1 in 10 Women are Affected by Endometriosis

www.endometriozis.org
HELLO

We are with you again with our 11th issue. In this issue as in the previous issues, you will find newly published articles, you will get a chance to observe point of views of several physicians from different specialties and you will find news from the world of endometriosis.

Our society has initiated a new project with Institute of Loans and Accommodations. Starting next month, we are going to visit student dormitories around Turkey and give seminars on 'Menstrual Wellbeing and Related Disorders'. Our board members, and other physicians who are members of our society will be volunteering in this project. We are very excited and honored to lead such an extensive social project nationwide.

We are very happy to announce that our book, 'Living with Endometriosis' which we have been preparing over the last year, is now published and on sale online. With this book we aim to support and increase the life standards of the endometriosis patients. A multidisciplinary team of writers came together in the creation this book, which we hope you will enjoy reading.

Turkish Philanthropy Funds has agreed to support our social projects. We are very honored to work with them. We are continuously strengthening our international relations both on academic and social platforms.

We would like to invite our colleagues to 2nd International Endometriosis School Istanbul which will take place on December 16-17, 2019. Engin Oral and Ertan Saridogan will be course directors. In addition to many international experts such as Joerg Keckstein, Mario Malzoni, Alessandra Di Giovanni and Natasha Curran, many Turkish specialists will be attending this meeting as well. Alessandra Di Giovanni will demonstrate live ultrasonographic examination on an endometriosis patient and Mario Malzoni will perform live laparoscopic endometriosis surgery.

11th EndoAcademy Meeting took place on October 20, 2019 at Kartal Dr. Lutfi Kirdar Research and Training Hospital’s conference hall in Istanbul. Endometriosis and chronic pelvic pain was discussed thoroughly. Gernot Hudelist joined this meeting from Austria with two talks and performed a live surgery. The meeting was broadcasted live through our social media accounts.

Our society’s founding president Engin Oral has chaired European Endometriosis League’s Session at the 8th Asian Conference on Endometriosis and he gave a talk on 'Management of Endometriosis in Patients Older Than 40'. One of our advisory committee members Kutay Biberoglu had a talk on 'Pelvic Pain Associated with Endometriosis – Progestins or Combined Contraceptive Pills’ and also chaired the session on medical treatment in endometriosis.

We are continuing our interviews with our international colleagues who are specialized in endometriosis. For this issue we have interviewed Caterina Exacoustos, who is world-renowned in endometriosis and ultrasonography. You can read a summary of the interview in this bulletin and watch the video on our website.

In this bulletin, in addition to the selected articles you can also read about articles written by Turkish authors on endometriosis in the past three months.

We hope to be with you in our next bulletin with more news and new developments in the field of endometriosis.

Best regards,

Turkish Endometriosis & Adenomyosis Society
Endometriosis Bulletin  October 2019 / Issue XI

Founding President Prof. Engin Oral, MD

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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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www.endometriosisturkey.com
POSSIBLE ROLE OF THE POSTERIOR COMPARTMENT PERITONECTOMY, AS A PART OF THE COMPLEX SURGERY, REGARDING RECURRENCE RATE, IMPROVEMENT OF SYMPTOMS AND FERTILITY RATE IN PATIENTS WITH ENDOMETRIOSIS, LONG TERM FOLLOW-UP.


Abstract

STUDY OBJECTIVE:

Beside the pain, there are 2 further problems in the management of endometriosis: the high recurrence rate (10% per year) and the high rate of impaired fertility. The objective of this study was to investigate the pathogenesis of these 2 factors.

DESIGN:

This is a retrospective cohort study, and the aim is to evaluate the complete excision of endometriotic lesions, including the posterior compartment of the peritoneum, with regard to postoperative outcome, focusing on relieving pain, increasing fertility rate, and decreasing recurrence rate.

SETTING:

Charité-University Clinic, Department of Gynaecology, Endometriosis research Centre.

PATIENTS:

Fifty-four patients were enrolled in this study, with severe deep infiltrating endometriosis (scored by ENZIAN) and superficial endometriosis, as well as endometriomas (revised American Society for Reproductive Medicine [rASRM] I = 3; II = 15; III = 10; and IV = 26).

INTERVENTIONS:

Posterior compartment peritonectomy (visible endometriotic lesions and inflamed altered peritoneum) was performed in all patients as part of a complex surgery: complete excision of endometriosis.

MEASUREMENTS AND MAIN RESULTS:

Postoperative outcomes were evaluated, based on the postoperative follow-up (up to 5 years) of 54 investigated patients. In 36 women (66%) preoperative complaints were eliminated. Furthermore, of 28 women seeking improved fertility, pregnancy was reported in 13 cases (46%). In 7 (54%) cases pregnancy occurred spontaneously, and in the remainder with assisted fertilization. In addition, long-term follow-up demonstrated a recurrence rate in 1.8% of patients.

CONCLUSION:

Overall, the number of complaints was significantly reduced. Only in the case of reproductive-aged women with ongoing postoperative complaints was it important to preserve the uterus. Although this pilot study on systematic posterior peritonectomy showed improvement in recurrence and fertility rate, the main question remains: will this surgical technique achieve better results and outcomes in the future? This has to be addressed in a prospective randomized study.

KEYWORDS:

Endometriosis; Infertility; Laparoscopy; Long-term follow-up; Pelvic pain; Peritomectomy; Peritoneum; Posterior compartment peritoneum; Recurrence rate
THE ASSOCIATION BETWEEN ENDOMETRIOSIS AND AUTOIMMUNE DISEASES: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Shigesi, N., Kvasnica, M., Kirtley, S., Feng, Q., Fang, H., Knight, J. C., ... & Becker, C. M. Human reproduction update, 25(4), 486-503.2019

Abstract

BACKGROUND: Endometriosis is a chronic gynaecological disorder that affects 2-10% of women of reproductive age. The aetiology of endometriosis is largely under-explored, yet abnormalities in the immune system have been suggested to explain the origin of ectopic endometrial tissues, and an association between endometriosis and autoimmune diseases has been proposed. Evaluation of current evidence investigating the association between endometriosis and autoimmune diseases from population-based studies will facilitate our understanding of the causes and consequences of endometriosis and provide a reference for better healthcare practices population-wide.

