

WE WOULD LIKE TO EXPRESS OUR GRATITUDE TO ALL OUR HEALTHCARE PROFESSIONALS WORKING ON THE FRONT LINES



1 in 10 Women are Affected by Endometriosis www.endometriozis.org

PREFACE
Hello,
In this 16 th issue of our bulletin, we hereby present to you our newest projects.
Year 2020 has been difficult for the whole world. During these hard times, as the Turkish Endometriosis & Adenomyosis Society we continued to work as hard as possible. We started our webinar series and organized live broadcasts so that our patients could find answers to their questions regarding endometriosis. We also have been keeping our international relationships strong. Hopefully in 2021 we, along with the rest of the world, will be able to work more actively in the "new normal" system.
We continued our Instagram Live Sessions on a monthly basis during the last quarter of 2020. In addition, we held three webinars during this period. In October, the webinar titled as 'Relationship Between Endometriosis and Cancer' and moderated by Taner Usta and Hale Goksever Celik took place. In this webinar, Fuat Demirkiran and Peter Oppelt from Austria shared their experiences. In November, we held the 'Recurrent Endometriosis' webinar moderated by Ahmet Kale and Cihan Kaya, in which Ertan Sarıdogan from UK and Alysson Zanatta from Brazil joined us as lecturers. Last but not the least, in December Huseyir Nazlikul, Mustafa Atasoy and Umit Inceboz shared their perspectives on 'Endometriosis and Complementary/Functiona Medicine in Literature: Evidence Based Approach', which was moderated by Cem Atabekoglu and Pinar Yalcin Bahat. This month Yucel Karaman and Tolga Karacan moderated the 'Adenomyosis: An Update' webinar on January 26th, during which Stefano Guerriero from Italy, Erkut Attar and Miklos Koppan from Hungary updated our knowledge on adenomyosis.
At the virtual AAGL Congress, the president of our society Taner Usta and Nura Fitnat Topbas Selcuki from our junior group represented our society with their presentations and ongoing studies. The World Endometriosis Congress and many other congresses are postponed due to the pandemic. The World Congress on Endometriosis is going to be held online on March 6-10 2021. Our junior group will take part in this congress with oral presentations and posters.
On March 12-13 2021, 'Adenomyosis: What we know, and we don't know?' ESHRE Campus Workshop organized by our society will be held online due to the pandemic, which was planned originally to take place in Istanbul.
In our next issue, we wish to share with you good news from Turkey and from all over the world. Wishing a happy and prosperous year for all of us.
Best regards,
Board Members of Turkish Endometriosis & Adenomyosis Society

Turkish Endometriosis & Adenomyosis Society Board of Directors 2019-2022



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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 you would like to ask, you can contact us via e-mail at dr_pinaryalcin@hotmail.com or baharyl86@gmail.com.

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Mira TAA, Yela DA, Podgaec S, Baracat EC, Benetti-Pinto CL. Eur J Obstet Gynecol Reprod Biol. 2020 Oct15;255:134-141

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A SELECTED ARTICLES

Pregnancy and delivery outcomes in women with rectovaginal endometriosis treated either conservatively or operatively.

Tuominen, A., Saavalainen, L., Tiitinen, A., Heikinheimo, O., Härkki, P. Fertility and Sterility,2020 on press

Abstract

Objective: To study reproductive outcomes, and pregnancy and delivery complications after conservative or operative treatment of rectovaginal endometriosis during long-term follow-up.

Design: Retrospective cohort study.

Setting: University hospital.

Patient(s): Women with rectovaginal endometriosis referred to hospital due to any indication from 2004 to 2013 (N = 543) who were treated initially either conservatively (group CONS, n = 183), or operatively (OPER, n = 360) either with resection of rectovaginal nodule (RVR, n = 192) or with concomitant bowel resection (BR, n = 132).

Intervention(s): Conservative or operative management.

Main outcome measure(s): Clinical pregnancy rate, live-birth rate, and assessment of the complications during pregnancy and delivery.

Results(s): Between women in the CONS group or OPER group, no differences were found in either clinical pregnancy rate (56%, n = 102 vs. 50%, n = 181) or live-birth rate (48%, n = 87 vs. 42%, n = 153). Of the pregnancies, 64% (n = 65) and 49% (n = 89), respectively, started after medically assisted reproduction. No differences emerge in the subanalysis of women <40 years-old



who wished to conceive. The most common pregnancy complication was preterm birth: 15% (n = 13) in the CONS group and 20% (n = 30) in the OPER group. The cesarean delivery rate also was high (46%, n = 40 vs. 49%, n = 76). Complications emerged in 21% (n = 10) versus 29% (n = 23) of vaginal deliveries and 45% (n = 18) versus 53% (n = 40) of cesarean deliveries. The most common delivery complication was excessive bleeding. The follow-up period was 4.9 years in the CONS group and 5.6 years in the OPER group.

Conclusion(s): Women with rectovaginal endometriosis have comparable and good reproductive prognosis regardless of the treatment method.

Keywords: Delivery complication; fertility; pregnancy complication; rectovaginal endometriosis.

2 Letrozole combined with oral contraceptives versus oral contraceptives alone in the treatment of endometriosis-related pain symptoms: a pilot study.

Zhao, Y., Luan, X., Wang, Y. Gynecological Endocrinology, 1-5,2020

Abstract

Background: To compare the efficacy and the tolerability of letrozole combined with oral contraceptives versus oral contraceptives alone in treating endometriosis-related pain.

Methods: A total of 820 women with endometriosis presented with endometriosis-related pain were enrolled with this study. Patients were randomly treated either with letrozole (2.5 mg/day) combined with oral contraceptives (Desogestrel and Ethinylestradiol Tablets) or oral contraceptives (Desogestrel and Ethinylestradiol Tablets) alone for 6 months. Changes in pain symptoms during treatment and in 1 months after treatment, 6-month follow-up and 12-month follow-up were evaluated. Adverse effects of each treatment protocol were recorded.

Results: At completion of treatment, the intensity of chronic pelvic pain continued to decrease during treatment and at 1-month after treatment it was significantly lower than at 6-month

follow-up and baseline level both in LE + oral contraceptives group (Mean \pm SD,1.5 \pm 1.4) and in oral contraceptives alone group(Mean \pm SD,2.9 \pm 1.2).The intensity of chronic pelvic pain and deep dyspareunia was significantly decrease at both 1-month after treatment and 6-month follow-up.

