anovulation in women suffering from endometriosis compared to that of women without endometriosis.

Design:

A single-center, cross-sectional study.

Setting: University hospital-based research center.

Patient (s): We included 354 women with histologically proven endometriosis and 474 women in whom endometriosis was surgically ruled out between 2004 and 2016.

Intervention: None.

Main Outcome Measure(s): Frequency of oligo-anovulation in women with endometriosis as compared to that prevailing in the disease-free reference group.

Results:

There was no difference in the rate of oligo-anovulation between women with endometriosis (15.0%) and the reference group (11.2%). Regarding the endometriosis phenotype, oligo-anovulation was reported in 12 (18.2%) superficial peritoneal endometriosis, 12 (10.6%) ovarian endometrioma, and 29 (16.6%) deep infiltrating endometriosis.

Conclusion(s):

Endometriosis should not be discounted in women presenting with oligo-anovulation.

Key Words:

Endometriosis, oligo-anovulation, antimüllerian hormone, deep infiltrating endometriosis

8 ASSESSMENT OF OVARIAN RESERVE AFTER CYSTECTOMY VERSUS 'ONE-STEP' LASER VAPORIZATION IN THE TREATMENT OF OVARIAN ENDOMETRIOMA: A SMALL RANDOMIZED CLINICAL TRIAL.

M. Candiani, J. Ottolina, E. Posadzka, S. Ferrari, L. M. Castellano, I. Tandoi, L. Pagliardini, A. Nocun, and R. Jach Human Reproduction, 33(12), 2205-2211, 2018

Abstract

STUDY QUESTION:

Does CO₂ laser vaporization offer better results in treating endometrioma in terms of ovarian reserve preservation compared to traditional cystectomy?

SUMMARY ANSWER:

Assessing both antral follicle count (AFC) and serum anti-Müllerian hormone (AMH) levels as measures of ovarian reserve, the results suggest that CO₂ technology may be an alternative treatment for endometrioma, causing minimal damage to adjacent healthy ovarian tissue.

WHAT IS KNOWN ALREADY:

Excisional surgery has been questioned as an ideal surgical approach for endometriomas because it is associated with potential reduction of ovarian reserve. Recently, vaporization with CO₂ laser in-line-of-sight, according to the 'three-step procedure', has been proposed as the best method to preserve ovarian function. However, no randomized controlled trials have been conducted to compare cystectomy and 'one-step' CO₂ fiber laser vaporization (without GnRH agonist therapy) with respect to the ovarian reserve.

STUDY DESIGN, SIZE, DURATION:

A multicentre randomized clinical trial including 60 patients was performed between July 2017 and February 2018. Computerized randomization was conducted to allocate them in a proportion of 1:1 either to Group 1 (laparoscopic stripping: cystectomy) or Group 2 (CO₂ laser vaporization). Patients in Group 1 underwent a standardized laparoscopic stripping technique; patients in Group 2 underwent drainage of the cyst content, biopsy and vaporization of the internal wall with a CO₂ fiber laser. Patients underwent pelvic ultrasound examination to determine the AFC and blood sampling to determine AMH levels before surgery and at 1- and 3-month follow-up.

PARTICIPANTS/MATERIALS, SETTING, METHODS:

Patients undergoing surgery for symptomatic endometriomas (infertility and/or pelvic pain) larger than 3 cm were randomized in two groups according to the surgical technique. Patients aged ≥ 40 years, or with deep infiltrating endometriosis/adenomyosis, or previously submitted to surgical procedures on the ovaries or to hysterectomy were excluded from the study. The primary endpoint was the comparison of intra-group AFC changes before and after surgery (Δ AFC) between the two groups (Δ AFC Group 1 versus Δ AFC Group 2). The secondary endpoint was the modification of serum AMH before and after surgery (Δ AMH) between the two groups (Δ AMH Group 1 versus Δ AMH Group 2).



MAIN RESULTS AND THE ROLE OF CHANCE:

The AFC of the operated ovary was significantly increased in Group 2 (laser vaporization) compared with Group 1 (cystectomy) after surgery (Group 1: from 4.1 ± 2.2 [mean \pm SD] at baseline to 6.3 ± 3.5 at 3-month follow-up; 95% CI: 0.9-4; Group 2: from 3.6 ± 1.9 at baseline to 8.6 ± 4.2 at 3-month follow-up; 95% CI: 2.8-7.1; $P = 0.016$); serum AMH levels were significantly reduced at 3 months in Group 1 (from 2.6 ± 1.4 ng/mL at baseline to 1.8 ± 0.8 ng/mL at 3-month follow-up; 95% CI: -1.3 to -0.2; $P = 0.012$) compared with no reduction in Group 2 (from 2.3 ± 1.1 ng/mL at baseline to 1.9 ± 0.9 ng/mL at 3-month follow-up; 95% CI: -1 to -0.2; $P = 0.09$).