OBJECTIVE AND RATIONALE: The aim of this study was to systematically review the literature on population-based studies investigating an association between endometriosis and autoimmune diseases and to conduct a meta-analysis of combinable results to investigate the extent and robustness of evidence.

SEARCH METHODS: Four electronic databases were searched (MEDLINE, Embase, Web of Science, and CINAHL) from each database inception date until 7 April 2018. Search terms included a combination of database-specific controlled vocabulary terms and free-text terms relating to ‘endometriosis’ and ‘autoimmune diseases’. Study inclusion criteria focused on peer-reviewed published articles that reported an association between endometriosis and autoimmune diseases, excluding case reports/series, review papers, meta-analyses, organizational guidelines, editorial letters, expert opinions, and conference abstracts. Quality assessment of included studies was performed based on GRADE criteria. Key information of eligible studies was abstracted into a standard form. Meta-analysis was performed for autoimmune diseases with combinable study results from at least three studies investigating an association with endometriosis. For cross-sectional studies and case-control studies, raw data from each study were documented to calculate a Mantel-Haenszel odds ratio with 95% CIs. For cohort studies, an inverse variance probability weighted model was used to pool study results to calculate a rate ratio (a hazard ratio or a standardized incidence rate) with 95% CIs.

OUTCOMES: A total of 26 published population-based cross-sectional, case-control, and cohort studies that investigated the association between endometriosis and autoimmune diseases met all eligible criteria and were included in the review. The studies quantified an association between endometriosis and several autoimmune diseases, including systemic lupus erythematosus (SLE), Sjögren's syndrome (SS), rheumatoid arthritis (RA), autoimmune thyroid disorder, coeliac disease (CLD), multiple sclerosis (MS), inflammatory bowel disease (IBD), and Addison's disease. However, the quality of the evidence was generally poor due to the high risk of bias in the majority of the chosen study designs and statistical analyses. Only 5 of the 26 studies could provide high-quality evidence, and among these, 4 supported a statistically significant association between endometriosis and at least 1 autoimmune disease: SLE, SS, RA, CLD, MS, or IBD.

WIDER IMPLICATIONS: The observed associations between endometriosis and autoimmune diseases suggest that clinicians need to be aware of the potential coexistence of endometriosis and autoimmune diseases when either is diagnosed. Scientists interested in research studies on endometriosis or autoimmune diseases should consider the likelihood of comorbidity when studying these two types of health conditions. Well-designed large prospective cohort studies with confounding control and mediation quantification, as well as genetic and biological studies, are needed to generate further insights into whether endometriosis is a risk factor for, or a consequence of, autoimmune diseases, and whether these two types of disorders share pathophysiological mechanisms even if they arise independently. Such insights may offer opportunities for the development of novel non-hormonal medications such as immuno-modulators or repurposing of existing immunomodulatory therapies for endometriosis.

KEYWORDS: Sjögren's syndrome; autoimmune diseases; celiac disease; endometriosis; inflammatory bowel disease; multiple sclerosis; population study; rheumatoid arthritis; systemic lupus erythematosus; thyroid disorder
ENDOMETRIOSIS AND THE MICROBIOME: A SYSTEMATIC REVIEW.

Abstract
Background
The aetiology and pathogenesis of endometriosis are still under investigation. There is evidence that there is a complex bidirectional interaction between endometriosis and the microbiome.

Objective
To systematically review the available literature on the endometriosis–microbiome interaction, with the aim of guiding future inquiries in this emerging area of endometriosis research.

Search strategy
MEDLINE, Embase, Scopus and Web of Science were searched through May 2019. A manual search of reference lists of relevant studies was also performed.

Selection criteria
Published and unpublished literature in any language describing a comparison of the microbiome state in mammalian hosts with and without endometriosis.

Data collection and analysis
Identified studies were screened and assessed independently by two authors. Data were extracted and compiled in a qualitative synthesis of the evidence.

Main results
Endometriosis appears to be associated with an increased presence of Proteobacteria, Enterobacteriaceae, Streptococcus spp. and Escherichia coli across various microbiome sites. The phylum Firmicutes and the genus Gardnerella also appear to have an association; however, this remains unclear.

Conclusions
The complex bidirectional relationship between the microbiome and endometriosis has begun to be characterized by the studies highlighted in this systematic review. Laboratory and clinical studies demonstrate that there are indeed differences in the microbiome composition of hosts with and without endometriosis.
Abstract

STUDY QUESTION:
Can plasma miRNAs be used for the non-invasive diagnosis of endometriosis in infertile women?

SUMMARY ANSWER:
miRNA-based diagnostic models for endometriosis failed the test of independent validation.

WHAT IS KNOWN ALREADY:
Circulating miRNAs have been described to be differentially expressed in patients with endometriosis compared with women without endometriosis, suggesting that they could be used for the non-invasive diagnosis of endometriosis. However, these studies have shown limited consistency or conflicting results, and no miRNA-based diagnostic test has been validated in an independent patient cohort.

STUDY DESIGN, SIZE, DURATION:
We performed genome-wide miRNA expression profiling by small RNA sequencing to identify a set of plasma miRNAs with discriminative potential between patients with and without endometriosis. Expression of this set of miRNAs was confirmed by RT-qPCR. Diagnostic models were built using multivariate logistic regression with stepwise feature selection. In a final step, the models were tested for validation in an independent patient cohort.

PARTICIPANTS/MATERIALS, SETTINGS, METHODS:
Plasma of all patients was available in the biobank of the Leuven Endometriosis Centre of Excellence. Biomarker discovery and model development were performed in a discovery cohort of 120 patients (controls = 38, endometriosis = 82), and models were tested for validation in an independent cohort of 90 patients (controls = 30, endometriosis = 60). RNA was extracted with the miR Neasy Plasma Kit. Genome-wide miRNA expression analysis was done by small RNA sequencing using the NEB Next small RNA library prep kit and the NextSeq 500 System. cDNA synthesis and qPCR were performed using the Qiagen miScript technology.