Conclusions: This treatment for endometriosis is a promising new modality that warrants further investigation.

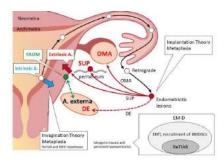
Keywords: Letrozole; aromatase inhibitor; endometriosis; oral contraceptives; pain

Relationship between adenomyosis and endometriosis; Different phenotypes of a single disease?

Maruyama, S., Imanaka, S., Nagayasu, M., Kimura, M., & Kobayashi, H. European Journal of Obstetrics & Gynecology and Reproductive Biology,2020 on pres

Abstract

Adenomyosis and endometriosis are common gynecological disorders, but their pathophysiology is still under debate. The aim of this review is to discuss whether adenomyosis and endometriosis represent two different entities or different phenotypes of a single disease. We searched PubMed electronic databases published between January 2000 and April 2020. Endometriosis is classified into three phenotypes; superficial peritoneal disease (SUP), ovarian endometrioma (OMA) and deep infiltrating endometriosis (DIE) lesions. Adenomyosis presents several different subtypes, including intrinsic adenomyosis, extrinsic adenomyosis, adenomyosis externa and focal adenomyosis located in the outer myometrium (FAOM). Human uterus is embryologically composed of archimetra, originating from the Müllerian duct, and neometra, arising from the non-Müllerian duct, and adenomyosis and endometriosis are diseases of archimetra. The outer myometrial layer of the uterus is composed of highly differentiated smooth muscle cells (SMCs), while the inner myometrial cells are immature. Inappropriate uterine contractions can cause retrograde menstruation and chronic inflammation in the pelvic cavity, then influencing the pelvic endometriosis. development of Furthermore. hyperperistalsis results in physiological and pathological changes



to the endometrial-myometrial junctional barrier, allowing invagination of the normal endometrial tissue into the inner myometrial layer. This can trigger the development of intrinsic adenomyosis. There are insufficient data available to draw conclusions, but extrinsic adenomyosis may result from pelvic endometriosis and FAOM from rectal and bladder DIE/adenomyosis externa. In conclusions, this paper contributes to the debate in the possibility that adenomyosis and endometriosis represent different phenotypes of a single disease.

Keywords: Adenomyosis; Endometriosis; Archimetra; Smooth muscle cells; Fibrosis

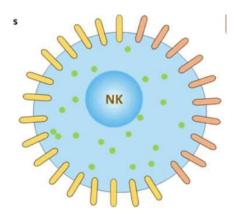
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Circulating CD56+ NKG2D+ NK cells and postoperative fertility in ovarian endometrioma.

Liu, Z. Q., Lu, M. Y., & Liu, B. Scientific reports, 10(1), 1-11,2020

Abstract

The current biomarkers for postoperative fertility assessment caused by ovarian endometrioma (OE) are insufficient. The present study hypothesized that the peripheral lymphocyte subpopulation can be used as a candidate biomarker of postoperative infertility in OE. The association of the number of circulating CD4/CD8 T, NK, and γδ T cells with postoperative fertility was assessed in 33 OE patients aged 20 ~ 40 years between June 2018 and January 2019. Concomitantly, 68 healthy female subjects were recruited. The changes in the baseline immune characteristics between the two groups were compared. The data demonstrated significant differences in the ratio of CD4/ CD8 T cells and the number of CD56+ NKG2D+ NK cells and y\delta T cells between OE patients and control subjects. The patients were followed-up till December 2019 and the number of CD56+ NKG2D+ NK cells in the cases was a significant predictor for postoperative fertility as determined by different COX regression models (crude HR = 0.220, 95% CI = 0.059-0.822; adjusted HR = 0.127,95% CI = 0.024-0.675).



A significant delay to successful pregnancy was noted in OE patients (median time, 173 vs. 99 days, log-rank P = 0.013). The present findings suggested that CD56+ NKG2D+ NK cells are a candidate biomarker of postoperative fertility in OE patients. Larger population studies are warranted.

Establishment of an immortalized stromal cell line derived from human Endometriotic lesion

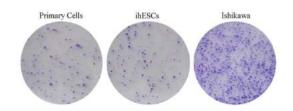
Huang ZX, Wu RF, Mao XM, Huang SM, Liu TT, Chen QH, Chen QX. Reprod Biol Endocrinol. 2020 Nov23;18(1):119

Abstract

Background: Endometriosis is a benign gynecological disease with obviously feature of estrogen-dependence and inflammatory response. The applications of primary endometriotic stromal cells in research of endometriosis are restricted for short life span, dedifferentiation of hormone and cytokine responsiveness. The objective of this study was to establish and characterize immortalized human endometriotic stromal cells (ihESCs).

Methods: The endometriotic samples were from a patient with ovarian endometriosis and the primary endometriotic stromal cells were isolated from the endometriotic tissues. The primary cells were infected by lentivirus to establish telomerase reverse transcriptase (hTERT)-induced immortalized cells. Quantification of mRNA and proteins was examined by quantitative real-time polymerase chain reaction (qRT-PCR) and Western Blot. CCK-8 assay and EdU labeling assay were assigned to assess the growth of ihESCs. Karyotype assay was performed to detect the chromosomes of ihESCs. Colony formation assay and nude mouse tumorigenicity assay were used to evaluate colony-formation and tumorigenesis abilities.

Results: ih ESCs continuously overexpressed hTERT via infection of lentivirus and significant extended the life span reaching 31 passages. The morphology, proliferation and karyotype of ihESCs remained unchanged. The expression of epithelial-mesenchymal



transition (EMT) markers, estrogen-metabolizing proteins and estrogen/progesterone receptors (ERs and PRs) were unaltered. Furthermore, the treatment of estrogen increased the proliferation and EMT of ihESCs. Lipopolysaccharides (LPS) and IL- 1β remarkably induced inflammatory response. The clonogenesis ability of ihESCs was consistent with primary cells, which were much lower than Ishikawa cells. In addition, nude mouse tumorigenicity assay demonstrated that ihESCs were unable to trigger tumor formation.

