

# Endometriosis Online Congress

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women with endometriosis

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## *Abstract Book*



## ACCEPTABILITY OF CANNABIDIOL (CBD) AS A POTENTIAL FERTILITY SPARING TREATMENT OPTION FOR WOMEN SUFFERING WITH CHRONIC PELVIC PAIN

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### Abstract

Chronic pelvic pain (CPP) is poorly understood; causative pathology is often not found; and currently available treatment options are limited. Most women with CPP suffer significant psychological, social and economic burden affecting their quality of life.

Cannabidiol (CBD) is a non-psychoactive treatment without fully elucidated analgesic mechanisms. WHO reported CBD may be useful in pain treatment, is well-tolerated, has a good safety profile and low abuse potential. Despite the significant consumer interest (13% of endometriosis sufferers in an Australian survey), available research is limited.

We aimed to determine if CBD is an acceptable treatment option for women with CPP and to elicit information on sufferer's current use of alternative self-management strategies.

### Methods

A voluntary, self-reported, anonymous questionnaire was administered to 200 pre-menopausal women (mean age 32.7 years) with CPP, attending a tertiary gynaecological clinic over a period of 6 months.

### Results

29% of responders claimed to have a diagnosis of endometriosis, 63.5% were not on hormonal treatments, 79.5% took regular analgesia and 53% had not had prior pelvic surgery. 16% were currently taking alternative unprescribed treatments. 13% had tried cannabis (prescribed/illicit) and 15.5% had tried CBD. 16 women specifically said cannabis products had helped alleviate CPP. 82.5% of respondents were willing to try CBD; 70.7% oral, 69.7% a skin patch, 72.3% a balm/gel and 33% a CBD infused tampon. Most women (75.5%) revealed their willingness to take part in a trial involving CBD as a treatment for CPP.

### Conclusions

Most women in our cohort were amenable to test CBD and enthusiastic to take part in further research to ensure efficacy, suitability and safety of CBD as a treatment for CPP. CPP urgently needs novel treatment options, especially those that allow the user to maintain fertility, therefore, CBD may be an acceptable, treatment option with the potential to revolutionise CPP management.

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## ART OF STIMULATION PROTOCOL OF INFERTILITY WITH ENDOMETRIOSIS PATIENT

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### Abstract

Endometriosis is a progressive disease with 20-40% incidence. The patients of endometriosis are poor responders to gonadotropin stimulation. The stimulation protocols need to be optimally planned to achieve good pregnancy rates. The controlled ovarian stimulation in these cases is done in an extremely judicious manner and best option would be to perform a tailor made stimulation or individualized stimulation protocol.

Intrauterine insemination is best suited for patients with Grade I & grade II endometriosis. The outcomes are better when IUI is combined with ovarian stimulation with Letrozole, Clomiphene citrate or Gonadotropins. Best results are when controlled ovarian stimulation with Gonadotropins, triggering with HCG along with monitoring is performed.

Infertile women with endometriosis had substantially lower success with IVF compared with tubal factor infertility, including lower ovarian response, reduced implantation rate and pregnancy rate. In addition, a more advanced disease is related to increasingly inferior outcome.

In two more recent meta-analyses on outcome of IVF in endometriosis, live birth rate was found to be similar in minimal/mild endometriosis and other indications for IVF, whereas in patients with moderate/severe endometriosis, the results were inferior, including fewer oocytes retrieved, lower implantation rate, and lower birth rate.

In vitro fertilization is performed using GnRh analogues, agonists or antagonists. It's observed that the average number of oocytes retrieved was higher in the agonist group compared to the antagonist group; there is higher pregnancy rate and number of embryos in the antagonist group compared to the agonist group in low AMH group. IVF gives encouraging results in endometriosis and is one of the best options for infertility, in selected cases.

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## ASSESSMENT OF QUALITY OF LIFE AND PSYCHOLOGICAL REPERCUSSIONS IN WOMEN WITH ENDOMETRIOSIS ACCORDING TO PAIN INTENSITY

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### Abstract

#### Introduction

Endometriosis is a chronic, inflammatory, estrogen-dependent disease, which is characterized by the presence of endometrial, glandular, and/or stromal tissue outside the uterine cavity. The incidence of endometriosis among women in menacme ranges from 6% to 10%. Symptoms vary, and include pain and infertility, with a significant impact on women's quality of life in the physical, psychological, social, and sexual spheres. In this context, depression and anxiety are strongly associated with endometriosis in women. Globally, endometriosis affects women's quality of life (QoL) and sexual function, both physically and emotionally. Thus, this study aimed to assess the QoL, anxiety, and depression in women with endometriosis, in addition to correlating these parameters with the intensity of pain.

#### Material and Methods

This multicenter cross-sectional study was conducted on 102 women with endometriosis from 2017 to 2020. The women were divided into two groups according to the pain intensity: group 1 (high pain, 62 women) and group 2 (low pain, 40 women). The Endometriosis Health Profile Questionnaire, Beck Anxiety Inventory, and Beck Depression Inventory were used to assess the quality of life and levels of anxiety and depression, respectively.

#### Results

Women in group 1 had a mean age of  $33.89 \pm 5.71$  years, while it was  $33.85 \pm 5.60$  years in group 2 ( $p=0.953$ ). In both groups, most women had deep endometriosis and were undergoing treatment, but group 2 had a longer treatment time ( $p=0.044$ ). Group 1 exhibited more depression and anxiety than group 2 ( $17.1 \pm 9.98$  vs.  $11.15 \pm 9.25$ ,  $p=0.003$  and  $23.71 \pm 12.92$  vs.  $12.58 \pm 10.53$ ,  $p=0.001$ , respectively). Women with high pain had a significantly worse quality of life than those with low pain ( $48.88 \pm 16.02$  vs.  $23.32 \pm 15.93$ ,  $p<0.001$ ).