MAIN RESULTS AND THE ROLE OF CHANCE:
We identified a set of 42 miRNAs with discriminative power between patients with and without endometriosis based on genome-wide miRNA expression profiling. Expression of 41 miRNAs was confirmed by RT-qPCR, and 3 diagnostic models were built. Only the model for minimal-mild endometriosis (Model 2: hsa-miR-125b-5p, hsa-miR-28-5p and hsa-miR-29a-3p) had diagnostic power above chance performance in the independent validation (AUC = 60%) with an acceptable sensitivity (78%) but poor specificity (37%).

LIMITATIONS, REASONS FOR CAUTION:
The diagnostic models were built and tested for validation in two patient cohorts from a single tertiary endometriosis centre. Further validation tests in large cohorts with patients from multiple endometriosis centres are needed.

WIDER IMPLICATION OF THE FINDINGS:
Our study supports a possible biological link between certain miRNAs and endometriosis, but the potential of these miRNAs as clinically useful biomarkers is questionable in women with infertility. Large studies in well-described patient cohorts, with rigorous methodology for miRNA expression analysis, sufficient statistical power and an independent validation step, are necessary to answer the question of whether miRNAs can be used as diagnostics markers for endometriosis.

STUDY FUNDING/COMPETING INTEREST(S):
The project was funded by a grant from the Research Foundation - Flanders (FWO). A.V., D.F.O. and D.P. are PhD fellows from the FWO. T.D. is vice president and Head of Global Medical Affairs Fertility, Research and Development, Merck KGaA, Darmstadt, Germany. He is also a professor in Reproductive Medicine and Biology at the Department of Development and Regeneration, Group Biomedical Sciences, KU Leuven (University of Leuven), Belgium and an adjunct professor at the Department of Obstetrics and Gynecology in the University of Yale, New Haven, USA. Neither his corporate role nor his academic roles represent a conflict of interest with respect to the work done by him for this study. The other co-authors have no conflict of interest.

KEYWORDS:
diagnosis; endometriosis; miRNA; non-coding RNA; plasma
Abstract

PURPOSE OF REVIEW: Postmenopausal endometriosis is a gynecologic disease, affecting 2-5% of postmenopausal women. Current literature assessing the prevalence, pathogenesis, and treatment of this uncommon condition is limited, stressing the necessity for future research. This review examines the current literature on postmenopausal endometriosis to help inform clinical decision-making and point to novel approaches for treatment and management.

RECENT FINDINGS: Although one unifying theory to explain the pathogenesis of endometriotic lesions has not been elucidated, estrogen dependence is central to the pathophysiological process. The total quantity of estrogen production is mediated by multiple enzymes in complex pathways. Recent studies have confirmed the presence of these necessary enzymes in endometriotic lesions thereby suggesting a local source of estrogen and a likely pathogenic contributor. More research is needed to fully elucidate the mechanism of local estrogen biosynthesis; however, the current data provide possible explanations for the presence of postmenopausal endometriosis in an otherwise systemically hypoestrogenic environment.

SUMMARY: All suspected endometriosis lesions should be surgically excised for optimization of treatment and prevention of malignant transformation. If hormone replacement therapy is initiated, combined estrogen and progestin is recommended, even in the setting of previous hysterectomy, given the risk of disease reactivation and malignant transformation of endometriotic lesions. Further research is needed to understand the true prevalence, cause, and progression in this patient demographic. Histologic studies evaluating tissue lesions and peritoneal fluid for estrogen receptors, estrogen metabolizing enzymes, immune cells, and nerve fibers will aide in clinical management and treatment planning.
NEWS FROM OUR SOCIETY

PAST ACTIVITIES

PROJECT WITH INSTITUTE OF LOANS AND ACCOMMODATIONS

Next month we are going to start giving seminars on ‘Menstrual Wellbeing and Related Disorders’ to the girls living at the dormitories of Institute of Loans and Accommodations. Our board members, and other physicians who are members of our society will be volunteering in this project. We are very excited and honored to lead such an extensive nationwide social project.

OUR BOOK ‘LIVING WITH ENDOMETRIOSIS’ IS ON SALE

We are very happy to announce that our book, ‘Living with Endometriosis’ which we have been preparing over the last year, is now published and on sale online. With this book we aim to support and increase the life standards of our endometriosis patients. We also hope that this book will be a useful tool for our colleagues who are interested in endometriosis. A multidisciplinary team of writers came together in the preparation process. We hope you will enjoy reading this book and recommend it to your patients.

You can use the links below to buy your copy.
SECTION 1

Introduction to Endometriosis and Current Treatments
Pinar Yalcin Bahat, MD, Prof. Engin Oral, MD
Medical Treatment: Prof. Umit Inceboz, MD

SECTION 2

Sexual Health: Cem Kece, MD
Nutrition: Pinar Yalcin Bahat, MD – Nilufer Akgun, MD
Exercise: Sibel Caglar Okur, MD
Psychiatry: Assoc. Prof. Cagri Poyraz, MD
Self-awareness: Zeynep Selvili Carmikli
Yoga and Meditation: Banu Cadirci (Yoga Therapist)

SECTION 3

Neural Therapy: Pinar Yalcin, MD – Prof. Huseyin Nazlikul, MD
Homeopathy: Levent Buda, MD
Acupuncture: Demet Erdogan, MD
Phytotherapy: Esra Arikar Beyaz, MD
Manuel Therapy: Sinel Caglar Okur, MD
Aromatherapy: Hulya Kayhan, DPharm
Ozone Therapy: Ruhi Cakir, MD
Music Therapy: Sebla Akbulut (Harp Therapist)
We are honored to announce that Turkish Philanthropy Funds has promised to support our projects. We would like to thank them for their support.