Conclusion: This study established and characterized an immortalized endometriotic stromal cell line that exhibited longer life span and kept the cellular morphology and physiological function as the primary cells. The immortalized cells remained normal feedback to estrogen and inflammatory response. Moreover, the immortalized cells were not available with tumorigenic ability. Therefore, ihESCs would be serviceable as in vitro cell tool to investigate the pathogenesis of endometriosis.

Hormonal treatment isolated versus hormonal treatment associated with electrotherapy for pelvic pain control in deep endometriosis: Randomized clinical trial.

Liu, Z. Q., Lu, M. Y., & Liu, B. Scientific reports, 10(1), 1-11,2020

Abstract

Objective: The aim of the study was to evaluate the clinical effectiveness of complementary treatment using self-applied electrotherapy treatment for pain control over the standard hormonal treatment alone for deep infiltrative endometriosis (DIE).

Study design: Multicentre randomized clinical trial. We included a hundred-one participants with DIE in electrotherapy (n = 53) (hormonal treatment + electrotherapy) or control group (n = 48) (only hormonal treatment) by 8 weeks of follow-up. The primary measurement was chronic pelvic pain (CPP) using a visual analogue scale (VAS) and deep dyspareunia. The secondary outcomes were the quality of life by endometriosis health profile (EHP-30) and sexual function by female sexual function index (FSFI).

Results: CPP relief was observed only in the electrotherapy group (pre:7.11 \pm 2.40, post:4.55 \pm 3.08, p < 0.001). In terms of deep dyspareunia, improvements were observed for both groups (electrotherapy pre:2.02 \pm 0.54-1.36 \pm 0.96, p < 0.001; control pre:1.95 \pm 0.86-1.68 \pm 0.82, p = 0.006). Considering the secondary



outcomes, a higher total score post-treatment for the EHP-30 was noted in both groups. Regarding sexual function, there was a statistically significant improvement in the FSFI score for the electrotherapy group (p < 0.001), with an increase in the scores for lubrication and pain domains (p = 0.013 and p < 0.001).

Conclusions: Electrotherapy treatment using transcutaneous electrical nerve stimulation proved to be a good complementary option for pain control, showing benefits in the reduction of CPP and deep dyspareunia and improving patient's quality of life and sexual function.

B NEWS FROM OUR SOCIETY PAST ACTIVITIES

As we wait for the battle against COVID 19 to end at our homes; we have continued our Instagram live broadcasts with our expert professors to answer the questions of our patients. Below are our broadcasts in last three months.



Q&A 10: Everything about endometriosis
Prof. Baris Ata, MD.
Assoc. Prof. Yusuf Aytac Tohma, MD.



Q&A 11: Everything about endometriosisProf. Baris Mulayim, MD.
Seher Sari, MD.



Q&A 12: Everything about endometriosisProf. Murat Api, MD.

Eda Ureyen Ozdemir, MD.



Q&A 13: Everything about endometriosisProf. Serhan Cevrioglu, MD.
Assoc. Prof. Cagdas Sahin, MD.



Q&A 14: Everything about endometriosisProf. Gonca Imir Yenicesu, MD.
Humeyra Demirkiran, MD.



Q&A 15: Everything about endometriosis
Prof. Engin Oral, MD.
Nilufer Akgun, MD.

Turkish Endometriosis & Adenomyosis Society Webinars 2020

The first webinar of Turkish Endometriosis & Adenomyosis Society was held in June 2020. Following our first webinar, we continued organizing webinars with the contribution of international endometriosis experts.



2-Relationship Between Endometriosis and Cancer

Moderators: Taner Usta, MD.

Hale Goksever Celik, MD.

Speakers: Fuat Demirkiran, MD.

Peter Oppelt, MD. (Austria)



3- Recurrent Endometriosis
Moderators: Ahmet Kale, MD.
Cihan Kaya, MD.

Speakers: Ertan Saridogan, MD. (UK)
Alysson Zanetta, MD. (Brazil)



4- Endometriosis and Complementary/ Functional Medicine in Literature: Evidence Based Approach

Moderators: Cem Atabekoglu, MD.
Pinar Yalcin Bahat, MD
Speakers: Huseyin Nazlikul, MD.
Mustafa Atasoy, MD.
Umit Inceboz, MD.



5- Adenomyosis: An Update

Moderators: Yucel Karaman, MD.
Tolga Karacan, MD.

Speakers: Stefano Guerriero MD. (Italy)
Erkut Attar, MD.
Miklos Koppan, MD. (Hungary)

PLANNED ACTIVITIES

ESHRE Campus Workshop

ESHRE Campus Workshop is going to be held by our society on $12 - 13^{th}$ of March, 2021. After the ESHRE Campus Workshop in 2016, which was in Istanbul, the second is going to be virtual due to the pandemic. There will be lectures by many international experts and we look forward to your participation in our workshop.

Friday 12 March

09.00-09.10: Introduction > Maria Isabel Acien & Andrea Romano

Session 1: Basis of Adenomyosis

Chairs: Umit Inceboz and Arne Vanhie

09.10-09.30: Definition, epidemiology of adenomyosis

Speaker: Grigoris Grimbizis (Greece)

09:30-09:50: Pathogenesis of Adenomyosis- Invagination or metaplasia?

Speaker: Olivier Donnez (France)

09:50-10:10: The coexistence of endometriosis, myomas and adenomyosis

Speaker: Ertan Saridogan (UK)

10:10-10:40: Discussion 10:40-10:50 COFFEE BREAK

Session 2: Mechanism of Pain and uterine bleeding in Adenomyosis: Basic aspects

Chairs: Taner Usta and Linda Tebache

10.50-11.10: The mechanism of pain in women with adenomyosis

Speaker: Katy Vincent (United Kingdom)

11.10-11.30: The mechanism of abnormal uterine bleeding in women with adenomyosis

Speaker: Malcolm Munro (USA)

11:30-11:50: Discussion 11:50-12:00 COFFEE BREAK

Session 3: Diagnostic Imaging in Adenomyosis

Chairs: Cihan Kaya and Maribel Acien

12.00-12.20: How do I diagnose adenomyosis with sonography?

Speaker: Caterina Exacoustos (Italy)

12.20-12.40: How do I diagnose adenomyosis with MRI?