LIMITATIONS, REASON FOR CAUTION:

The key limitations of the trial were the low accuracy of AFC in estimating the ovarian reserve in ovaries with endometriomas, the limited study size and the relatively short follow-up, which do not allow us to draw definitive conclusions.

WIDER IMPLICATIONS OF THE FINDINGS:

The present study suggests that CO₂ technology may treat endometrioma with minimal damage to the adjacent healthy ovarian tissue; however, this study should be considered as a preliminary clinical trial, intended to stimulate future larger trials to address this clinically relevant issue.

STUDY FUNDING/COMPETING INTEREST(S):

None.

9 ACCURACY OF ANOGENITAL DISTANCE AND ANTI-MÜLLERIAN HORMONE IN THE DIAGNOSIS OF ENDOMETRIOSIS WITHOUT SURGERY

Abstract

Objective:

To assess the predictive ability of a combination of anogenital distance (AGD) and anti-Müllerian hormone (AMH) to diagnosis the presence of endometriosis without surgery.

Methods:

The present study included women diagnosed with endometriosis and a control group who attended the "Virgen de la Arrixaca" University Hospital, Murcia, Spain, between September 1, 2014, and May 31, 2015. Serum concentrations of AMH were measured, and two AGD measurements were obtained: from the anterior clitoral surface to the upper verge of the anus (AGDAC), and from the posterior fourchette to the upper verge of the anus (AGDAF). Data were assessed by receiver operator characteristic (ROC) curves.

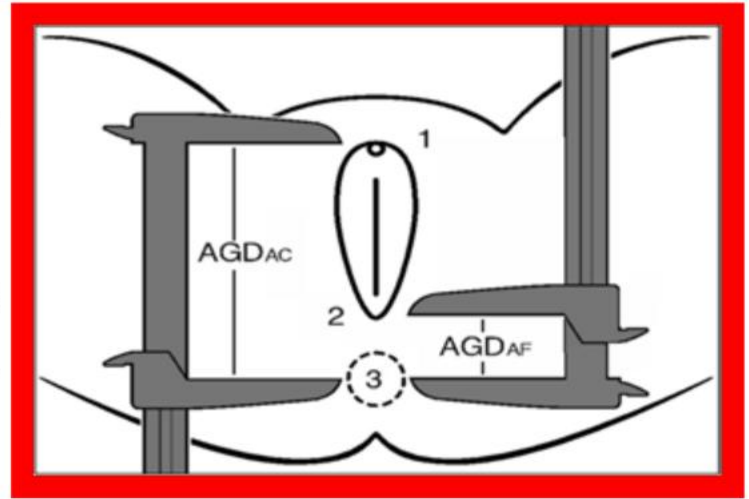
Results: Women in the endometriosis group (n=57) had significantly shorter AGDAF (22.8 ± 4.6 vs 27.2 ± 5.7 mm; $P < 0.001$) and lower AMH (2.2 ± 2.5 vs 3.3 ± 1.9 ng/mL; $P < 0.003$) compared with the control group (n=93). Women with serum AMH below the clinical cut-off (1 ng/mL) were 17.40-times more likely to have endometriosis (95% confidence interval [CI] 5.64–53.82). The area under the ROC curve of combined AMH and AGDAF was 0.77 (95% CI 0.70–0.85).

Conclusion:

The model for predicting endometriosis on the basis of AMH and AGD could be useful for clinicians and epidemiologists to improve diagnosis and prognosis of this condition.

KEYWORDS

Anogenital distance; Anti-Müllerian hormone; Endometriosis; Predictive model; Prenatal exposures; ROC curve



B NEWS FROM OUR SOCIETY

PLANNED ACTIVITIES

Endoacademy Meetings IX

9th Endoacademy will take place in February in Istanbul. With our guest Mr. George A. Pistofidis MB.BS. FRCOG from Greece we are going to discuss endometriosis and adenomyosis.

George A. Pistofidis

Director of Gynecological Endoscopic Surgery at Levkos Stavros Clinic, Athens

Consultant at Gennima Fertility Centre, Athens

Consultant in Obstetrics and Gynecology at Mitera Maternity & Surgical Centre Athens

Member of the board of the Hellenic Gynecological Endoscopic Society

Director of ACET laparoscopic training centre, Athens



FEBRUARY 10, 2019 ENDOMETRIOSIS PROGRAMME

Moderators: Ahmet Kale, Ercan Baştu		
1st SESSION		
ENDOMETRIOMA Chairman: Bülent Baysal		
09:00-09:20	For which patients should surgery be performed?	Cem Demirel
09:20-09:40	For which patients should IVF be performed?	Hakan Yarıalı
09:40-10:00	How to perform endometrioma surgery?	Taner Usta
10:00-10:20	How to manage patients with endometrioma aged 16 and 42?	Engin Oral
10:20-10:30	Discussion	
10:30-10:50	Coffee Break	
2nd SESSION		
Adenomyosis and Deep Endometriosis Chairman: Cem Çelik		
10:50-11:10	Can we diagnose adenomyosis clinically?	Ayşe Seyhan
11:10-11:40	How to manage adenomyosis?	George Pistofidis