Since 2007 Turkish Philanthropy Funds has been funding more than 200 projects focused on addressing economic, social and environmental needs in Turkey and around the world. Use the link below for more information.

https://donate.tpfund.org/campaign/turkish-endometriosis-and-adenomyosis-society/c242884

8TH ASIAN CONFERENCE ON ENDOMETRIOSIS

Our society’s founding president Engin Oral has chaired European Endometriosis League’s session at the 8th Asian Conference on Endometriosis and he gave a talk on ‘Management of Endometriosis in Patients Older Than 40’. One of our advisory committee members Kutay Biberoglu had a talk on ‘Pelvic Pain Associated with Endometriosis – Progestins or Combined Contraceptive Pills’ and also chaired the session on medical treatment in endometriosis.
Engin Oral and Taner Usta participated in the ESHRE Campus ‘Deep Endometriosis’ Workshop, which took place in Muenster Germany.

We would like to invite our colleagues to 2nd International Endometriosis School Istanbul which will take place on December 16-17, 2019. Many international specialists will be joining us in this informative meeting. Alessandra Di Giovanni will demonstrate live ultrasonographic examination on an endometriosis patient and Mario Malzoni will perform live laparoscopic endometriosis surgery. We will be happy to see our colleagues at this meeting where they will get a chance to experience both a theoretical and a practical approach. For registration please contact: endo@globalturizm.com.tr
2nd International Endometriosis School
Istanbul
December 16 - 17, 2019
Medtronic Innovation Center, Istanbul - Turkey

Course Directors: Engin Oral, Ertan Sarıdoğan
Course Coordinators: Taner Usta, Ercan Baştu

www.endometriozis.org/endometriozisokulu2
www.endometriosisturkey.com/endometriosisschool2
2nd International Endometriosis School
Istanbul
December 16 - 17, 2019, Medtronic Innovation Center, Istanbul - Turkey
Course Directors: Engin Oral, Ertan Saridoğan
Course Coordinators: Taner Usta, Ercan Baştu

Day I (December 16, Monday)

08:00 - 08:20  Registration
08:20 - 08:30  Opening: The aim and objectives of the International Endometriosis School
Preschool Evaluation of The Participants (Keypad)
Ertan Saridoğan (UK)

Session I
Chairs: Yücel Karaman (Turkey), Banu Kumbak Aygün (Turkey)
08:30 - 09:00  Diagnosis, classification and staging of peritoneal disease, endometrioma and deep infiltrating endometriosis
Joerg Keckstein (Austria)
09:00 - 09:30  Imaging in endometriosis and adenomyosis
Alessandra Di Giovanni (Italy)
09:30 - 10:00  Endometriosis and infertility: reproductive outcomes
Hakan Yarali (Turkey)
10:00 - 10:30  Current approach to management of adenomyosis
Joerg Keckstein (Austria)
10:30 - 10:50  Discussion
10:50 - 11:10  Coffee Break

Session II
Chairs: Ümit Inceboz (Turkey), Hale Göksever Çelik (Turkey)
11:10 - 11:40  Medical treatment options for patients with endometriosis
Ercan Baştu (Turkey)
11:40 - 12:10  Pain management in endometriosis
Natasha Curran (UK) to be transmitted live from London, UK
12:10 - 12:40  Management of endometriosis at the extremes of reproductive years
Engin Oral (Turkey)
12:40 - 12:50  Discussion
12:50 - 15:30  Live Transmission Session From Acibadem University Altunizade Hospital
(This session consists of 2 parts; First: Ultrasonografic Live case demonstrations,
Second: Live surgery transmission)
Chair: Ercan Baştu (Turkey)
Live Ultrasonografic Demonstration of Endometriosis Cases
Expert Sonographer: Alessandra Di Giovanni (Italy)
Live Surgery
Surgeon: Mario Malzoni (Italy)

Session III
Chairs: Fatih Şendağ (Turkey), Onur Topçu (Turkey)
15:30 - 16:00  Surgical techniques for endometriomas
Bülent Urman (Turkey)
16:00 - 16:30  Deep endometriosis: the road map
Taner Usta (Turkey)
16:30 - 17:00  How can we prevent complications during endometriosis surgery: tips and tricks
Mario Malzoni (Italy)
17:00 - 17:30  Management of recurrent endometriosis after surgical treatment
Ertan Saridoğan (UK)
17:30 - 17:50  Discussion
2nd International Endometriosis School
Istanbul
December 16 - 17, 2019, Medtronic Innovation Center, Istanbul - Turkey
Course Directors: Engin Oral, Ertan Saridoğan
Course Coordinators: Taner Usta, Ercan Baştu

Day II (December 17, Tuesday)

Session IV
Guidelines, Bowel Endometriosis and Complications
Chairs: Hulusi Zeyneloğlu (Turkey), Bülent Berker (Turkey)
08:30 - 08:50 Useful anatomy for pelvic laparoscopic surgery
Ahmet Kale (Turkey)
08:50 - 09:20 Bowel endometriosis: indication and surgical techniques
Bilgi Baca (Turkey)
09:20 - 09:50 Current guidelines on endometriosis
Ertan Saridoğan (UK)
09:50 - 10:00 Discussion

Hands On Training
Coordinator: Taner Usta (Turkey)
Trainers: Ahmet Kale (Turkey), Banş Mülayım (Turkey), Cem Demirel (Turkey), Çağatay Taşkıran (Turkey), Onur Topçu (Turkey)
10:00 - 10:30 Pig model for laparoscopy - Evaluation
10:30 - 12:30 Training on live animal tissue
Practice of different energy types in live animal model
Bladder injury and repair
Dissection of the ureters and major pelvic vessels
12:30 - 13:10 Lunch
13:10 - 16:00 Training on live animal tissue
Ureteric injury and reanastomosis
Bowel injury and repair
Hysterectomy
16:00 - 16:20 Coffee Break
16:20 - 17:20 Wrap-up
Ertan Saridoğan (UK), Engin Oral (Turkey), Taner Usta (Turkey), Ercan Baştu (Turkey)
End of the course - Delivery of Certificates of Attendance
17:20 - 17:30 Postschool evaluation of the course by the participants (Keypad)
11th EndoAcademy Meeting took place on October 20, 2019 at Kartal Dr. Lutfi Kirdar Research and Training Hospital in Istanbul. Up-to-date information on endometriosis has been shared and discussed with the participants.
NEWS FROM THE WORLD OF ENDOMETRIOSIS