#### Conclusion

Women with endometriosis and high pain intensity have a worse quality of life, and more severe levels of anxiety and depression.

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# COMPARISON OF DIENOGEST VERSUS ORAL CONTRACEPTIVE USE IN THE MEDICAL TREATMENT OF ENDOMETRIOSIS WITH QUALITY OF LIFE SCALE SF-36 MEASUREMENTS AND CA-125/AMH LEVEL; A COHORT STUDY

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## Abstract

### Objective

In our study, we aim to compare the effectiveness of oral contraceptive treatments and dionegegest, primarily by considering the quality of life scale, and secondarily to compare the treatments by considering the Ca125 and AMH values.

### Study Design

Clinical and examination findings (Gynecological examinations and TVUSG and/or TRUSG and/or TAUSG evaluations) evaluated based on ESHRE and ASRM Guideline criteria are compatible with endometrioma/endometriosis, or a previous laparotomy/laparoscopic surgery pathology result is compatible with endometrioma/endometriosis, and patients whose pelvic MRI imaging report was compatible with endometrioma/endometriosis were selected. Among the patients who were recommended medical treatment instead of surgical treatment, patients selected as Dionegegest 2mg + Ethinylestradiol 0.03 mg (Dienelle) treatment were considered as group 1, and patients deemed suitable for treatment with 2mg Dionegegest (Visanne) were considered group 2. Pre-treatment Ca-125/AMH values and quality of life assessments were recorded with the SF-36 quality of life scale.

### Results

There was no significant difference between drug groups in terms of Education Status, BMI, Family History, Smoking, Alcohol consumption, age, age at menarche, menstruation pattern, duration of menstruation, infertility, gestational status, job loss due to pain complaints, operation, and MRI findings ( $p>0.05$ ). There was no significant difference between the drug groups regarding the quality of life before and after treatment. ( $p>0.05$ ). There was no significant difference between drug groups in terms of TVUSG, CA125, AMH findings. ( $p>0.05$ ).

### Conclusion

Evaluating the data we have, the efficacy and success of the two treatment protocols were the same. It seems more logical to prefer cost-effective OC treatments with a low side-effect profile instead of high-cost DNG. Following the guidelines accepted step therapy in treating mild or moderate endometriosis, cyclic OC may be recommended as first-line therapy.

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## DEEP INFILTRATIVE ENDOMETRIOSIS IN THE BLADDER, SURGICAL RESECTION BY LAPAROSCOPY. CASE REPORT AND REVIEW OF THE LITERATURE

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### Abstract

#### Background

Bladder endometriosis is a rare urological disease that usually appears in women of childbearing age due to endometrial ectopic tissue growing at the expense of estrogens.

#### Clinical Case

36-year-old nulligesta patient with five years of primary infertility and disabling primary dysmenorrhea, with pain (8/10) and analgesic intake (not specified) during menstruation; mild dysuria at the onset of micturition and 5 x 1 nocturia and dyschezia. On bimanual pelvic examination a lump was palpated towards the right adnexa, mobile, approximately 5 cm. The left adnexa were not palpated. The endovaginal ultrasound described a cyst in the right ovary, with hyperechogenic contents with a “ground glass” image, measuring 5.5 x 3.5 x 3.5 x 3 cm. An ovarian endometrioma was suspected. Surgical laparoscopy was proposed based on the suspicion of deep and infiltrative endometriosis.

#### Conclusion

Cases of bladder endometriosis are rare; its treatment is still debated. Treatment is surgical. It is relevant to keep in mind this disease in women with a history of urinary symptoms of hematuria, dysuria, dyspareunia and disabling dysmenorrhea.

#### Keywords

Bladder endometriosis; Urological disease; Endometrial ectopic tissue; Estrogens; Dysmenorrhea; Dyspareunia; Gynecological examination; Dysuria; Laparoscopy

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## DIAGNOSING ENDOMETRIOSIS USING ARTIFICIAL INTELLIGENCE ON ULTRASOUND

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### Abstract

#### Introduction

Endometriosis is a non-malignant process that affects more than 11% of American women 15-44. It causes severe dysmenorrhea, dyspareunia, and chronic pelvic pain. Because 30-50% of women with endometriosis are infertile, there is a significant need to diagnose patients early. While the current gold standard for diagnosis is laparoscopy with tissue diagnosis, ultrasound detection would provide a safer, more cost-effective diagnostic tool than surgery and/or MRI. We aimed to 1) evaluate the feasibility of diagnosing endometriosis via ultrasound; 2) investigate the accuracy of AI in the diagnosis of endometriosis.

#### Methods

In this IRB-approved study, two groups of 50 subjects (50 normal and 50 with diagnosed endometriosis) were defined. The endometriosis group included subjects > 21 years old, diagnosed with endometriosis via laparoscopy or laparotomy, and assessed via transabdominal and transvaginal ultrasounds at Rutgers. The normal group met the same criteria except for the diagnosis of endometriosis. Subjects who had undergone hysterectomies or oophorectomies were excluded. A multitask neural network was evaluated on both sets of ultrasounds. All proposed networks were trained for 50 epochs using the early stopping technique to avoid overfitting, a learning rate of 0.001 for the first epoch, and a learning rate decay of 0.1 every 15 epochs with mini-batches of size 32. All images were normalized to have zero mean and unit variance and resized to the suitable size for each network during training. All techniques were implemented in Python using the Pytorch framework.

