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Superior hypogastric plexus block as an effective treatment method for endometriosis-related chronic pelvic pain: an open-label pilot clinical trial

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ABSTRACT
We aimed to investigate the effect of superior hypogastric plexus (SHP) block on pain relief and quality of life of patients with refractory endometriosis. Sixteen patients with refractory endometriosis underwent SHP block. The outcome measures included visual analogue scale (VAS) for chronic pelvic pain, VAS for dysmenorrhoea, and VAS for dyspareunia. The short-form endometriosis health profile (EHP-5) was used to measure quality of life. All the outcome measures were evaluated at weeks 0, 1, 4, 12 and 24. The mean baseline VAS scores significantly improved after the SHP block ($p < .001$ for all). The mean overall EHP-5 score also significantly improved from $54.3 \pm 18.2$ to $24.6 \pm 13.3$ ($p < .001$). The positive effects of SHP were not diminished over time. No serious adverse effect was noticed in any of the patients. Preliminary results suggest that SHP block could be used as an effective method in pain control and improvement of quality of life in refractory endometriosis.

IMPACT STATEMENT
What is already known on this subject? Safety and efficacy of SHP block in the treatment of CPP has been revealed in earlier investigations. However, the efficacy of SHP block for pain management in patients with refractory endometriosis has not been investigated in earlier investigations.

What do the results of this study add? SHP block is an effective method for pain control and improvement of quality of life in patients with refractory endometriosis. The positive effects of this treatment did not diminish over 24-weeks follow-up of the study. No serious adverse effect was noticed in any of the patients.

What are the implications of these findings for clinical practice and/or further research? Preliminary results suggest that SHP block could be used safely and effectively for controlling pain and improvement of quality of life in patients with refractory endometriosis.

Introduction
Endometriosis is identified as one of the most common and debilitating diseases of women in reproductive ages (Mishra et al. 2015). It is detected in 25–50% of infertile women (Missmer et al. 2004; Meuleman et al. 2009), which is 6–21 times higher than fertile women (Rawson 1991; Louis et al. 2011). Moreover, endometriosis is found in 45–82% of females with chronic pelvic pain (CPP; Missmer and Cramer 2004; Sun-Wei and Wang 2006). The impact of endometriosis on the quality of life of affected patients is significant, which is the results of the pain experience (dysmenorrhea, dyspareunia, CPP), as well as psychological stress and depression caused by endometriosis-associated infertility (Jones et al. 2004b).

Several types of therapy are available for pain control in endometriosis. Certain painkillers have demonstrated to be effective for the reduction of endometriosis pain by inhibiting prostaglandin synthesis and suppressing the inflammatory response (Allen et al. 2017). Dienogest and other hormonal therapy are commonly used for suppression of ovulation and reduction of peripheral oestrogen synthesis. It has been revealed that 2 mg daily dienogest effectively alleviates the endometriosis-associated pain, reduces endometriotic lesions, and improves the quality of life of the patients (Schindler 2011). Surgical removal of the lesion and restoration of the pelvic floor could be regarded as an adjunct to medical therapy in the management of endometriosis-associated pain (Zanelotti and Decherney 2017). However, endometriosis could be resistant to treatment in a considerable number of...
patients, and research continues to find new therapeutic options to treat refractory endometriosis (Verma and Konje 2009) effectively.

The superior hypogastric plexus (SHP), as a retroperitoneal structure, is located bilaterally between the fifth lumbar and the first sacral vertebra in a sacral promontory. This network innervates the pelvic floor and genitalia through the nerves of hypogastric plexus that is the main cause of pelvic pain (Jones and Rock 2015). Safety and efficacy of SHP block have been reported in the treatment of CPP, especially in patients with pelvic cancers and secondary dysmenorrhea (Plancarte et al. 1997; Yang et al. 2018). However, the efficacy of SHP block in pain management in patients with refractory endometriosis has not been investigated in earlier investigations. In this study, we aimed to evaluate the effect of SHP block on pain and quality of life of patients with refractory endometriosis who were irresponsible to medication therapy.