EEL

5th European Congress on Endometriosis will take place in Prague this year. You can reach detailed information using the following link: https://www.eec2019.com/

WES 2020

Abstract submission has already started for the 14th World Congress on Endometriosis. For further information you may use the following link: http://endometriosis.ca/world-congress/wce2020/#2

WCE 2020

Abstract submission extension
Submission deadline 27 October 2019

14th World Congress on Endometriosis

8 - 11 May 2020
INTERVIEW WITH AN ‘ENDO SPECIALIST’

Interview with Assoc. Prof. Caterina Exacoustos, MD

A short curriculum vitae
Caterina Exacoustos received her medical education at the Rome Medical School of the Università Cattolica del Sacro Cuore. After completing her residency and research at the same institution, she is currently working as an associate professor of gynecology in Universita di Tor Vergata Roma. She is world renowned in her research on transvaginal ultrasonography, endometriosis, ovarian masses, endometrial pathology and infertility. In 2010, Dr. Exacoustos was invited as a visiting academician to the University of Connecticut for her expertise on 3D transvaginal ultrasonography. Today, she is well known in the world of endometriosis research for her studies on vaginal ultrasound in the diagnosis of endometriosis. Dr. Exacoustos is also an editor of several journals like Fertility and Sterility, Human Reproduction, Ultrasound in Obstetrics and Gynecology, and the Journal of Minimally Invasive Gynecology.

Hi Dr Exacoustos, this is Dr Salih Yilmaz. On behalf of our association, I would like to thank you for taking the time to do this interview. Today we will talk about endometriosis and adenomyosis.

You have been dealing with endometriosis for many years, what pushed you to be interested in endometriosis?
Like everyone else, I was not really interested in endometriosis at first. I was more interested in early pregnancy and birth. Over time I became interested in pelvic pain. After talking to patients during their ultrasound examinations and hearing their symptoms, pain and poor quality of lives, I thought I could diagnose endometriosis using ultrasound. Ultrasound should be the first method of choice for diagnosis. Ultrasound can easily be performed in the examination room, and can easily show us uterus and ovaries, but we do not investigate for specific findings of endometriosis. I had the chance to evaluate patients with no previous diagnosis of endometriosis. Then I conducted a number of researches. I expanded my basic knowledge and I tried to define endometriosis and adenomyosis using ultrasound.

How do you think endometriosis management should be?
Endometriosis is not a disease that a gynecologist can solve alone. Good teamwork is required. I was very lucky to have the opportunity to work with very good surgeons. Diagnosis alone is not enough. You have to approach the patient with a good team. You should definitely try medical treatment, perform good quality surgery, and communicate well with your patient for the best treatment approach. In short, endometriosis is not a disease that a person can solve alone; it is a team work.
You have described how endometriosis and adenomyosis can be recognized using ultrasound. Could you tell us if ultrasound alone would be enough for diagnosis or would we need to use additional diagnostic techniques?

As I said before, ultrasound is the first choice in diagnosis. We must remember this every time. When we perform ultrasound, we must always keep endometriosis in mind, especially deep infiltrative endometriosis. I can't say for certain that there won't be any need for other diagnostic methods. In my practice I always start with ultrasound. When in doubt magnetic resonance imaging (MRI) can be used for assurance. MRI may be the second step in diagnosis. We can improve our ultrasound techniques and evaluate upper abdomen better. Thanks to MRI we improved our ultrasound techniques in diagnosis of adenomyosis, but ileoceleal endometriosis can still be diagnosed better with MRI. However, uterosacral ligament involvement and bowel involvement can be evaluated with ultrasound thoroughly. When evaluating a case, assessment should be done knowing whether MRI or ultrasound would be more suitable for that particular patient. MRI should be done and images should be evaluated by someone who is also an expert on endometriosis. The same goes for the person who is performing an ultrasound. We should improve our diagnostic skills using ultrasound.

For the ultrasonographic recognition of endometriosis, what do you suggest for our young colleagues?

Current gynecologists are much more fortunate than before. Back then ultrasound was not available everywhere, but now everyone has their own ultrasound. We should teach our young colleagues how to perform ultrasound better. In addition to basic ultrasound techniques, we should teach them how to evaluate ovaries and organs outside of the pelvis. We should also teach them how to perform good laparoscopy. Back then there were few people who can perform laparoscopy but now it is an essential surgical technique.

What do you think about adenomyosis? Is it preceding endometriosis?

Can it be detected easier with new technology and techniques compared to before?

To be honest, we've started looking at adenomyosis recently. It is definitely a very important disease. It is very important not only for bleeding problems but also for infertility. Adenomyosis is not only a problem we see in the elderly, but also in young women. Over the years, we have started to examine the junctional zone, inner myometrium and outer myometrium in more detail and have detected adenomyosis. It is a disease in which you get very good results when you detect it and first treat it medically and then if necessary move on with surgery. A clear detection of the location of adenomyotic loci with preoperative transvaginal ultrasound or even better the perioperative ultrasound detection of adenomyosis can be helpful in diagnosis.

What developments do you expect in the field of endometriosis and adenomyosis in the future? In which part should there be developments?

First of all, there is room for improvement in diagnosis and medical treatment. Surgical treatment should be avoided. So far, we have performed a lot of surgery and we still continue to do so. Performing surgery so frequently also creates problems for patients. Operating on the ovaries and intestines can create complications which can add burden on the patients. We need to consider all aspects before taking the next steps in treatment. Of course, there should be improvements in diagnosis.

What do you think about March, worldwide endometriosis awareness month?

We cannot reduce awareness on endometriosis to one thought. Because the perspectives on endometriosis and treatment approaches all over the world are very different. For instance, approach is very different in Europe and in America. More surgery is being done in Europe. Whereas Italy is more research oriented. The important thing is: we need to establish rules on how to treat patients and patients with endometriomas. We should not reduce ovarian reserve by treating too much. There should not be an approach to remove every cyst seen because we reduce the ovarian reserve of younger patients. We’ll see what will happen in the world. However, we still need to increase awareness worldwide.