Speaker: Isabelle Thomassin-Nagarra (France)

12:40-13:00: Discussion 13:00-14:00 LUNCH BREAK

Session 4: Clinical management

Chairs: Ahmet Kale and Carla Tomassei

14.00-14.20: Medical treatments of women with adenomyosis

Speaker: Silvia Vannuccini (Italy)

14.20-14.40: Surgical treatments of women with adenomyosis

Speaker: Vasilios Tanos (Cyprus)

14.40-15:00: Discussion

Keynote session

Chairs: Engin Oral and Antonio Simone Laganà

15.00-15.30: Is adenomyosis the same disease as endometriosis?

Speaker: Philippe Koninckx (Belgium)

15.30-15:50: Discussion

15:50-16:00 closing remarks day one > Andrea Romano

Saturday 13 March

Session 6: Adenomyosis during adolescence

Chairs: Pınar Yalcin Bahat and Umberto Leone Roberti Maggiore 09.00-09.20: Juvenile cystic adenomyosis-a congenital malformation

Speaker: Maribel Acién (Spain)

09.20-09.40: What to do in young pallents with adenomyosis

Speaker: Gabriele Tridenti (IT)

09:40-10:00: Discussion

Session 7: Infertility and pregnancy in adenomyosis

Chairs: Hale Goksever Celik and Michelle Nisolle

10.00-10.20: Adenomyosis related infertility: what are the treatment options?

Speaker: Engin Oral (Turkey)

10:20-10:40: Is endometrial receptivity and IVF outcome affected in women with

adenomyosis?

Speaker: Edgardo Somigliana (IT)

10:40 – 11:00: Adenomyosis and obstetrical outcomes

Speaker: Laura Buggio (IT)

11:00 - 11:30 Discussion

11:30 – 11:45 Closing remarks > Maria Isabel Acien & Andrea Romano & Oral Engin

NEWS FROM THE WORLD OF ENDOMETRIOSIS

EEL WEBINARS



Monthly webinars of European Endometriosis League (EEL) continued during the last quarter of 2020. In November, Shaheen Khazali discussed the issue of "Management of ureteric endometriosis", which was moderated by Joerg Keckstein. Then, on 15th of December, 2020, Ertan Saridogan gave a lecture titled as "What do we know about adolescent endometriosis".

For more information, you can visit www.endometriosis-league.eu/home or follow the European Endometriosis League or Euro Endo League accounts on social media.

EEL Bullettin



The December 2020 issue of EEL Bulletin has been published. The bulletin, which is planned to be sent to EEL members 4 times a year, aims to inform the members of the association the announcements and developments. The full version of the can be accessed euroendometriosis.com.

ESHRE 2021



Due to the pandemic, the 36th ESHRE Annual Meeting was held online on 5 - 8th of July, 2020. The 37th Annual Meeting of ESHRE (European Society of Human Reproduction and Embryology) will be virtual and will be held on 27-30th of June, 2021.

WCE 2021



14th World Endometriosis Congress was planned to be held in Dubai in September, however it will be held online on 6-10th of March, 2021 due to the pandemic.

ASRM 2020



ASRM 2020 Congress was held online between 17-21st of October, 2020 due to the pandemic.

AAGL 2020



49th Global Congress of Minimally Invasive Gynecologic Surgery was held online due to the pandemic. President of Turkish Endometriosis&Adenomyosis Society, Taner Usta, and Nura Fitnat Topbas Selcuki represented our society with their presentations.

ISGE 2020



An online meeting by ISGE (International Society of Gynecologic Endoscopy) was held on 5-6th of December, 2020; with participation of international speakers.

6TH EMEL CONFERENCE



 6^{th} conference of EMEL (Emirates Endometriosis League) on endometriosis and uterine disorders, was postponed to $12-13^{th}$ of March, 2021, due to the pandemic.

ACE 2020







The joint congress of Endometriosis Association of Sri Lanka and Asian Society of Endometriosis & Adenomyosis, which was planned to be held in 2020, was postponed to 2021 due to the pandemic.

ENDOMETRIOSIS 2021



Endometriosis meeting which was originally planned to be held in Rome by Mario Malzoni, was postponed to $8-11^{th}$ of May, 2021 due to the pandemic.

INTERVIEW WITH AN 'ENDO SPECIALIST'



GERNOT HUDELIST, MD. Interview: Ezgi DARICI, MD.

A Short Curriculum Vitae

Gernot Hudelist, M.D, MSc, is a consultant, minimally invasive surgeon, and clinical lecturer focusing on fertility surgery, endometriosis and gynecological oncology. He studied advanced gynecological endoscopy at the St. Lukes Cancer Center, Guildford and studied in Austria and the UK as well. Dr. Hudelist is a visiting professor at the Medical University of Vienna, teaches and works as an endometriosis and minimally invasive surgeon at St. John of God Hospital and Rudolfinerhaus Private Clinic. He is the author of more than 120 scientific publications on endometriosis and gynecological oncology, a member of the advisory board of the European Endometriosis League (EEL), and a member of the Austrian Society of Endocrinological Oncology.

Turkish Endometriosis & Adenomyosis Society (EAD): Today we will interview with Doctor Gernot Hudelist from Vienna. Hello Dr. Hudelist welcome.

Gernor Hudelist: Hello Ezgi, thank you for inviting me to this interview, it is a pleasure tobe with you.

EAD: Thank you, we have a few questions for you. First of all, you have been studying endometriosis for many years. Could you tell us how your journey started?

GH: Actually, I always wanted to focus on gynecological surgery. To summarize, my story is as follows; I researched various regions of Austria and Germany to get a good education in gynecological endoscopy and luckily there was a suitable position in the city where I grew up. At that time, Professor Keckstein was the head of the endometriosis department. I applied to a position at his clinic and let him know that I wanted to be a gynecological surgeon. That's how everything started. I have always been interested in gynecological oncology. I worked in England in 2006. I came back after studying there for 1.5 years. Later, after working as a consultant physician with Professor Keckstein for three more years, I moved to Vienna.

EAD: What do you think is the most challenging part of this disease for doctors?

GH: The most challenging part is to accurately understand the extent of the disease using non-invasive methods and, in light of this, to determine the most appropriate patient specific treatment. As we know, there is no need to surgically treat every patient with endometriosis. Secondly, surgical treatment is the most challenging part in a patient with diffuse endometriosis. In my opinion, for a gynecological surgeon, such operations are even more challenging than gynecological oncology. Because you have to find a way around between completely excising the disease and fertility-sparing during surgery. This surgery is not all about R0 resection, it's about preserving and ameliorating the reproductive function where the disease seriously affects the organ.