FEBRUARY 10, 2019 ENDOMETRIOSIS PROGRAMME

11:40-12:00	Adenomyosis and abnormal uterine bleeding: how to manage?	Levent Şentürk
12:00-12:30	How to diagnose and manage deep endometriosis in clinical practice?	George Pistofidis
12:30-12:50	Insulin resistance in PCOS and the role of inositol in treatment	Faruk Buyru
12:50-13:05	Discussion	
13:05-14:00	Lunch	
3rd SESSION		
ADENOMYOSIS AND ENDOMETRIOSIS INTERACTIVE VIDEO PRESENTATION AND CASE DISCUSSIONS (90 MIN) Moderator: George Pistofidis		
14:00-15:30	Panelists: Yücel Karaman, Bülent Urman, Ahmet Kale, Ercan Baştu	
CLOSING ENDOACADEMY		

Participation is free of charge.
For registration please send your e-mail to yasemindervisoglu@figurint.com



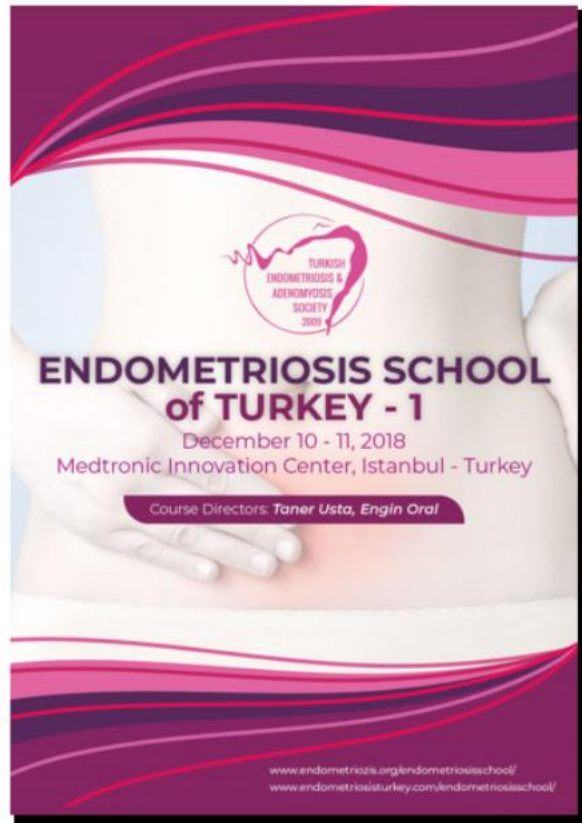
PAST ACTIVITIES

Endometriosis School of Turkey I

On December 10-11, 2018, 1stEndoschool has taken place. National and international specialists have given seminars. On the first day there was a video presentation and personal experiences were discussed. **Prof. Mario Malzoni, MD., Prof. Joerg Keckstein, MD., and Mr. Shaheen Khazali, MD.,** MRCOG., MSc. shared with us their surgical expertise on endometriosis cases. **Alessandra Di Giovanni, MD.** gave a seminar on ultrasonographic diagnosis of deep infiltrative endometriosis. On the first day in the afternoon live surgery session Prof. Joerg Keckstein, MD. showed us laparoscopic techniques on a deep infiltrative endometriosis case.

Second day started with a theoretical education on pig anatomy and laboratory rules and then until 4 pm surgical techniques were demonstrated and practical training on pig models was possible. Attendants had a chance to see and learn advanced laparoscopic techniques. Following the practical laboratory training session, a two-hour discussion session took place. With a lot of positive feedbacks from the participants we can conclude that it has been a very productive two days and a successful project.

We hope to see you in the upcoming meeting.