In your country, how is the management of a patient with endometriosis? Do these patients directly have access to doctors specialized in endometriosis?

Just like many other countries, there are endometriosis treatment centers in our country. If the patient is consulted here, she receives a multimodal assessment and treatment. But in Italy, as in Germany, there is no certification program. For this reason, the patient cannot understand whether the doctors at a certain center is certified or experienced in endometriosis. Some centers are more focus on the financial aspect of the treatments whereas others focus on the patient. They want to start a certification system in Italy, but it is a difficult process. Because it is hard to document which doctors in a center are experienced in surgery and which are experienced in ultrasound. Even if the surgeon in a center is very experienced, his team or those who make the necessary assessment for preoperative diagnosis may not be good. There are centers in Italy that have very good surgeons and teams. However, this set-up and approach is very different across Europe. You can be a very good surgeon, but you may not be as good in medical treatment or in ultrasound. Therefore, it is very important to work with a good team.

I would like to thank your society for this kind invitation.
ARTICLES ON ENDOMETRIOSIS FROM OUR COUNTRY FROM THE LAST THREE MONTHS

1. Bioactivity-guided isolation of flavonoids from Urtica dioica L. and their effect on endometriosis rat model.

Abstract
ETHNOPHARMACOLOGICAL RELEVANCE:
Urtica dioica L. has been used traditionally for centuries. U. dioica leaves and roots are used as a blood purifier, emmenagogue, and diuretic, as well as to treat menstrual hemorrhage, rheumatism, and eczema. The present study aimed to evaluate the activity of U. dioica L. aerial parts in endometriosis rat model.

MATERIALS AND METHODS:
To evaluate the effects of the plant in endometriosis, n-hexane, ethyl acetate (EtOAc), and methanol (MeOH) extracts were prepared from the aerial parts of the plant and utilized in a rat surgical endometriosis model. In this model, adhesion scores of endometriotic implants and the spherical volumes of ectopic uterine tissues were evaluated. In addition to these parameters, tumor necrosis factor alpha (TNF-α), vascular endothelial growth factor (VEGF), and interleukin-6 (IL-6) levels of the peritoneal fluids were evaluated. Furthermore, histopathological studies were conducted on the endometriotic tissues.

RESULTS:
Post-treatment implant volumes and adhesion scores were significantly reduced in the reference and the MeOH extract treated groups. Significant differences were found between the peritoneal TNF-α, VEGF, and IL-6 levels of MeOH extract treated group and those of control group. Moreover, histopathological findings supported the biological activity results. Furthermore, isolation studies were conducted on the MeOH extract, which showed prominent activity in the rat endometriosis model. Rutin (1), isoquercetin (2), the mixture of kaempferol-3-O-rutinoside (nicotiflorin) (3a) and isorhamnetin-3-O-rutinoside (narcissin) (3b) (3), the mixture of kaempferol-3-O-glucoside (astragalin) (4a) and isorhamnetin-3-O-glucoside (4b) (4) were isolated from the active fraction.

CONCLUSIONS:
The present study demonstrated that aerial parts of U. dioica exhibited promising activity in the endometriosis rat model due to its flavonoids.

2. Diagnostic Efficacy of T2 Dark Spot, T2 Dark Rim Signs, and T2 Shading on Magnetic Resonance Imaging in Differentiating Endometriomas From Hemorrhagic Cysts.

Abstract
OBJECTIVE:
This study aimed to evaluate the diagnostic efficacy of T2 dark spot, T2 dark rim, and T2 shading signs on magnetic resonance imaging in the differentiation of endometriomas from hemorrhagic cysts.

METHODS:
Seventy-two hemorrhagic lesions were included in this retrospective study. The presence of T2 dark spot, T2 dark rim, and T2 shading signs in the lesions and the presence of complete or incomplete rim in lesions exhibiting T2 dark rim signs were evaluated.

RESULTS:
Of T2 lesions, 50 were diagnosed with endometrioma and 22 were diagnosed with hemorrhagic cyst. Twenty-six of 50 endometriomas and none of the hemorrhagic cysts showed T2 dark spot sign. T2 shading was observed in 90% of endometriomas and 18% of hemorrhagic cysts. Incomplete T2 dark rim was detected in 67% of endometriomas and 21% of hemorrhagic cysts.

CONCLUSIONS:
T2 dark spot and T2 dark rim signs could be useful for distinguishing endometriomas from hemorrhagic cysts.
3- Endometriomas with low-risk malignancy potential in ultrasonography with high human epididymal protein 4 and risk of ovarian malignancy algorithm: a cases series

Tolga Karacan, Eser Ozyurek, Seyma Yesiralioglu, Huseyin Kiyak, Taner Usta & Engin Oral  Gynecological Endocrinology, 1-5.2019

Abstract

Endometriosis is an estrogen-dependent disease that affects 5 to 15% of women of reproductive age. Data from large-cohort and case-control studies indicate an increased risk for ovarian cancers in women with endometrioma. Recently, as an ovarian cancer biomarker, human epididymal secretory protein E4 (HE4) has been increasingly investigated in the differentiating of endometrioma from ovary malignancy and in confirming the benign structure of the endometrioma. This case series study describes women who underwent surgery due to increased serum HE4 levels and higher Risk of Ovarian Malignancy Algorithm (ROMA) index, in whom the final pathology was reported as benign, although, ultrasonography and magnetic resonance imaging (MRI) findings showed features of "typical" endometrioma.