#### Results

Three neural network algorithms, EfficientNetB2 (AUC=0.8278), ResNet50 (AUC=0.8219), and DenseNet121 (AUC=0.8457) were used to detect endometriosis. To improve accuracy, number of images was increased via data augmentation, improving AUC values (EfficientNetB2=0.8758, ResNet50=0.8839, DenseNet121=0.8995).

#### Conclusions

Many clinical applications have successfully analyzed ultrasound images using multitask neural networks. Our pilot study successfully detects endometriosis. We expect to identify early-stage endometriosis via a similar approach, which would reduce the need for diagnostic laparoscopy. Future work includes increasing the cohort size to validate results and developing our own multitask algorithm to improve prediction quality.

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## DIFFERENCES IN INTENSITY AND QUALITY OF BOWEL SYMPTOMS IN PATIENTS WITH COLORECTAL ENDOMETRIOSIS: A CASE-CONTROL STUDY

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### Abstract

#### Purpose

Patients suffering from colorectal deep endometriosis (DE) experience gastrointestinal symptoms with almost the same frequency as gynaecological pain symptoms. Preoperatively existing gastrointestinal symptoms may translate into pathological Gastrointestinal Quality of Life Index (GIQLI) and Low Anterior Resection Syndrome scores (LARS). This prospective questionnaire-based case control study aims to assess the prevalence of gastrointestinal complaints reflected by changes in LARS and GIQLI scores in patients with colorectal deep endometriosis prior to surgical treatment and compare those to a healthy control group.

#### Methods

The study was conducted at tertiary referral centre for endometriosis, Department of Gynaecology of the Hospital St. John of God in Vienna, Austria and included a total of 97 patients with histologically confirmed colorectal DE with radical surgical treatment and 96 women in which DE was excluded via transvaginal sonography by an expert sonographer or visually during a previous caesarean section within 12 months of inclusion. Gastrointestinal symptoms reflected by LARS and GIQLI scores were evaluated presurgically and in controls.

#### Results

A total of 193 premenopausal patients were included in this study. A mean GIQLI of  $90.7 \pm 22.0$  and  $129.4 \pm 11.1$  was observed among patients and controls, respectively, showing a significantly higher morbidity concerning gastrointestinal symptoms and decreased quality of life (QoL) compared to healthy controls ( $p < .001$ ). The LARS score results demonstrated that 18.6% of the patients with bowel DE presented with a major LARS and 27,8% with a minor LARS presurgically compared to 2.1% and 9.4% of control patients ( $p < .001$ ).

#### Conclusion

Patients with colorectal DE experience a high intensity and quality of gastrointestinal symptoms translating into a decreased QoL and pathological GIQLI and LARS scores already presurgically. As a consequence, these instruments should be interpreted with caution in a postoperative setting and should routinely be evaluated presurgically in order to evaluate baseline values of changes in bowel function in women undergoing colorectal surgery for DE.

#### Keywords

Endometriosis, deep endometriosis, low anterior resection syndrome (LARS), gastrointestinal quality of life index (GIQLI)

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## DIFFERENT SEGMENTAL RESECTION TECHNIQUES AND SURGICAL OUTCOMES IN PATIENTS WITH COLORECTAL ENDOMETRIOSIS: A COMPREHENSIVE REVIEW OF THE LITERATURE

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### Abstract

#### Introduction

Segmental resection (SR) for colorectal endometriosis includes different surgical variations. The present work aims to analyze the available literature to assess the possible effects of different segmental resection techniques on surgical outcomes.

#### Materials and Methods

Pubmed, Clinical Trials.gov, Cochrane Library, and Web of Science were comprehensively searched from 1997 to 2021 in order to perform a systematic review. The MESH terms "bowel endometriosis", "colorectal endometriosis" combined with "segmental resection", 'colorectal resection', "radical surgery" and 'treatment', 'outcomes', 'complications' were utilized, combining terms with the search functions "AND" and "OR". Studies including patients undergoing SR for colorectal endometriosis including adequate follow-up, data on early-late postoperative complications, postoperative sequelae, and the recurrence rate of endometriosis were enrolled in this review. Selected articles were divided in two groups: Nerve-sparing resection (NSR), and conventional SR not otherwise specified (SRNOS). When sufficient data were available, subgroup analyses according to different surgical techniques, artery and nerve sparing (ANSR) and NSR was performed to compare the outcomes of both techniques.

#### Results

A total of 7549 patients, represented across 63 studies were included in the data analysis. In total, 22 studies, including 2543 patients reported on outcomes of NSR and the remaining 41 publications comprising 5006 patients failed to mention the preservation of neither the nerve nor arteries (SRNOS). 8 studies in the NSR group including 424 patients reported on also sparing arteries with the nerves reported the use of ANSR technique. The mean size of the resected DE lesions and patients' BMI were comparable among the 2 groups. A mean of  $3.6 \pm 4\%$  of rectovaginal fistula development (RVF) was reported in patients who underwent SR compared to  $1.5 \pm 1.3\%$  and  $2.3 \pm 2.7\%$  in SRNOS and NSR, respectively. Anastomotic leakage rates varied from 0% to 3.2% and in ANSR and NSR cohorts 0% to 8% versus patients undergoing SRNOS 0% to 8.6%. Urinary retention and long-term bladder catheterization were frequently reported in ANSR and NSR. There was insufficient information about pain or the recurrence rates in the 2 groups.