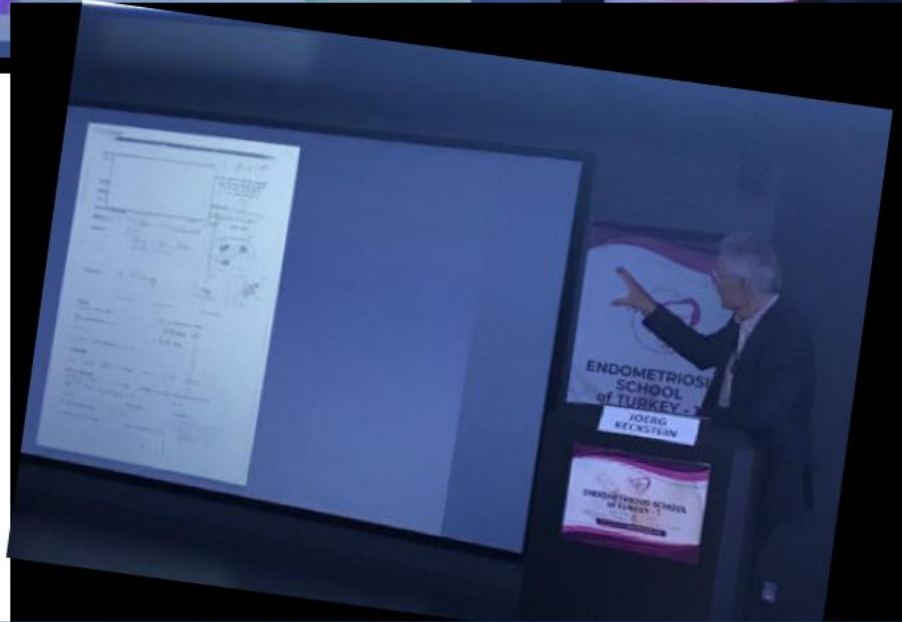
Young Team of Endometriosis



From upper left: Aysel Ozkaynak, MD., Isik Sozen, MD., Isil Ayhan, MD., Eda Ureyen, MD., Dilek Buldum, MD., Salih Yilmaz, MD., Pinar Yalcin Bahat, MD., Gulfem Basol, MD., Seher Sari, MD., Assoc. Prof. Hale Goksever Celik, MD., Cihan Kaya, MD., Aysegul Mut, MD., Humeyra Demirkan, MD., Bahar Yuksel Ozgor, MD., Goknur Topcu, MD., Ezgi Darici, MD., Tolga Karacan, MD.







Prof. Engin Oral, MD., is president-elect of European Endometriosis League (EEL)



The founding president of our Endometriosis & Adenomyosis Society **Prof. Engin Oral, MD.**, has been announced to be the president-elect of the **European Endometriosis League (EEL)** at the board meeting which took place on **November 23rd** at the **4th European Endometriosis Congress**. European Endometriosis Leagues which was founded in 2005 is one of the most important organizations in the field of endometriosis. EEL works to raise awareness on endometriosis and encourages research to enhance our understanding of the disease primarily in Europe, but it is also a well-known all around the world.

We are talking about endometriosis with adolescent girls

In order to raise awareness on endometriosis we are teaching high school girls what endometriosis is.

Our first seminars took place at **American Collegiate Izmir and Izmir Saint-Joseph Highschool**. **Prof. Umit Inceboz, MD.**, taught a total of 300 girls the subject endometriosis and reproductive health. The emphasis was given to the advantages of early diagnosis in endometriosis. The seminars lasted for two weeks and we had positive feedbacks from the students. We are in contact with other high schools. We hope to reach as many students as possible. We would like to thank school administrations for their kind collaboration and the students for their interest in the subject.





40th Vodafone Istanbul Marathon

On November 11, 2018 a team of our members joined 10K and 15K runs at the 40th Vodafone Istanbul Marathon to raise awareness on endometriosis. We encountered a lot of people during the run asking us questions about the disease. We were very pleased with the amount of interest and were happy to be a part of the Istanbul Marathon. We would like to thank our members and volunteers who ran for our society.





TSRM 2018 Reproductive Health and Infertility Congress

On November 8-11, 2018 TSRM Reproductive Health and Infertility Congress took place. On the first day of the congress **Assoc. Prof. Hale Goksever Celik, MD.** gave an oral presentation on 'Current Paradigm on Etiology of Endometriosis'. On the second day one of the board members **Prof. Engin Oral, MD.** gave a presentation on 'Advanced Endometriosis and ART' whose session was chaired by our president **Prof. Yucel Karaman, MD.**



We cycled for endometriosis in Samsun

On November 3rd, 2018 we organized the first bicycle tour 'we are cycling for endometriosis' in **Samsun**. Under **Seher Sari, MD.**'s organization endometriosis patients and volunteers came together to bicycle and raise awareness. We thank everyone who have participated in this event. We are happy to announce that we are planning similar events in other cities as well.



Informative Meeting on Endometriosis and Reproductive Health (Ankara – Antalya – Van – Samsun)



One of our members **Eda Ureyen, MD.**, on Tuesday the 20 of November between 13:45 and 15:30 at Turuncu Café in Kecioren, Ankara and on December 25th at Yukselen College in Serik, Antalya held an informational meeting on the subject 'Reproductive Health and Endometriosis'.



Salih Yilmaz, MD., organized a similar meeting in December at 100. Years University in Van.



Seher Sari, MD., held one of these meetings under the title 'Informative Meeting on Endometriosis' for YEDAS workers in Samsun.