4- The Importance of Serum Prolidase Activity in Endometriosis


ABSTRACT

Objective: In this study, our objective was to evaluate the abnormal collagen destruction and turnover and the prolidase activity in the etiopathogenesis of endometriosis, which may deteriorate the collagenous structure of extracellular matrix (ECM). Materials and Methods: For the assessment of the prolidase activity, venous blood samples were obtained from 37 patients, who had applied to the outpatient department of the Medical Faculty at Ondokuz Mayis University with complaints of pelvic pain, dysmenorrhea and infertility between October 1st, 2011 and February 15th, 2012, underwent clinical and ultrasonographic examination, prediagnosed with endometriosis, and scheduled for laparoscopy or laparotomy. A total of 22 patients, who were diagnosed with endometriosis via intraoperative exploration and/or pathological examination, constituted the study group and the remaining 15 patients, who did not have any pathological finding or were diagnosed with a benign disease except for endometriosis, constituted the control group. Serum samples obtained from all patients were first centrifuged and then stored in a freezer at -70 C until the time of analysis. During the analysis, the prolidase activity was measured following the necessary biochemical enzymatic processing. Results: We found a statistically significant difference between stage 4 and stage 1,2,3 patients in the study group regarding the CA 125 levels (p=0.018). On the other hand, there was no statistically significant difference between stage 1,2,3 patients in the study group and the control group for serum prolidase levels (p=0.778). There was a statistically significant difference between stage 4 endometriosis patients in the study group and the control group considering the serum prolidase levels (p=0.026). Conclusion: We conclude that serum prolidase activity has a critical function in the development of the endometriotic lesions. In endometriosis patients, the increase in the serum prolidase activity may play an important role in the progress to more advanced stages and in the development of infertility.

5- A Rare Cause of Recurrent Dysuria; Endometriosis of the bladder; Case Report


Abstract

Primary bladder endometriosis is rare and the cause is not fully known. In this article, we present a 37-year-old female patient who underwent transurethral resection for primary bladder endometriosis. The patient's complaints were hematuria, dysuria and pollakuria associated with menstrual cycle for 4 months. After cystoscopic and radiological evaluation in our clinic, transurethral resection of the mass was decided. A 23*21 mm diameter solid bladder mass was excised by transurethral resection. In the postoperative follow-up of the patient by cystoscopy, no recurrence was observed until 6 months.

Keywords: Endometriosis; Hematuria; Urinary Bladder
6. Promising activity of Anthemis austriaca Jacq. on the endometriosis rat model and isolation of its active constituents.

Abstract
Anthemis austriaca Jacq. flowers are traditionally used to alleviate abdominal pain, hemorrhoids, ovary diseases and pneumonia. This study aimed to investigate the effects of A. austriaca flowers, which are frequently used in gynecological disorders, on the rat endometriosis model. The rat endometriosis model was used to evaluate the potential activity of the plant in endometriosis. The dried plant material was extracted with n-hexane, ethyl acetate (EtOAc), and methanol (MeOH), successively. The obtained extracts from A. austriaca flowers were applied to the rats. The adhesion scores, endometrial foci areas, and cytokine levels of the peritoneal fluids were measured on surgical induction of endometriosis in rats. The adhesion scores, endometriotic volume, and cytokine levels of the peritoneal fluids were reduced in the EtOAc, MeOH, and buserelin acetate-treated (reference) groups. The MeOH extract reduced the adhesion scores and endometrial foci areas from 3.1 to 1.1 (p < 0.01) and from 86.4 to 40.5 (p < 0.01), respectively and also the MeOH extract reduced tumor necrosis factor (TNF)-α, vascular endothelial growth factor (VEGF), and interleukin (IL)-6 levels of the peritoneal fluids from 13.7 to 3.8 (p < 0.01), from 28.4 to 16.3 (p < 0.05) and from 50.2 to 24.3 (p < 0.01), respectively. Therefore, isolation studies were conducted on the EtOAc and MeOH extracts. After the MeOH extract was fractionated using RP-18 column, the obtained subfractions were evaluated again on the endometriosis rat model. Subfractions A and C of the MeOH extract displayed statistically significant activity on the endometriosis rat model. Phytochemical investigation resulted in the isolation of 4-β-D-glucopyranosyloxy-6-methyl-2H-pyran-2-one (1) from Fr. A and quercetin (2), apigenin-7-O-(3″-O-acetyl)-β-D-glucopyranoside (3), apigenin-7-O-(6″-O-acetyl)-β-D-glucopyranoside (4), apigenin-7-O-β-D-glucopyranoside (5), quercetin-7-O-β-D-glucopyranoside (6) from Fr. C. Moreover, β-sitosterol-3-O-β-D-glucopyranoside (7) was isolated from the EtOAc extract. As a conclusion, the MeOH extract obtained from A. austriaca flowers contributed to the regression of endometriosis. In addition, flavonoids and sterols of the plant were detected as the possible compounds responsible for the activity.

7. The feasibility of the platelet count and mean platelet volume as markers of endometriosis and adenomyosis: a case control study.

Abstract
INTRODUCTION:
The aim of the study is to investigate the role of platelet count (PC) and mean platelet volume (MPV) in determining adenomyosis and endometriosis.

MATERIAL AND METHODS:
This was a retrospective case control study that included adenomyosis, endometriosis and control groups. The adenomyosis group included 84 women diagnosed between January 2013 and January 2015 based on hysterectomy specimen. The endometriosis group included 102 patients underwent diagnostic laparoscopy and confirmed by histopathologic examination. Lastly, the control group included 88 women had no medical problem and underwent tubal ligation.

RESULTS:
MPV (fl) was significantly lower in adenomyosis group (8.5) compared to endometriosis (9, p<0.05) and control groups (9, p<0.01). Modified platelet activity (MPV/PC) was significantly lower in adenomyosis group compared to control group (p<0.01). Bivariate logistic regression model was used to assess the odds ratio of risk factors and serum markers related to endometriosis and adenomyosis. Variables showing significant differences based on post-hoc Bonferroni test were included in the logistic regression model for comparison of each disease with the control group. MPV was not found to be a risk factor both for presence of endometriosis and adenomyosis after adjusting for demographic and clinical characteristics.

DISCUSSION:
Our study suggested that PC and MPV were not useful diagnostic markers for endometriosis or adenomyosis. Further research on how platelet indices and other inflammatory markers are related to inflammation might help better understand their potential as markers for these diseases.
8. The effects of endometrioma size and bilaterality on ovarian reserve.