EAD: What is the most important part of the evaluation and examination of a patient with endometriosis?

GH: At this point, I can say that the hardest part is to listen to the patients because if you are closely interested in endometriosis you constantly encounter patients with pelvic pain and as a doctor you can get to the point where you are filled with pain descriptions and complaints. Not only pain, but also problems with sexual intercourse, psychological problems, impaired reproductive function. Patients can be very demanding in the face of these problems. I think this is very complicated. Patients have real reasons for being both mentally and psychologically affected by this chronic condition and I think it is very difficult talking to these patients and offering them the most appropriate individual treatment option. That's why I personally think, primarily, it's about communication. The second is about achieving diagnosis with simple methods, like a solid dialogue with the patient, clinical examination and sonography. These methods are useful for approaching the patient with chronic pelvic pain and endometriosis.

EAD: You are one of the leading names in endometriosis sonography. There are some recommended imagining techniques such as sonovaginography or gel contrast vaginography. Is there a special technique you use in your daily practice?

GH: Not really. Personally, I was taught that it is necessary to use ultrasound always as a tool to understand what to expect in the operating room. Sonography for me, is a tool for obtaining better ideas about surgical problems. We do not treat all these patients surgically for sure. Sonography helps me to understand what challenges I will encounter during surgery, what other specialties I should cooperate with, and makes the operation easier enabling me to plan the surgery step by step. Regardless of what technique you use, regardless of a Ferrari or a standard ultrasound device what actually matters is what you are looking at, where you should actually look, and to know how the things you are looking for seem like with ultrasound. My personal opinion is, all techniques and discussions about MRI, whether it should be applied or should not, bowel preparation whether it is necessary or not, and gel sonography whether it should be performed or not, do not constitute a primary importance.

EAD: Besides sonography, you are also a skilled endometriosis surgeon. Can you give us some tips on how to avoid complications during surgery? Do you have some tips and tricks for beginners?

GH: As I told you at the beginning, if you know what you will encounter and know what to do, your chances of complications are less. The better you preoperatively evaluate the big picture, the less likely you will be in a difficult situation during surgery. Second, we all know that there are evidence-based medical recommendations such as the use of protective ileostomy to reduce anastomotic leakage in widespread endometriosis surgery, and we all know them. Ultimately, it is your patient experience that matters. This is the case with any job you manually work with your hands. If you are a shoe manufacturer and you only make two pairs of shoes a year, it is difficult to sell them. If you are a surgeon and you have endometriosis surgery twice a year, you are less likely to get good results with the surgery. There is similar data in gynecological oncology. The more often you do complicated procedures, the better the result. It is important to focus, have rigorous training, and maintain your skills at a high level.

EAD: So, you are saying that practice makes perfect?

GH: Yes, and keep the skill going! I think that to keep your complication rates within an acceptable range as a center you need to have a minimum number of cases similar to oncology centers, which is about 20 complicated cases per year. In order for interdisciplinary surgeons to work together in harmony, these operations need to occur more than once a year, or more than twice a year. I support the idea of referral to a tertiary center where there is a specialized, well trained surgical team doing the surgeries frequently and regularly.

EAD: And my last question. Do you have any suggestions for young colleagues who want to become experts in the field of endometriosis?

GH: I'm looking at you Ezgi, you came to Austria to observe me and I think the most important thing is to be inspired. If you are inspired, if you really want to do something because you think it is interesting, if you are fascinated by the idea of doing it, this is the motto of everything. If you have that spirit, that spirit will guide you and allow you to overcome difficult times. Things change, hospitals change, colleagues change, but if that spirit is in you, this is what matters the most. If you want to succeed and you stick with this idea which is the most important and the rest will come eventually.

FROM THE LAST THREE MONTHS

1. The effectiveness of Teucrium chamaedrys L. extracts on endometriotic implant regression in rat endometriosis model

Sule Ozel, Ipek Suntar , Nilufer Ercan Gokay , Tugba Taskin Turkmenoglu , Murside Ayse In Veterinary Research Forum. Faculty of Veterinary Medicine, Urmia University, 2020.

Abstract: The aim of the present study was to investigate the therapeutic effects of Teucrium chamaedrys L. (Lamiaceae) in the experimentally induced endometriosis in rats. Endometrial tissue was implanted into the abdominal wall of thirty Sprague Dawley rats; the rats with endometriosis were randomized into five groups and treatment procedure was performed for three weeks. The treatment groups were orally treated with three different extracts of Teucrium chamaedrys. Buserelin acetate (20.00 mg) was given as a reference drug. Vehicle was administered alone to the control group. All rats were sacrified at the end of the experiment. The endometriotic implants were measured, intra-abdominal adhesions were scored and the tissue samples were histopathologically investigated. After the treatment procedure, the volumes of endometrial implant and adhesions were detected to be significantly decreased in the T. chamaedrys extracts treated groups compared to the control group. Therapeutic effect of the T. chamaedrys extracts could be attributed to the both nonpolar and polar secondary metabolites. The study conceived that the different polarity extracts of T. chamaedrys could be beneficial in the treatment of endometriosis.

2. Prevalence of Caesarean Section Scar Endometriosis: 10-years Experience of a Tertiary Center and Retrospective Evaluation of 40 cases.

Erdoğan, A., & Erdoğan, P. Erciyes Medical Journal, Ahead of print

Abstract

Objective: Caesarean scar endometriosis (CSE) is the presence of ectopic endometrial tissue at the site of the previous caesarean section (CS) scar. The prevalence vary between 0,04 and 0,53. We aimed to evaluate the women with CSE in last 10 years in Niğde.

Materials and Methods: The medical records of Ömer Halisdemir University Training and Research Hospital and the single private hospital were retrospectively analyzed through electronic databases between January 2010 and January 2020. Pathological reports with the diagnosis of abdominal wall endometriosis were distinguished. The ones excised from a CS scar were included into the study. For each patient clinical, obstetric and surgical characteristics were recorded.