We reached women either suffering from chronic pelvic pain or are already diagnosed with endometriosis. We thank the participants for their interest.

We also would like to thank all our younger members who are working all around the country to raise awareness on endometriosis.

© NEWS FROM THE WORLD OF ENDOMETRIOSIS

Endo Dubai

ENDO DUBAI
2019



This year the 4th symposium will take place in February. You can find the program details under the following link:
<https://endo-dubai.ae/>

D INTERVIEW WITH AN 'ENDO SPECIALIST'

December 11, 2018 – Interview with Mario Malzoni

-Hello Professor Malzoni. I am Isil Ayhan from the Endometriosis & Adenomyosis Society. First of all, I would like to thank you for this opportunity. I am curious to learn since when have you been interested specifically in endometriosis surgery?

-About 20 years ago. I was very young. I had a chance to work at a semi private clinic where my father, who is now 76 years old, was working back then. My father was a gynecological oncology specialist, but he was like a general surgeon and operated on complicated cases. He was a very hard-working physician. I started in 1995 with open surgery. In 1997 I continued my work at the Columbia University with my instructor Harry Reich. He pioneered laparoscopic hysterectomy in 1998 in New York. I started doing endometriosis surgery in 1997-1998 and I opened up an endometriosis center in Italy.

-How many endometriosis operations do you perform in one year?

-We have two centers; one in Avelino and the other one in Rome. Although both of these centers are private the one in Avelino operates as if it were a state clinic. Only in Avelino me and my team, we have laparoscopically operated on almost 1200 cases. 80% of these cases were endometriosis patients. The problem is that all the endometriosis patients not only from Italy but worldwide are referred to our center. We only operate on severe endometriosis cases. Thus, our operations are usually complicated.

-How many of these are deep infiltrative endometriosis patients?

-All of them, because we don't operate on simple endometrioma cases. Almost all of our patients have deep infiltrative endometriosis, except maybe a group of less than 10%. We operate not only on the ovaries. We also deal with intestines, bladder, and the ureters.

-How do you prepare the patients for surgery? Do you ask for consultations from other specialties like general surgery or urology?

-We perform a total intestinal cleaning the day before the surgery. If we are planning a rectal shaving, discoid resection or segmental resection of the intestines, we prepare the patients earlier, so that their intestinal cleaning is already done 24hours before the surgery. We believe that a gynecological surgeon is fit to operate in the pelvic area, because a gynecologist has more experience in the pelvis than a general surgeon. Thus, we operate on patients with intestinal or ureter endometriosis loci without consulting urologist or general surgeons.

-What do you think about robotic surgery? There is a worldwide increase in the interest in robotic surgery. What are the advantages and disadvantages for the surgeon and the patient?

-It took me three years to get used to the idea of robotic surgery. Now I believe that it is very helpful in endometriosis cases. If you have a good team working together every day you can operate faster and the operations can be cost effective. You don't necessarily need robotic surgery.

-Then you prefer laparoscopy?

-Definitely.

-As for my last question; how could we as young gynecologists can improve our surgical skills. What would you recommend?

-Avoid obstetrics.

-Is it possible?!!:)

-Of course, it is! I did it, all the members of my team did. None of the physicians who are working with me do obstetrics. They only perform surgery. They do surgery all they long to become a good surgeon.



E ARTICLES ON ENDOMETRIOSIS FROM OUR COUNTRY FROM THE LAST THREE MONTHS

Usefulness of hematological parameters for differential diagnosis of endometriomas in adolescents/young adults and older women.

Seckin B, Ates MC, Kirbas A, Yesilyurt H.

International Journal of Adolescent Medicine and Health, 0(0), pp,2018(on press)

Abstract

Background Inflammatory processes have been considered to be involved in the pathogenesis of endometriosis. However, the predictive role of inflammatory hematological parameters in endometriosis is not clear. The aim of this study was to analyze the clinical value of hematologic markers in the differential diagnosis of endometriomas in younger and older reproductive age women. Materials and methods A retrospective chart review was done for 502 patients who underwent surgery: 267 with endometriomas (endometrioma group) and 235 with other benign adnexal cysts (control group). Patients were placed into subgroups as younger (adolescents/young adults, aged <25 years) and older (aged ≥25 years) women. Total and differential white blood cell count, neutrophil-to-lymphocyte ratio, platelet indices and platelet-to-lymphocyte ratio (PLR) were evaluated with receiver operating characteristic curve analysis for differential diagnosis of endometriomas. Results The mean serum levels of PLR, plateletcrit (PCT), platelet count and CA-125 (reference range below 35 IU/mL) were significantly higher in the endometrioma group ($p < 0.001$). The area under the curve (AUC) for CA-125 was 0.85 [95% confidence interval (CI), 0.82-0.88] ($p < 0.001$) for the entire group. However, platelet count, PLR, and PCT showed poor discriminative ability for detecting endometriomas with AUC values of 0.59 (95% CI, 0.55-0.65, $p < 0.001$), 0.58 (95% CI, 0.53-0.63, $p = 0.002$) and 0.61 (95% CI, 0.56-0.66, $p < 0.001$), respectively. In age-stratified analysis, these platelet indices had also low diagnostic performance in both age groups. Conclusions Hematologic markers do not adequately differentiate ovarian endometriomas from other benign cysts in neither adolescents/young adults nor older women.