#### Conclusion

Current data on different SR techniques are inhomogenous and not sufficient to reach a conclusion regarding a possible advantage of one technique over the other.

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## ENDOMETRIOSIS: A PROBABILITY IN CUTANEOUS FISTULA

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### Abstract

Extra-pelvic endometriosis is a rare clinical condition. Utero cutaneous fistula is a communication between the endometrial cavity and the skin. Tubo cutaneous fistula is a communication between the fallopian tube and the skin. These are rare forms of extra pelvic endometriosis requiring surgical treatment.

### Case reports

We report 2 cases of cutaneous fistula. Case 1 was a 32 year old patient with a utero - cutaneous fistula with continuous dull aching pain since three years aggravated during menstrual cycle with a visual analogue score (VAS) of pain of 9. MRI showed an endometriotic utero cutaneous fistula, connecting from the endometrium to the abdominal wall. Case 2 was a 28 year old with a right tubocutaneous fistula with right pelvic mass with cyclical pain (VAS of 10 ) and swelling since 1 year.

### Results

Case one was treated with an en - block excision of the fistula tract from the endometrium to the abdominal wall. She had peritoneal and superficial endometriosis and is on medical management with continuous oral contraceptive pills for 1 year. In case two, right salpingectomy with excision of the bladder nodule and excision of fistula tract was performed. Both patients had a history of a cesarian delivery without any postoperative complications.

### Conclusion

The standard treatment in such cases is surgical excision of the lesion within safe margins. Long term follow up and hormonal therapy may be required in preventing recurrence of endometriosis.

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## ENDOMETRIOSIS OF THE VERMIFORM APPENDIX SIMULATING AN ACUTE APPENDICITIS

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### Abstract

#### Introduction

Endometriosis of the vermiform appendix is a rare condition, defined as the presence of ectopic endometrial tissues located in the walls of the appendix. According to the literature, the body of the appendix is affected in 56%, without mucous membrane involvement. There is a high incidence of association with uterine fibroids and menstrual dysfunction, especially in women of reproductive age.

#### Clinical Case

A 22-year-old patient was admitted to the Surgery Unit. The onset of the disease was characterized by acute, sharp pain in the right lower abdomen, accompanied by vomiting and anorexia during the last two days. Gynecological history was complicated by irregular menstrual cycles, especially during the last year. The patient administrated hormonal treatment due to infertility during the last year. General exam determined fever 37.5°C and fatigue. The patient was hemodynamically stable. The exam of the abdomen revealed muscular defense and pain in the right lower abdomen. Kohler, Rowzing, and Bartomier-Michelson symptoms were positive. A vaginal exam determined tenderness and pain in the right lower quadrant, absence of ovarian tumors, painless posterior fornix, and moderate vaginal discharge. Leukocytosis, as well as imaging changes, confirmed the diagnosis of acute appendicitis. An appendectomy was performed. The slightly congested, 8.0x0.5 cm vermiform appendix was found; a 1.5 cm tumor was seen in the distal part, mobile, with a recent blood clot, limited to serous; with the intact mucosal epithelium. A small amount of hemorrhagic fluid was found in the pelvis. The specimen was sent for pathology evaluation. The histopathological exam showed ectopic endometrial glands, with thickened stroma, in the subserosal and muscular layers; hemorrhage in the appendix body; the inflammatory reaction in the walls of the appendix was ruled out. The patient recovered without complications; the acute abdominal symptoms disappeared. Abdominal pain has recurred due to the association of genital endometriosis (in ovaries, fallopian tubes).

#### Conclusions

Appendiceal endometriosis is a rare condition, difficult to diagnose relying only on a clinical approach. The histopathological exam confirms the condition, in the absence of an inflammatory reaction in the appendix walls. The association of genital endometriosis requires gynecological treatment and follow-up.

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## INCREASED LEVELS OF INTERLEUKIN-18 IN FOLLICULAR FLUID FROM WOMEN WITH ENDOMETRIOSIS

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### Abstract

#### Introduction

Women with endometriosis have been shown to present poor fertilization and oocyte cleavage rates. The mechanisms are unclear but it may be related to impaired oocyte function, possibly due to an inflammatory milieu in the pelvis of these women. The NLR family member leucine rich repeat and pyrin domain containing 3 (NLRP3) forms the NLRP3 inflammasome that mediates innate immune responses via IL-1 $\beta$  and IL-18 and participates in a variety of inflammatory conditions. IL-18 is a pro-inflammatory cytokine that is structurally similar to IL-1 $\beta$  and strongly induces a Th1 response.

#### Objective

The aim of this study was to examine whether follicular fluid (FF) and granulosa cells (GCs) from women with endometriosis (n=14) deviated with respect to production of the inflammatory cytokine interleukin (IL)-18 compared with granulosa cells from women, undergoing IVF for male or tubal infertility (n=10).

#### Material and Methods

GCs were obtained from FF collected at the time of oocyte retrieval from women undergoing for IVF. The IL-18 levels were investigated by enzyme-linked immunosorbent assay (ELISA) and quantitative real-time PCR (qRT-PCR) in FF and GCs, respectively.

#### Results

The basal production of IL-18 cytokine was higher in cells from women with endometriosis when compared to controls in FF ( $p < 0.05$ ). No statistically significant differences in mRNA expression level of IL-18 in the GCs.

#### Conclusions

It suggests that the higher amounts of follicular IL-18 are not dependent of GCs production. Whether aberrant cytokine IL-18 in FF from women with endometriosis may disturb fertilizing capacity of oocytes requires study.