Results: Fourty women were included into the study with an average age of 31,6±5,9 years. The diameter of the CSE lesion was positively correlated in medium strength with BMI at the time of CS (r=0,448, p=0,019). Similarly the diameter of the lesion and weight gain during pregnancy were correlated in medium strength (r=0,423, p=0,014). The onset of symptoms was correlated in medium strength with lactation period (r=0,539, p=0,001). The rate of correct initial diagnosis was significantly higher in years 2015-2019 than in years 2010-2014 (p=0,004). The CSE prevalence was 0,15 in the present study.

Conclusion: High BMI values at the time of CS and weight gain during pregnancy might be contributors of CSE development. Furthermore lactation might have protective effects against CSE.

3. Differential expression of Oct-4, CD44, and E-cadherin in eutopic and ectopic endometrium in ovarian endometriomas and their correlations with clinicopathological variables.

Usta, C. S., Turan, G., Bulbul, C. B., Usta, A., Adali, E. Reproductive Biology and Endocrinology, 18(1), 1-10,2020

Background

Endometriosis is an estrogen-dependent inflammatory disease that often causes infertility and chronic pelvic pain. Although endometriosis is known as a benign disease, it has demonstrated characteristics of malignant neoplasms, including neoangiogenesis, tissue invasion, and cell implantation to distant organs. Octamer-binding protein 4 (Oct-4) is a molecular marker for stem cells that plays an essential role in maintaining pluripotency and self—renewal processes in various types of benign and malignant tissues. CD44 is a multifunctional cell surface adhesion molecule that acts as an integral cell membrane protein and plays a role in cell—cell and cell—matrix interactions. E-cadherin is an epithelial cell—cell adhesion molecule that plays important role in the modulation of cell polarization, cell migration, and cancer metastasis. The aim of this study was to investigate the expression patterns of Oct-4, CD44, and E-cadherin in eutopic and ectopic endometrial tissues from women with endometrioma.

Methods

In the present study, Oct-4, CD44, and E-cadherin expressions were evaluated in eutopic and ectopic endometrial tissue samples from women with endometrioma (n = 32) and compared with those of control endometrial tissue samples from women without endometrioma (n = 30).

Results

Immunohistochemical expression of Oct-4 was significantly higher in the ectopic endometrial tissue samples of women with endometrioma than in the control endometrial tissue samples (p = 0.0002). Conversely, CD44 and E-cadherin expressions were significantly lower in the ectopic endometrial tissue samples of women with endometrioma than in the control endometrial tissue samples (p = 0.0137 and p = 0.0060, respectively). Correlation analysis demonstrated significant correlations between Oct-4 expression and endometrioma cyst diameter (p = 0.0162), rASRM stage (p = 0.0343), and total rASRM score (p = 0.0223). Moreover, CD44 expression was negatively correlated with the presence of peritoneal endometriotic lesions (p = 0.0304) while E-cadherin expression was negatively correlated with the presence of deep infiltrating endometriosis (p = 0.0445).

Conclusions

Increased expression of Oct-4 and decreased expression of adhesion molecules in endometriotic tissues may contribute to the development and progression of endometriosis.

4. Expression of monocyte chemotactic protein 2 and tumor necrosis factor alpha in human normal endometrium and endometriotic tissues.

Aksak, T., Gümürdülü, D., Çetin, M. T., Polat, S. Journal of Gynecology Obstetrics and Human Reproduction, 101971,2020

Endometriosis is a gynocological disease characterized by the presence of the endometrial glands and stroma outside the uterine cavity. This disease affects % 6-10 of women with reproductive age and it causes serious problems such as pelvic pain, dysmenorrhea and infertility. Although endometriosis is one of the most investigated disease of gynecology, its pathogenesis is not clear completely. In recent years, many studies revealed the inflammatory nature of endometriosis. Many of the immune cells and their secretory products cytokines and chemokines has been detected in body fluids of women with endometriosis. Cytokines are protein or glycoprotein in structures and hormon-like molecules that act generally in a paracrine fashion to regulate immun responses. They involved in chemotaxis, cell proliferation, cell activation, motility, adhesion and morphogenesis. Tumor necrosis factor alpha (TNF- α) is a proinflammatory cytokine secreted by the macrophages, monocytes, neutrophiles, T cells and natural killer cells. It stimulates increase in the level of the chemokines in body fluids. Monocyte chemotactic protein 2 (MCP-2) is a chemokine act to recruit and activate monocytes into sites of inflammation area. The aim of this study to investigate the ultrastructural properties and whether the expression and localization of TNF-α and MCP-2 in the eutopic endometrium (normal endometrium of women with endometriosis) and endometritic tissues of women with endometriosis. Eutopic endometrial and endometriotic tissue samples were obtained from women with endometriosis between 20-41 y and normal endometrial tissues were collected from 5 women without endometriosis as a control group. Tissues were processed for light and electron microscopy and examined. The epithelial cells of endometriotic tissues were revealed strongly cytoplasmic TNF- α and MCP-2 immunreactivities. Eutopic endometrial tissues were also stained prominently for both TNF- α and MCP-2. Furthermore, a significant increase in stromal macrophages were observed in endometriotic tissues. Moreover, the ultrastructural observations on the normal and endometriotic tissues were exhibited microvilli-rich cells and ciliated cells. These findings suggest that TNF- α and MCP-2 may be involved in normal endometrial biology and in the pathogenesis of endometriosis.

5. Evaluation of Serum Endocan Levels in Endometriosis: A case-control study: Evaluation of Serum Endocan Levels in Endometriosis: A case-control study.

Güralp, O., Acikgöz, S., Tüten, N., Ekmekci, H., Schild-Suhren, M., Malik, E., Tüten, A. La Clinica Terapeutica, 171(6),2020

Objective

To evaluate the possible associations between serum endocan levels and endometriosis.

Study Design

A total of 60 women with histologically proven endometriosis and 40 women who underwent laparoscopy due to unexplained infertility without endometriosis were evaluated in a case-control study. Serum endocan, CA125, CA19.9, and CA15.3 levels were measured. Demographic, clinical, and laboratory parameters were compared.