KEYWORDS:

adolescents; endometrioma; lymphocyte; neutrophil; platelet

The levonorgestrel-releasing intrauterine system is associated with a reduction in dysmenorrhoea and dyspareunia, a decrease in CA 125 levels, and an increase in quality of life in women with suspected endometriosis.

Yucel N, Baskent E, Karamustafaoglu Balci B, Goynumer G.

Aust N Z J Obstet Gynaecol, 58: 560-563,2018

Abstract

BACKGROUND AND AIMS:

The aim of this study was to investigate the effectiveness of a levonorgestrel-releasing intrauterine device (LNG-IUS) in the symptomatic relief of pain in women with endometriosis and additionally, to assess the changes in women's life quality and serum cancer antigen (CA) 125 levels.

MATERIALS AND METHODS:

All women who had an LNG-IUS inserted for the treatment of dysmenorrhea, chronic pelvic pain or both for more than six months over a two-year period were included in the study. Each woman was asked to complete questionnaires of the Short Form-36 and visual analogue scales (VAS) in the first visit and the third, sixth, ninth and twelfth months after the LNG-IUS insertion. CA 125 levels were measured at each visit.

RESULTS:

Forty-five women were included in the study. At the end of 12 months, mean dysmenorrhoea VAS score decreased from 6.13 to 2.88, mean dyspareunia VAS score from 6.04 to 2.61 and CA 125 level from 50.67 to 22.45. Endometriomas reduced in size in six women (mean size decreased from 31 to 20 mm) and disappeared in three.

CONCLUSIONS:

Several favourable outcomes were found following LNG-IUS insertion: (i) dyspareunia and dysmenorrhoea were clearly reduced; (ii) the size of endometriomas were decreased; (iii) CA 125 levels significantly decreased; (iv) a few women experienced the typical systemic adverse effects of progestogens; however, LNG-IUS-related adverse events were generally tolerable and the discontinuation rate was as low as 6.66% (3/45).

HOXA-10 gene expression in ectopic and eutopic endometrium tissues: Does it differ between fertile and infertile women with endometriosis?

Özcan C, Özdamar Ö, Gökbayrak ME, Doğer E, Çakırođlu Y, Çine N.

European Journal of Obstetrics and Gynecology and Reproductive Biology , 233 , 43 – 48,2018

Abstract

OBJECTIVE:

To compare HOXA-10 gene expression in eutopic endometrium samples, between fertile and infertile endometriosis patients and the fertile control cases, and in endometrium and endometrioma specimens, between severe and moderate endometriosis cases.

STUDY DESIGN:

Prospective clinical study included women without infertility and endometriosis (Group 1); women without infertility but with endometrioma (Group 2); and infertile women with endometrioma (Group 3). In addition, the Group 2 and 3 cohort were assessed based on the findings obtained during laparoscopy, based on the (rAFS) scoring, as women with a rAFS score of 16-40 were evaluated in Group A, whereas those with rAFS score above 40 were considered in Group B. HOXA-10 gene expression was evaluated in both secretory endometrium tissue and endometrioma specimens.

RESULTS:

Eutopic endometrium samples from group 2 (reference gene = 0,680 vs. target gene = 0,362) and group 3 (reference gene = 0,641 vs. target gene = 0,183) patients revealed a 1,871-fold and 3,509-fold decrease in HOXA-10 gene expression, respectively, as compared to group 1. Endometrial HOXA-10 gene expression was 1,778-fold down-regulated in group 3 women (reference gene = 1,510 vs. target gene = 0,850), when compared to group 2. Both eutopic endometrium and endometrioma tissue samples from severe endometriosis patients revealed 1,259-fold (reference gene = 1,523 vs. target gene = 1,210) and 1,338-fold (reference gene = 1,274 vs. target gene = 0,952), down-regulation in HOXA-10 gene expressions, respectively, as compared to moderate cases.

CONCLUSION:

Endometrial HOXA-10 gene expression in women with endometriosis is significantly down-regulated than in those without endometriosis. Endometriosis patients with infertility have significantly lower levels of endometrial HOXA-10 gene expression than endometriosis without infertility; thus decreased expression of this gene may, directly or indirectly, be related with the endometriosis-associated infertility. Severe endometriosis cases express, in their both endometrium and endometrioma tissues, significantly lower levels of HOXA-10 gene than moderate endometriosis cases.