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# INDEPENDENT COMPLEXATION OF CURCUMIN WITH COPPER AND NICKEL ENHANCES ANTIOXIDANT ACTIVITY, INDUCES SELECTIVE CYTOTOXICITY AND IMPROVES CELLULAR UPTAKE IN OVARIAN ENDOMETRIOSIS DERIVED STROMAL CELLS

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## Abstract

### Introduction

Endometriosis, a multifactorial endometrial disorder, affects approximately 7-10% of women in their reproductive age and is generally associated with 30%-50% infertility. The current treatment options, surgical intervention and medical management, are primarily associated with limitations such as high recurrence rate, and adverse side effects that restrict their long-term use in women desiring pregnancy. An urgent need for the development of newer therapeutic options with minimal side-effects is, therefore, well realized. Curcumin, a promising multifaceted nutraceutical, successfully targets the intricate pathological network involved in the progression of endometriosis. However, clinical use of curcumin is limited due to its low systemic bioavailability and hydrolytic instability. It is evidenced that complexation of curcumin with transition metal addresses these challenges by influencing the physiochemical and biological properties of curcumin molecule, thereby making metallo-curcumin complexes an ideal therapeutic agent. Thus, the present study attempts to investigate the effect of conjugation of different transition metals (Copper, Zinc, Iron, Manganese and Nickel) with curcumin on stability, antioxidant activity, cytotoxicity and cellular uptake in endometriotic stromal cells.

### Methods

Multi-spectroscopic investigations were carried out to characterize the synthesized complexes and evaluate their stability, antioxidant and hemocompatible behavior. In addition, primary endometrial stromal cells were isolated from endometrial biopsies collected from infertile patients with and without ovarian endometriosis. The concentration and time dependent effects of the metallo-curcumin complexes on cellular proliferation, morphology and uptake were examined using flow cytometry and microscopic techniques.

### Results

Copper and nickel-curcumin complexes exhibited significantly higher stability, and antioxidant activity in comparison with the parent curcumin molecule and other metallo-curcumin complexes. In addition, both these complexes showed selective toxicity and uptake as indicated by decreased proliferation, altered morphology and time dependent cellular accumulation in endometriotic stromal cells. The mechanism of uptake was found to be energy dependent active transport indicating the potential role of metal transporters in cellular uptake of these complexes in endometriotic stromal cells.

### Conclusion

Copper-curcumin and nickel-curcumin complexes seem promising as anti-endometriotic agents and warrant further mechanistic investigation in preclinical models.

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### Abstract

One of the most common forms of endometriosis is the ovarian endometrioma. The adverse effect of surgical treatment of ovarian endometriosis to ovarian reserve is well understood and reported in the literature.

**The aim of the study** was to compare the efficacy and safety of ovarian endometrioma treatment for maintaining ovarian reserve using PRP-therapy in laparoscopy and transvaginal sclerotherapy.

The study included 71 women of reproductive age: 20 women (I) underwent sclerotherapy under sonographic control followed by PRP injection into ovarian tissue. 21 women (II) underwent laparoscopic cystectomy followed by PRP injection. 30 women underwent laparoscopic cystectomy (C). In patients before surgery and 3, 6 months after surgery were estimated AMH and calculated antral follicle count (AFC).

### Results

Before surgery, values of AMH and AFC did not differ between the groups. AMH of group I in 3 and 6 months after surgery remained almost unchanged. In group II, AMH first decreased and after 6 months increased almost to the initial level. In group C, its indicators decreased by 1.7 ( $p<0.001$ ) and 1.86 ( $p<0.001$ ) folds, respectively. After 3 months median of AMH in the groups I and II was 1.49 and 1.46 folds respectively higher than in the group C and after 6 months by 1.6 and 1.5 folds, respectively. After 3 months AFC was practically not changed  $p=0.53$  in group I. After 6 months it increased from the initial level  $p=0.0078$ . After 3 months was observed decreasing of AFC of group II  $p<0.001$ , and after 6 months it had recovered to the initial values  $p=0.21$ . In group C, its indicator after 3 months decreased almost 2 folds  $p<0.001$ , and in the repeated measurement on the 6th month it also remained in smaller quantities than the initial numbers  $p<0.001$ .

### Conclusions

The use of sclerotherapy in combination with PRP-therapy for ovarian endometriomas improves the ovarian reserve values, in comparison with the classical laparoscopic stripping of endometriomas. And the combination of the use of laparoscopic excision of the endometrioma with PRP-therapy makes it possible to save ovarian reserve than when PRP-therapy is not used.

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## NEW ALGORITHM FOR CHOOSING TREATMENT TACTICS FOR PATIENTS WITH EXTERNAL GENITAL ENDOMETRIOSIS INCLUDING mircoRNA let-7