Results

There was no significant difference between the groups regarding age, body-mass-index, parity, and serum CRP and WBC levels. Serum endocan (p<0.001), CA125 (p<0.001), CA19.9 (p=0.022) and CA15.3 (p=0.013) levels were significantly higher in the endometriosis group compared to the control group. The correlation analysis showed that serum endocan level was positively correlated with the stage of the disease, CRP, and WBC, but not with remaining parameters, age, BMI, dysmenorrhea score, CA125, CA19.9, and CA15.3. Serum CA125 can predict endometriosis (Cut off=26.2 IU/mL, AUC=0.955) with a sensitivity of 89% and specificity of 88%. Serum endocan can predict endometriosis (Cut off=454 ng/mL AUC=0.749) with a 93% sensitivity and 61% specificity.

Conclusion

The serum endocan levels were significantly elevated in women with endometriosis compared to the control group. Serum endocan can predict endometriosis with a sensitivity of 93% and specificity of 61%

6. Colorectal invasion of endometriosis

Ozdemir, H., Ozdemir, Z. U., Gul, M. O. Annals of Medical Research, 27(10), 2020

Abstract

Aim: Endometriosis is a common gynecological disorder affecting women of reproductive age. The localization and stage of endometriosis determine the clinical course of the disease. In this study, colorectal invasion in endometriosis cases were evaluated retrospectively.

Material and Methods: Between January 2011 and December 2019, female patients aged 18-60 that had undertaken colonoscopy examinations, appendectomies, colorectal resections and bowel shave was performed to remove mass in the intestinal wall. All results were evaluated retrospectively. After histopathological examinations, the results obtained, including findings of endometriosis were included in the study.

Results: The mean age of patients was found to be 41.78±2.03. 30078 patients who had colonoscopy and rectosigmoidoscopy only two endometriosis was found(0.06%). Five out of 554 colorectal resection specimens (0.9%) and 8 out of 1516 appendectomy specimens were detected with endometriosis. Endometriosis was detected in 3 other cases with an invasive mass on the colon wall during gynecological operations and finally, in one patient holding the entire intestinal system along with the peritoneal surfaces in the abdomen. Altogether 19 cases of endometriosis were detected, 42% was invasion of the appendix tissue (most common) and the rectum being second with 21% most common localization.

Conclusion: Colorectal invasion of the endometriosis is a rare clinical condition. The radiological appearance of the lumen obstruction could be confused with malignancy, cases that have not been diagnosed can visit emergency services with ileus due to lumen obstruction. In these cases surgical treatments are the best treatment option.

7. Abdominal Wall Mass Associated with Endometriosis.

Atak, T., Bozkurt, S., Yener, O., Çoşkun, H. Medical Journal Of Bakırkoy, 7(3), 122-124,2020

Endometriosis is defined as the presence of endometrial tissue outside the uterus. It is mostly localized to the pelvic viscera and the peritoneum in women during the reproductive period. It may also be present in the layers of the abdominal wall after cesarean section or other gynecological operations. Pelvic pain and infertility are frequently observed in patients with endometriosis. We presented four cases that underwent surgery for a mass in the abdominal wall which were histopathologically diagnosed as endometriosis.

8. Determination of PD-1 expression in peripheral blood cells in patients with endometriosis.

Okşaşoğlu, B., Hepokur, C., Misir, S., Yildiz, Ç., Sönmez, G., Yanik, A. Gynecological Endocrinology, 1-5.2020

Abstract

In patients with endometriosis, ectopic endometrial tissues can escape from immune system control and survive in other tissues. The pathophysiology of endometriosis is still not fully understood. In this study, we aimed to clarify the pathophysiology of endometriosis, which is thought to be a benign but infiltrative cancer type, which has many similarities with cancer biology by determining PD-1 expression in patients with endometriosis. In this study, n = 73 cases who underwent surgery or examination at the Obstetrics and Gynecology Clinic of Sivas Cumhuriyet University Faculty of Medicine and diagnosed as endometriosis in the biopsy material taken with the pre-diagnosis of endometriosis constituted the patient group. The control group consisted of n = 64 healthy subjects without concomitant malignancy or chronic inflammatory disease. Venous whole blood samples were obtained from the study groups. PD-1 and PD-L1 levels were determined by the ELISA method from serum and plasma samples. PD-1 gene expression level was determined by RT-PCR. The PD-1 level was found to be approximately 350 ± 150 ng/L and 45 ± 17 ng/L in endometriosis and control group, respectively. While the PD-L1 level was approximately 760 ± 108 ng/L in the patients, this level was 140 ± 14 ng/L in the controls. According to the RT-PCR results, the expression of the PD-1 gene 10 times higher compared to the controls. Conclusion: The identified increase of PD-1 levels and gene expression in endometriosis groups show that immunotherapy may be used in the treatment of endometriosis.

9. Non-invasive diagnosis of endometriosis and moderate-severe endometriosis with serum CA125, endocan, YKL-40, and copeptin quadruple panel.

Guralp, O., Kaya, B., Tüten, N., Kucur, M., Malik, E., Tüten, A. Journal of Obstetrics and Gynaecology, 1-6, 2020

Abstract

Considering the complex pathogenesis of endometriosis, which is associated with many cellular or molecular processes, such as

proliferation, angiogenesis, inflammation, we evaluated the diagnostic value of a quadruple panel of serum markers CA125, endocan, YKL-40 and copeptin, for the prediction of endometriosis and moderate – severe endometriosis. Seventy women with endometriosis and 70 women without endometriosis were evaluated. Serum CA125, endocan, copeptin and YKL-40 levels were significantly increased in women with endometriosis compared to the women without endometriosis and in the minimal – mild endometriosis group compared to the no-endometriosis group. YKL-40, endocan and copeptin levels were significantly increased in the moderate – severe endometriosis group compared to the mild –moderate endometriosis group but the difference in CA125 levels remained non-significant. The quadruple panel score had an AUC of 0.954, a sensitivity of 96.5% and specificity of 84.6% for prediction of moderate – severe endometriosis. Zero or one positive marker had a sensitivity of 91.4% and specificity of 88.57% to rule out endometriosis. In conclusion, a quadruple panel of serum markers-CA125, endocan, YKL-40, and copeptin may be beneficial for the diagnosis of endometriosis and especially moderate – severe endometriosis. Further studies are needed to prove the efficacy of this panel.