The prognostic significance of stage I ovarian clear cell and endometrioid carcinomas arising from endometriotic cysts: is it a myth?

Ayhan A., Akilli H., Haberal N.

Archives of gynecology and obstetrics, 1-6,2018

Abstract

PURPOSE:

The aim of this study was to determine the clinicopathologic features and the prognostic significance of Stage I ovarian clear cell and endometrioid carcinomas arising from endometriotic cysts.

MATERIALS AND METHODS:

Patients with either Stage I ovarian clear cell or endometrioid carcinoma were divided into three groups. *Group 1: Patients with cancers arising from endometriotic cysts *Group 2: Patients with ovarian and pelvic endometriosis *Group 3: Patients without endometriosis Patient characteristics (overall survival and disease-free survival) were compared between groups.

RESULTS:

Of the 78 patients who participated in this study, 39 were in group 1, 13 were in group 2, and 26 were in group 3. The mean age in groups 1, 2, and 3 were 46 years, 54 years, and 48 years, respectively ($p = 0.39$). Tumoral characteristics, including capsule rupture, positive cytology, grade, and the presence of synchronous endometrial cancer were similar in both groups. The 5-year overall survival rate in groups 1, 2, and 3 were 100, 90, and 93%, respectively ($p = 0.4$). Moreover, the recurrence rates did not differ significantly between groups. Furthermore, subgroup analysis of clear cell carcinoma and endometrioid adenocarcinoma separately showed no effect of endometriosis on disease-free survival (DFS) or overall survival (OS).

CONCLUSION:

Clear cell or endometrioid ovarian carcinoma arising from ovarian and/or pelvic endometriosis shares the same clinicopathologic characteristics with their counterparts that do not arise from endometriosis and patients have similar overall and disease-free survival.

KEYWORDS:

Endometriotic cyst; Gynecologic oncology; Prognosis; Stage I EOC

Caecal Appendiceal Intussusception Caused by Endometriosis: A Case Presentation of Laparoscopic Management

Gokhan Posteki, Alican Guresin, Sertac Ata Guler, Kilic Ersin, Turgay Simsek, Nihat Zafer Utkan

Turkish Journal of Colorectal Disease, 28(1), 34-37,2018

Abstract:

Appendiceal Intussusception can present itself as the invagination of only the appendix or affect the colon as a whole. It is very rare and can

be caused by foreign objects, lenfoid hyperplasia, polypoid lesions, neoplasia or endometriosis. Endometriosis very rarely leads to appendiceal intussusception. Patients usually present with acute appendicitis like symptoms. In this case an explorative laparoscopic surgery was done on a patient with a prediagnosis of acute appendicitis. Appendiceal intussusception was detected during laparoscopy and surgical treatment was performed.

Key words: Acute appendicitis, appendix, intussusception, endometriosis.

Colon resection for endometriosis.

Erol T, Reis E, Koç Ö, Taşbaş B.

Turkish journal of surgery, 1-3.2018

Abstract:

Endometriosis affects women during the reproductive period and can cause functional disorders. Sometimes general surgical intervention is

necessary owing to disease boundary. The sigmoid colon and rectum are particularly affected because of their close relationship. In this case, treatment must be individualized according to the patient and symptoms. If the lesion penetrated the entire bowel wall, bowel

F ENDOMETRIOSIS AND OTHER SPECIALTIES



Prof. Huseyin Nazlikul, MD.

Prof. Huseyin Nazlikul, MD. has a specialty in Neuraltherapy and Complementary Medicine. Since 2004 he is the president and founding member of the Complementary Medicine and Regulation Society and Neuraltherapy and Regulation Society. He is the second president of Manuel Medicine Society and the honorary president of Acupuncture and Regulation Society. He is the scientific board member of IGNH (International Gesellschaft fuer Neuraltherapie nach Huneke = Huneke International Neuraltherapy Society), extended board member of ZAEN, a faculty member of the German Pain Research and Therapy Society and European Anti-aging Society.

WHAT IS NEURALTHERAPY NEURALTHERAPY IN TREATMENT OF ENDOMETRIOSIS

Neuraltherapy is a regulatory treatment done with low doses of local anesthetics (procaine and lidocaine).

Neuraltherapy activates and regulates the electrical web of our body which is the vegetative (autonomous) nervous system (ANS). The local injections performed to special points on the body regulate 3 circulatory systems: blood circulation, lymphatic fluid circulation and nerve transmission. When blood circulation (perfusion) of a tissue increases the tissue is nourished. When lymphatic circulation is activated the tissue is drained from its metabolites and thus cleansed. An increase in nervous transmission enhances tissue regulation. Thus, a well-nourished, cleansed and well-regulated tissue has an increased capacity to heal itself.