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<sup>1</sup>Dr. Pokrovenko

### Abstract

For the first time the molecular genetic marker such as let-7 mircoRNA was included in the complex of examination of women with external genital endometriosis and a new algorithm was used to select the optimal treatment tactics for patients with this pathology. The proposed algorithm of diagnosis and treatment allowed to preserve the ovarian reserve in women of reproductive age by reducing and optimizing the methods of surgery, the use of modern approaches in the field of IVF. Mann-Whitney analysis showed a significant difference in let-7 microRNA levels between groups of patients with endometriosis and patients in the control group. At the same time, another representative biomarker miRNA mir-9 in a similar analysis did not give a statistically significant difference. The median value of let-7 microRNA was 4.43, when analyzing the mean values of the indicator and comparing endometriosis group 1 (mild and moderate) and endometriosis group 2 (moderate and severe endometriosis), we obtained an average value of 3.96 in the latter group, thus the indicator let-7 "4" was chosen for use in the new algorithm. To test the effectiveness of the algorithm, a study was conducted on 32 women with EGE, treatment tactics were determined taking into account the indicator of a new biomarker (group 3, n = 32). Results compared with the group of patients with EGE in the main part of the study, all women from whom underwent laparoscopic treatment (group 1 + 2, n = 64). A statistically significant difference between these groups was found in the indicator "Time to treatment" ( $p = 0.001$ ). After that, the results of treatment in both groups were evaluated. In group 1 + 2, due to the fact that all patients had the surgical treatment, we noted a decrease in ovarian reserve -AMH and AFC in 1.8 times, which is a negative fact. To comparing the results before and after treatment in the test group of the algorithm there was no difference in ovarian reserve due to reduced frequency of surgical treatment, use of modified sclerotherapy techniques and ART methods, while the effect of treatment as a significant difference in pain intensity was achieved.

### Full name of each author followed by their COI

Prof. Mikhailo Medvediev

## NON PUERPERAL LACTATION INDUCTION: A VIABLE OPTION

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### Abstract

#### Introduction

Breastfeeding and developing mother-infant relationship is big challenge in surrogate pregnancy. Though protocols for lactation induction were proposed long back, very few reports are published. We present a case of successful lactation induction in genetic mother who was able to breastfeed her biological child after pregnancy by surrogacy.

#### Material and Methods

Genetic mother was case of adenomyosis and endometriosis and suffered recurrent implantation failure. Lactation was induced with help of hormonal therapy, pharmacological and non-pharmacological galactagogues, mechanical nipple stimulation and continuous motivation for the purpose. The protocol was started when surrogate mother reached 28 weeks of gestation.

#### Results

Genetic mother was given low dose combined oral contraceptive pills (COPs) once daily continuously and tablet Domperidone 10 mg three times a day which was increased to 20 mg three times a day. Her breasts became heavy and increased in size as per her. COPs stopped when surrogate host reached 34 weeks. By this time genetic mother had spontaneous milk secretions from breast. Following withdrawal bleeding, the genetic mother was explained to add natural non-pharmacological galactagogues along with same dose of domperidone and to start pumping both the breasts each for 5-7 minutes every 3 hours during daytime. When surrogate host reached 36 weeks pregnancy, genetic mother was advised breast pumping at least once at night time also. By this time she was able to pump 4-5 spoons of milk. Her serum prolactin levels were 90 ng/ml.

#### Conclusions

Lactation induction can be a viable option even in non-puerperal mothers who want to give benefits of breastmilk to their infants.

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Rashmi Vohra

## **SERUM PROLACTIN LEVEL FOR EARLY PREDECTION OF PRECANCEROUS AND ENDOMETRIAL CARCINOMA IN CASES OF PERIMENOPAUSAL AND POSTMENOPAUSAL ABNORMAL UTERINE BLEEDING**

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### **Abstract**

#### **Introduction**

Endometrial adenocarcinoma is the most common malignant neoplasm of the female genital tract comprising 6% of female cancers. Aim of the work: To develop a risk prediction model to see is there role of serum prolactin level and early prediction of precancerous and endometrial carcinoma in perimenopausal and postmenopausal abnormal uterine bleeding.

#### **Material and Method**

This study was conducted on 200 Patients referred to one of the participating centres because suffering of perimenopausal and postmenopausal bleeding. 100 cases with perimenopausal bleeding and 100 cases with postmenopausal abnormal uterine bleeding.

#### **Results**

In our study age distribution of premenopausal patients is mostly between 40-45 years (60%) and age distribution of postmenopausal patients is between 50-55 years (70%). Most of the perimenopausal patients in the study multiparous (95%) and the same in postmenopausal patients in the study multiparous (93%).

#### **Conclusion**

The level of prolactin varies according to the type of AUB. Majority of the participants had prolactin level within the normal range. Around 25% of the participants had prolactin level above normal level in perimenopausal patients and 16% of postmenopausal patients.

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## STANDARDISATION OF THE SUTURING TECHNIQUE OF LAPAROSCOPIC ADENOMYOMECTOMY WITH “T” SHAPED INCISION

Kade, Sandesh<sup>1</sup>

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### Abstract

The appropriate surgical treatment of adenomyosis remains still a subject of debate.

There have been no attempts of standardizing the technique of laparoscopic suturing which according to us is the most significant factor in avoiding future antenatal rupture in subsequent pregnancy.

Incision is T shaped or inverted T shaped. The flaps have to be tailored to have at least 0.5 cm thickness under the serosa. As the technique of suturing is not standardised, we often find that many surgeons struggle to complete the job. The closure demands more reconstruction than just mere approximation. The incision converts

The operative site into two triangular and one horizontal flap. These flaps need to be overlapped and compactly sutured to offset the lost muscle layer and reconstruct the uterus.

Standardised steps of suturing:

We always use barbed suture because it exerts uniform tension on the suture line due to the helical placement of barbs along the long axis of suture and aids compact suturing. We always perform contralateral suturing in which the natural axis of driving the needle is from right side to left.

Step 1 – horizontal arm of T incision is closed first from right to left side of the incision. Care should be taken to prevent dead space. This is the easiest of all steps.

Step 2 – technique of suturing or overlapping the left flap so as to partially cover the first layer in lower half and raw wound in upper part. The left flap in lower part gets sutured to the serosal surface of horizontal flap by few sutures and then the sutures pass through the raw adenomyoma bed and flap compactly press and avoid dead space.