Abstract
The aim of this study was to investigate the effects of endometrioma (OMAs) size and bilaterality on ovarian reserve. The patients with OMA were determined by ultrasonographic examination. Fifty patients with unilateral OMA (Group A), 30 patients with bilateral OMA (Group B), and 60 women without ovarian cysts (Group C) were included in this study. AMH levels were measured, and antral follicle count (AFC) was determined. The mean serum AMH levels were significantly lower in Group B than Groups C and A, and were significantly lower in Group A than Group C. There was a significant correlation between serum AMH level and OMA size in Group A (R = -.372, p = .008). OMAs per se appear to be associated with damage to the ovarian reserve. Increased OMA size is related to decreased AMH levels in patients with OMA. Bilateral OMAs have a more destructive effect on ovarian reserve. IMPACT STATEMENT What is already known on this subject? Previous Studies have demonstrated the effect of surgery on ovarian reserve but there have been contradictory findings reported about the effects of OMAs per se on serum AMH levels and it has not been clear what the relation between OMAs size and AMH levels is, if any. What the results of this study add? In this study, we found decreased AMH levels in patients with OMA. The results showed significant negative correlation between OMA size and AMH levels. The patients with bilateral OMAs had lower AMH levels than the unilateral ones. What the implications are of these findings for clinical practice and/or further research? Increasing OMA size might be harmful to ovarian reserve. Further studies should be done to evaluate whether increasing the size of the OMA is associated with a progressive decline in ovarian reserve and to better clarify the role of the OMAs per se or of laparoscopic surgery in the determination of damage to the ovarian reserve.

Meral, S. European Journal for Person Centered Healthcare, 7(2), 265-295.2019

ABSTRACT
Background, aims and objectives: Endometriosis is a perplexing and chronic disease, with an unknown cause and no cure, affecting around 10-15% of women of reproductive age. Symptoms of the condition include severe menstrual cramps, pelvic pain before, during and after periods, nausea, fatigues, infertility, excessive bleeding and pain when moving bowels. Diagnosis can only be established via a laparoscopy and delays have been reported to occur from an individual patient level and a medical level. The study aimed to observe the impact that endometriosis has on women’s lives and contribute to the knowledge provided by the existing qualitative literature.

Methods: The study adopted a qualitative approach and utilised secondary data in the form of videos published on YouTube. Six videos were chosen which were transcribed verbatim and data analysed using interpretative phenomenological analysis (IPA). The analysis conveyed three superordinate themes: making sense, effect on quality of life, and support.

Results: The women reflected on the journey they endured which began by experiencing menstrual cramps and gradually worsened with the onset of additional symptoms. These symptoms had a negative impact on daily living and a reduction in their quality of life (QoL). Women revealed feeling isolated, which stemmed from the lack of support from medical professionals, friends and family. Despite many visits to doctors, the pathway to diagnosis was delayed. Symptoms were normalised by doctors, friends and family members, which reduced the legitimisation of the condition.

Conclusion: Overall, there is a lack of sufficient knowledge, support and acceptance for women suffering with endometriosis. Suggestions for future research and practice include focusing on how to improve women’s quality of life, exploring effective self-management interventions, introducing educational interventions and developing person-centered models of care which could contribute to earlier diagnosis and less suffering.
Chronic pelvic pain is chronic or recurrent, persistent pain that is detected in pelvic structures for 6 months or more. An organic cause may or may not be detected. It is more common in women. It is usually associated with negative cognitive, behavioral, sexual and emotional consequences, as well as symptoms such as lower urinary tract, sexual, intestinal, pelvic floor or gynecological dysfunction.

Treatment of chronic pelvic pain include medical treatment with a wide spectrum with nonsteroidal anti-inflammatory drugs, opioids, antidepressants, anticonvulsive drugs, hormones, etc., physical therapy and exercises, interventional pain applications and surgical treatments.

Interventional pain treatments are applied to patients who have insufficient response to medication and physical therapy, who do not consider surgical treatment, and who do not have a serious problem in psychological evaluation. Patients should not have a general or local infection in the intervention area. There should be no bleeding disorders and blood thinner treatments should be readjusted. Permanent procedures can be tried in patients with a positive response of greater than 50% in diagnostic and prognostic applications.

For myofascial pain syndromes with involvement of pelvic muscles, trigger point injections can be applied. These injections include local anesthetics, steroid mixtures, botulinum toxin, medical ozone and dry needling.

Injection treatments are applied to central, somatic and sympathetic nerves. These applications include specialized techniques that require experience. C-arm fluoroscopy, computed tomography and ultrasonography guidance have been used in recent years. Patients are prepared under sterile conditions in special intervention rooms and under sedation. According to the positive response obtained by temporarily stopping the pain conduction by using local anesthetics for diagnostic purposes, cryotherapy or pulsed or conventional radiofrequency thermocoagulation (RFT) therapy is applied physically or chemically permanent block such as the use of alcohol, phenol, glycerol. However, long-term therapeutic effects can be achieved with deposteroid used together with local anesthetic and recurrent blocks.

Epidural injection via sacral hiatus is applied as central block. This procedure is usually preferred in the treatment of coccydynia. However, it is also used in therapy of various pelvic pain symptoms.

The most common somatic blocks include pudendal nerve block, obturator block, ilioinguinal and iliohypogastric block. In addition, pulsed RFT can be applied to the sacral root dorsal ganglia (S1-5) following its block and/or appropriate stimulus.

Superior hypogastric plexus block and ganglion impar block are examples of sympathetic blocks. Superior hypogastric plexus block is analogous to presacral neurectomy. In cases where superior hypogastric block is not sufficient, inferior hypogastric block is also applicable. Sacral stimulation is applied as a neuromodulation technique. Retrograde and anterograde techniques have been described for this application, but sacral 3 transfemoralinal techniques are the most commonly used ones. Permanent implantation is performed if the electrode placed temporarily displays a control of 50% or more of the associated symptoms and/or pain. Besides urogenital and rectal problems, it is effective in constipation, interstitial cystitis, perianal and pelvic pain. In addition, epidural or spinal port/pump system can be placed in some cancer or non-cancerous pelvic pain and pain control can be applied by using medication.

Chronic pelvic pain is a difficult area to treat. It requires multidisciplinary evaluations and treatment practices. Algology techniques contribute to the treatment applications in this field as the most frequently used application in the diagnosis and treatment of patients.
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