The key point for the regulation and pain treatment is the balance between the afferent and efferent answer of the sympathetic nervous system (SNS). Sympathetic nervous system is responsible for the neurogenic inflammation and pain response (nociception) of our body. ANS and SNS both mediate the release of pain mediators, the transmission of pain response, the formation of the reflex arc as an answer to pain and the initiation of the inflammatory response. Pain cannot be perceived without the sympathetic nervous system. In order to treat pain and inflammation a thorough understanding of the organs' sympathetic, spinal and parasympathetic innervation is important.

When evaluated from the perspective of neuraltherapy and regulatory medicine endometriosis is a disease of chronic inflammation! With a neuraltherapeutic approach the treatment of inflammation is possible!

A multidisciplinary approach is required for the management of endometriosis.

Neuraltherapy plays an important role in management of pain and regulation of the overall wellbeing of the patient. It also increases the tissue perfusion and by down regulating inflammatory process eliminates pain. During pain management a wholesome and regulatory approach with neuraltherapy and a multidisciplinary treatment improves patient's overall life quality.

Understanding inflammation from a neuraltherapist' perspective and a solution is possible.

Neurogenic inflammation is the common problem of endometriosis and other chronic diseases. Inflammation underlies endometriosis.

Neurogenic inflammation is a physiologic process which is caused by the proinflammatory mediators released from cutaneous nerve endings. Although neurogenic inflammation and immunologic inflammation occur at the same time they are clinically different. Neurogenic inflammation is associated with nervous system and inflammatory reactions.

By the above-mentioned mechanism, locally produced sensory stimulus is transmitted to the central nervous system through efferent nerves which in return triggers an inflammatory reaction.

According to multiple chemical sensitivity syndromes' lock and key theory when respiratory system detects chemical irritants inflammatory responses are activated at several secondary organ systems. Similar to this a neuronal pathway is also a possible explanation.

Proinflammatory cytokines released by peripheral immune cells (ECM: Extracellular Matrix, first step of VNS) are critical signals of communication with CNS. Following this initial signal, a communication starts between immune system and nervous system. Information reaches CNS through humoral and neural pathways and this in return induces a neuronal cascade of proinflammatory cytokine production. These newly produced cytokines play key roles in the peripheral inflammatory processes.

Central nervous system is an advanced web which covers all of the human body and connects all cells and organs and it transmits each good or bad stimulus to every part of the body. The main function of the neurovegetative system is to connect humoral, cellular, neural and hormonal regulatory mechanisms and to involve these mechanisms in the systematic reaction. Thus, a failure in one of these mechanisms would result in a general disfunction of the system. A disease would not affect just one organ but would affect the whole body. Local anesthetic injection at the distressed tissue does not only regulate the neurovegetative system but it also affects and regulates other mechanisms as well. Once the electrical transmission in nerves and tissues is restored the associated physical functions are regulated and the patient returns to his healthy state.

In addition, especially with functional diseases (such as endometriosis) and pain response to neuraltherapy is fast and the therapy is very effective. For this reason, neuraltherapy is useful at any clinical situation or at pain clinics for diagnosis and treatment. Recent research in neuraltherapy on patients with chronic pain has successfully explained the long-term effects of the therapy by pathophysiology of pain. Peripheral and central sensitization fields point out the possibility of disruption of neuroplasticity and vicious circle with the use of local anesthetics. When regarded from this perspective neuraltherapy causes a desensitization of pathologic pain in patients with chronic pain.

Neuraltherapy relies on the regulatory and plasticity mechanism of the nervous system: Direct stimulus (with needle) and at the same time selective inhibition of the stimulus (with local anesthetics) affects organization and perfusion of the nervous system. Thus, vicious circle caused by pain is disrupted and regulated.

Chronic pelvic pain experienced by patients with endometriosis can be treated via these mechanisms. When the patients are evaluated with visual analog scale, an improvement in their pain assessment can be observed.

Similar to dysmenorrhea, pain symptoms such as dysuria, dyschezia, dyspareunia seen in patients with stage 1-2 endometriosis can be treated in a couple of sessions. At the same time the inflammation process of endometriosis can be regulated and so the progression can be inhibited. In addition, owing to the effects of neuraltherapy on the serotonin and dopamine levels in the central nervous system, patients also benefit from the positive effects on their psychological status.

Neuraltherapy as an addition to our primary treatment increases patient's well-being and helps to relieve of many adverse symptoms. Thus, it is an effective complementary therapy in endometriosis patients.

Best regards

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Article Full texts uploaded by **Prof. Banu Kumbak Aygun, MD**.

<http://www.endometriosisderneği.org/en/library/article-summaries>



OUR WEBSITES

Our websites have been renovated. You can reach all the webpages through the following link.

Endometriosis&Adenomyosis Society

Website

(www.endometriosis.org)



Endometriosis ve Adenomyozis Derneği

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