The left flap suturing ends with a final step passing through the apex and passing it under the right flap from inside out.

Step 3 – overlapping the right flap so as to cover left triangular flap in upper part and horizontal flap in lower part.

### Conclusion

Standardising the steps makes surgery predictable, duplicatable, easy, safe, and effective.

### Full name of each author followed by their COI

Sandesh Kade N/A

## THE CHANCES OF HAVING A CHILD IN PATIENTS WITH ENDOMETRIOSIS UNDERGOING A BIOPSYCHOSOCIAL TREATMENT APPROACH (SINOSOMATICS)

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### Abstract

#### Introduction

Patients with endometriosis are considered to have reduced chances to deliver a baby.

#### Objective

To evaluate the cumulative live birth rate (CLBR) of patients with endometriosis treated with a biopsychosocial approach (Sinosomatics).

#### Methods

Subgroup analysis of 72 patients with confirmed endometriosis from our registry of 212 patients who started treatment with Sinosomatics for infertility between 2014 and 2016, with follow-up through May 2020. Sinosomatics combines psychotherapy with somatosensory stimulation (acupuncture, moxibustion, cupping), herbs and nutritional supplements. Fertility treatment was provided by ART specialists, as needed. Data on diagnosis, history of infertility, prior ART treatments, mode of conception, and pregnancy outcome were prospectively documented.

#### Results

At enrollment, the mean age of patients was 35.1 years ( $\pm 4.2$  SD) and the mean duration of infertility was  $4.5 \pm 3$  years. As per May 2020, 61 women (85%) became pregnant at least once. Overall, 51 out of 72 women (71%) delivered a healthy baby, among them 19 out of 24 patients (79%) without prior IVF and 32 out of 48 patients (67%) with a history of  $\geq 1$  failed IVF before registry entry (11 out of 19 patients (58%) with  $>4$  failed IVFs). 23 out of 51 live births (45%) followed natural cycle IVF/ICSI, 12 (24%) conventional IVF/ICSI/kryo-conservation, 10 (20%) spontaneous conception, 2 (4%) IUI, and 4 (8%) egg or embryo donation. CLBR including donor cycles was 25 out of 29 (86%) for women  $< 35$  years, 24 out of 32 (75%) for women between 35 and 39 years, and 2 out of 11 (18%) for women  $\geq 40$  years. 2 out of 51 deliveries (4%) were premature, twin rate was 8% ( $n=4$ ). Median time to delivery after starting Sinosomatics was 19 months (IQR, 12 to 28.3).

#### Conclusion

In our previous RCT (Meissner et al., 2016) we demonstrated that a systemic biopsychosocial treatment approach that reorganizes traumatic life experiences can significantly and long-lasting reduce chronic pain in patients with endometriosis. The current analysis of endometriosis patients from our infertility registry adds that up to the age of 40 there is a high chance of having a child even after failed IVF treatment, with pregnancies occurring in 65% after natural cycle IVF/ICSI or spontaneously.

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## THE EFFECT OF ACUPUNCTURE ON DYSMENORRHEA: A SYSTEMATIC REVIEW OF THE LAST 5 YEARS

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### Abstract

#### Introduction

Dysmenorrhea is defined by pain associated with menstruation. With a prevalence rate between 50% and 90%, it can impact daily routines and life quality. 62-75% of adolescents undergoing laparoscopy for chronic pelvic pain and/or dysmenorrhea have been diagnosed with endometriosis. The same happens with 70% of adolescents with pelvic pain that does not improve with non-steroidal anti-inflammatory drugs and/or combined oral contraceptive. If evidence is found on the benefits of acupuncture on the treatment of dysmenorrhea, being a safe therapy with few side effects, acupuncture may be considered as a complementary therapeutic technique.

Possible mechanisms of dysmenorrhea are the hyper-production of uterine prostaglandins, which results in myometrial hypercontractility and arterial vasoconstriction. Acupuncture seems to reduce a variety of pain-related substances released by glial cells such as the proinflammatory cytokines, interleukins and prostaglandins, which might provide the mechanistic background to justify its possible benefits.

The objective is to analyze the literature published on Pubmed which may validate the effect of acupuncture on dysmenorrhea.

#### Material and Methods

The database used was Pubmed-Mesh, and the search was performed using the following keywords with the following search strategy: (("Acupuncture"[Mesh] OR "Acupuncture Therapy"[Mesh] OR "Acupuncture, Ear"[Mesh] OR "Acupuncture Analgesia"[Mesh]) OR "Moxibustion"[Mesh]) AND "Dysmenorrhea"[Mesh]) in January 2022.

#### Results

A total of 7 articles were found and the literature was analyzed and merged.

#### Conclusions

After analyzing the articles found, a consistent decrease in the pain intensity was observed with acupuncture and moxibustion interventions in specific acupuncture points. Furthermore, acupuncture and moxibustion seems to have a long-term effect. According to the available data, acupuncture seems to be a safe intervention and may be considered as a complementary therapeutic technique for dysmenorrhea.

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## THE USE OF DEEP LEARNING IN THE DIAGNOSIS OF ENDOMETRIOSIS

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### Abstract

#### Objectives

The use of artificial intelligence (AI) in obstetrics and gynecology (OB/GYN) is a fast-growing area of research. AI has been more recently used in gynecology in the categorization of endometrial lesions such as endometrial cancers, polyps, hyperplasia, and myomas. The aim of this review is to summarize the types of Machine-Learning which are currently being investigated in obstetrics and gynecology with emphasis in the evaluation of endometriosis.