Impact statement

What is already known on this subject? Many serum markers including CA125 have been investigated so far and suggested to be associated with endometriosis. However, none of these markers is sensitive and specific enough to diagnose endometriosis. What do the results of this study add? A quadruple panel score (CA125, endocan, YKL-4 and copeptin) had an AUC of 0.954, a sensitivity of 96.5% and specificity of 84.6% for prediction of moderate – severe endometriosis.

What are the implications of these findings for clinical practice and/or further research? A high score may be beneficial to warn the surgeon about the risk of moderate to severe endometriosis if the patient will be operated anyway. A negative test of the quadruple panel may show high odds that there is no endometriosis which may prevent unnecessary surgery

10. Tumour markers and histopathologic features of ovarian endometriotic cysts.

Selcuk, S., Kucukbas, M., Koc, N., Cam, C., Ozkaya, E., Eser, A., Karateke, A. Journal of Obstetrics and Gynaecology, 1-6,2020

Abstract

Endometriosis is one of the most common benign gynaecologic diseases and its clinical presentation is generally ovarian endometrioma. We aimed to assess the association of tumour markers with histopathological structure of ovarian endometriomas to assess their roles in clinical management. Data from 86 women who underwent laparoscopic surgery for ovarian endometrioma were evaluated. The possible risk factors for inadvertently removed normal ovarian parenchyma (IRNOP) during laparoscopic cystectomy and the relationship between tumour markers and histopathologic parameters of ovarian endometrioma were assessed. Age and the depth of penetration of endometrial tissue into the cyst wall showed a significant positive correlation with thickness of IRNOP. There was a significant negative correlation between IRNOP and the thickness of fibrosis on cyst wall. Thickness of fibrosis and the depth of penetration represented significant positive correlations with tumour markers (CA 125, CA 15-3, and CA 19-9), respectively. This is the first study that reveals the association between tumour markers and the histopathologic features of ovarian endometrioma. The outcome of the present study indicated that lower levels of tumour markers may permit a conservative management, rising levels may help in timing of a possible surgical intervention and high levels may help in counselling postoperative outcomes.

Impact statement

What is already known on this subject? Endometriosis is defined as a benign gynaecologic disease, and the vast majority of women who suffer from endometriosis are of reproductive age. Ovarian endometriotic cysts are found in one-fifth to one-half of patients with endometriosis. Laparoscopic cystectomy is accepted as the gold standard for the surgical management of ovarian endometriotic cysts because of the procedure's several clinical advantages, such as lower recurrence and higher pregnancy rates. However, studies have indicated that laparoscopic excision of an ovarian endometrioma capsule could be associated with a reduction in both the ovarian volume and the follicle count.

What do the results of this study add? Our retrospective data indicate that tumour markers may have role in planning the management of ovarian endometriomas.

What are the implications of these findings for clinical practice and/or further research? Low tumour markers levels may permit a conservative management, elevating levels may help in timing of a possible surgical intervention and finally high levels may help in counselling the patient about her possible postoperative outcomes.

11. Do women with endometriosis have increased arterial stiffness?

Kilic D, Guler T, Sevgican CI, Kabukcu C, Buber I, Mehmet K, Arslan M, Attar E, Kilic ID. Kardiol Pol. 2020 ahead of print, 2020

Abstract

Background: Endometriosis is a common gynecological disease, which is associated with systemic inflammation and atherogenic risk markers. Therefore, cardiovascular risk can be increased in women with endometriosis.

Aims: To evaluate arterial stiffness using cardio-ankle vascular index (CAVI) in women with endometriosis and women without

Methods: In this study 44 endometriosis patients and 76 age-matched controls were analyzed. Diagnosis of endometriosis was

made on histopathological or magnetic resonance examination. Arterial stiffness using CAVI were evaluated in the study group with and without endometriosis.

Results: Median age, body mass index and waist circumference were similar between the endometriosis and control group (30.0 [24.25-35.0] years vs. 26.0 [24.0-35.0] years, 23.31 [20.82-24.98] kg/m2 vs. 23.74 [21.13-26.78] kg/m2, and 69.0 [64.0-75.0] cm vs. 72.0 [65.0-81.25] cm, respectively). Median C-reactive protein (CRP) levels were increased in women with endometriosis (0.27 [0.14-0.68] vs. 0.12 [0.06-0.24] mg/dL, P < 0.001). Women with endometriosis and control group showed similar left ventricular (LV) ejection fraction, LV mass index (LVMI), and relative wall thickness. Systolic and diastolic blood pressure (BP) results were comparable between the two groups. Mean CAVI levels in the endometriosis group were higher when compared to controls (5.961 [0.644] vs. 5.554 [0.654]; P = 0.001). Elevated arterial stiffness in endometriosis patients persisted after adjustment for age and LVMI.

Conclusions: In this study, the results suggest that there was increased arterial stiffness in women with endometriosis compared to controls, using CAVI. Physicians should be aware of possible increased cardiovascular risk in these patients.

12. The COVID-19 pandemic and patients with endometriosis: A survey-based study conducted in Turkey. Yalçın Bahat, P., Kaya, C., Selçuki, N. F., Polat, İ., Usta, T., Oral, E. International Journal of Gynecology & Obstetrics, 151(2), 249-252,2020

Abstract

Objective: To apply rapid online surveying to determine the knowledge and perceptions of the COVID-19 pandemic on patients with endometriosis in Turkey.

Methods: An online survey was conducted by the Turkish Endometriosis & Adenomyosis Society and administered to patients with endometriosis who agreed to participate in the study. The survey included 25 questions prepared by an expert committee of four professionals (two gynecologists and two endometriosis specialists).

Results: Of the 290 questionnaires sent out, 261 (90%) were returned. A total of 213 (83.86%) patients reported that they were afraid of having endometriosis-related problems during the pandemic period. In addition, 133 (53.63%) patients thought the management of their endometriosis was affected because of the pandemic.

Conclusion: Clinical studies clearly indicate that endometriosis is a condition associated with high levels of chronic stress. The COVID-19 pandemic has led the public to experience psychological problems such as post-traumatic stress disorder, psychological distress, depression, and anxiety. The majority of patients with endometriosis were afraid of having endometriosis-related problems during the pandemic period. The majority of elective endometriosis surgeries have not been postponed. Patients were highly aware of the pandemic and practiced social distancing and hygiene. Only 4 (1.59%) patients with endometriosis required hospitalization.

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