#### Methods

The NCBI/PMC library was searched using the following terms: “((Deep Learning) OR (Artificial Intelligence)) AND OB/GYN”. A total of 172 articles resulted. The term “Convolutional Neural Network” was added to the search due to its prevalence in the original search. The terms “(Convolutional Neural Networks) AND (endometriosis)” were used to investigate the use of machine-learning in diagnosis of endometriosis, yielding 50 results.

#### Results

Types of AI described for use in obstetrics and gynecology include Artificial Neural Networks (ANN), Convolutional Neural networks (CNN), Deep Residual Learning Frameworks, Dense Connected Convolutional Networks (DCNN), and Fully Convolutional Neural Networks (FCNNs).

Typically, these neural networks have a training phase and testing phase. The training phase consists of feeding pre-labeled or categorized data to an algorithm which then “learns” to classify this data. In the test phase, the algorithm is blind to category and sorts the new images based on what it learned in the training phase. A validated CNN achieved 80.8% accuracy for endometrial lesions. An 86% accuracy was achieved using an FCNN to differentiate fibroid from normal endometrial structures on recorded videos. However, no current research has tried classifying endometriosis lesions except one mention of CNN used in diagnosis of endometriosis.

#### Conclusion

AI, specifically CNN, has shown promise as a clinical tool to aid clinicians in diagnosis and categorization of endometrial tissue. Endometriosis has imaged-based diagnosis such as laparoscopy and ultrasound. These algorithms have potential to be used in diagnosis and/or staging of endometriosis. Further research regarding the feasibility and best machine learning tools is warranted.

#### Full name of each author followed by their COI

Kayla Piiwaa, N/A; Adrian Balica, N/A

## UROLITHINS MODULATE ENDOMETRIOSIS PROGRESSION RELATED GENES IN-VITRO

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### Abstract

#### Objective

Urolithins are a subfamily of metabolites generated by the human intestinal microbiota from ellagitannins and Ellagic Acid, which are polyphenols mainly found in red fruits. In previous studies, it has been demonstrated that they have anti-inflammatory, anticancer, antioxidant, antimicrobial and antiestrogenic effects. Moreover, we demonstrated the anti-proliferative, anti-migratory, anti-invasive and pro-apoptotic effects of Urolithin A (UA) and urolithin B (UB) in endometriosis *in-vivo* and *in-vitro*. In addition, it is well known that angiogenesis is one of the mayor process involved in endometriotic lesions establishment and progression. Taking these data into account, the aim of the present work was to evaluate the effect of UA and UB on the expression of a variety of genes related to angiogenesis, migration and invasion *in-vitro*.

#### Material and Methods

12z endometriotic cells were stimulated with UA, UB or vehicle (Basal) or with culture media alone (Control) for 24 h. Afterwards, cells were collected, total RNA was extracted and gene expression was analyzed by quantitative real time RT-PCR using Taq-Man probes.

#### Results

UA decreased the expression of VEGF, RHOJ, IL1B, FGF2 and IL6 pro-angiogenic and proinflammatory genes ( $p<0.05$ ) while UB only diminished RHOJ and IL1B expression ( $p<0.05$ ). Neither UA nor UB caused significant changes on HIF1a expression. In addition, UA decreased the expression of CD44 and CDH2 ( $p<0.05$ ) but had no effect on CDH1 expression while UB had no significant effect on CD44, CDH1 and CDH2 levels.

#### Conclusion

These results suggest that UA would have antiangiogenic effects on endometriotic lesions since it diminishes the expression of proangiogenic factors on endometriotic cells. Also UA anti-invasive and anti-migratory effects could be mediated by CDH2 and CD44 down regulation in endometriotic cells. In conclusion, Urolithins would be a promising therapy for endometriosis being UA a better choice than UB.

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## USE OF PROBIOTICS IN ENDOMETRIOSIS PATIENTS: SYSTEMATIC REVIEW

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### Abstract

Over the years, the perception of consider the upper female reproductive tract including uterus, fallopian tubes and ovaries, as sterile environment has fundamentally changed. The uterine cavity contains a large quantity of microorganism; this microbiota seems to play a decisive role in reproductive outcomes and diseases like endometriosis. Frequently, imbalances occur in microbiota composition, known as dysbiosis, compromising immunosurveillance and modifying immune cell profiles. Progressively, this immune dysregulation might progress into a chronic state of inflammation contributing to the pathogenesis of endometriosis, an increasingly common problem in the female population.

A healthy vagina microbiota is defined by *Lactobacillus* presence, reason why endometriotic microbiota has been consistently associated with diminished *Lactobacillus* dominance, as well as an elevated quantity of bacterial vaginosis-related bacteria and other opportunistic pathogens.

In the last years, the administration of probiotics is continuously progressing due to its capacity of modulate dysbiosis of the microbiota. Most of clinical trials have been carried out using oral probiotics even though achieving the correct impact in reproductive tract was difficult because of this implies that probiotics must resist to the low pH of the upper gastrointestinal region. According to this, the use of vaginal probiotics became popular by allowing a direct and targeted colonizing action to restore the altered vaginal microbiota.

The main objective of this work was to present a compilation of the results of different recent studies in which the clinical impact of probiotics in endometriosis patients was analysed to report the beneficial effects of probiotics related to the restoration of healthy microbiome. These studies might allocate future focus on customizing the administration of probiotics as nutraceutical treatment in endometrial disorders.

### Full name of each author followed by their COI

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