**Patients and methods**

This study was approved by the ethics committee of our institute under the code of IR.IUMS.REC.1396.29814. The protocol of trial was registered in the Iranian Registry of Clinical Trial (ID: IRCT2017082923684N3). All patients signed a copy of the informed consent form.

In an open-label pilot clinical trial, patients with the confirmed diagnosis of endometriosis according to the criteria of the world endometriosis society (Johnson et al. 2017) and no response to surgical and medical treatments were included in the study. The ‘no response’ was defined as no reduction in endometriosis-associated pain, increased pain, or pain recurrence after treatment cessation. The inclusion criteria were the age of between 18 and 45 years, stage IV of endometriosis (score of 40 based on the American Society of Reproductive Medicine scoring system) confirmed by laparoscopy, mean visual analogue scale (VAS) of ≥5, and at least 3 months past the date of last medical treatment. Patients with pelvic inflammatory disease, irritable bowel syndrome, fibroids and adenomyosis, urinary problems, and coagulation disorders were excluded from the study. Before the enrolment, the presence of endometriosis, such as ovarian and deep infiltrating lesion, was identified by gynaecological clinical examinations and imaging analysis using transvaginal Doppler ultrasound.

**Intervention procedure**

All the procedures were done by a pain group composed of a pain specialist and an interventional radiologist. First of all, the expected outcome and potential complications were fully explained to the patients. In the operation setting, the patient was placed in a prone position. Then, a peripheral venous catheter was inserted, and sedative drug (fentanyl and midazolam) was administered. Subsequently, a nasal oxygen cannula was implicated in monitoring the vital signs of the patients. The skin was marked 7 cm from the middle line on both sides. Local anaesthesia using 1% lidocaine, two 22G 15-cm needles (Dr Japan Co., Tokyo, Japan), were inserted from both sides under fluoroscopic guidance. The needle tips were located at the junction of the L5 and S1 vertebral bodies in the lateral fluoroscopic view (Figure 1(A)). After negative blood aspiration, 3 ml of contrast solution was injected. The smooth posterior line at the anterolateral margin of the vertebral bodies in the lateral view and paramedian region in the anteroposterior view was confirmed the proper positioning of needles (Figure 1(B,C)). Then, 10 ml of bupivacaine (0.25%) along with 40 mg triamcinolone was injected from each needle. The patients left the hospital 2–3 h after the injection and were prescribed to use ibuprofen, if necessary. Preventive hormonal therapy (progesterone pills) was performed during the 24 weeks follow-up of the patients as indicated.

**Outcome measurements**

The effect of SHP block on the pain level of patients with refractory endometriosis was assessed using the evaluation of VAS for CPP, VAS for dysmenorrhea, and VAS for dyspareunia. The Persian translation of short form endometriosis health profile (EHP-5) was used to measure health-related quality of life (HRQol; Goshfateh et al. 2011). The EHP-5 contains 11 four-point scale (0–4) items, including pain, control and powerlessness, emotional well-being, lack of social support, self-image, work, intercourse and worries about infertility, treatment, and relationship with children and medical professionals. The final score is transformed into a 0 (indicating best possible health condition) to 100 (indicating worst possible health condition) scale (Jones et al. 2004a; Goshfateh et al. 2011). All the outcome measures were evaluated before the intervention (week 0) as well as 1, 4, 12 and 24 weeks after the intervention.

**Statistical analysis**

According to the study of Cao et al. the mean baseline VAS score of the patients was 6.4 ± 3.8 which decreased to 0.82 ± 1.5 after complete resection of endometriosis (Cao et al. 2015). Based on these values, a power of 95%, effect size of 1.8, and α error of 0.05, a number of 7 patients was found to be enough to detect a statistically significant difference using a paired t-test. To increase the power of the study we included 16 patients.

We used SPSS for Windows, version 16 (Chicago, IL) for the statistical evaluation of data. Qualitative variables were presented as number and percent. Quantitative data were presented as mean ± standard deviation (SD). Repeated measure analysis of variance (ANOVA) or its nonparametric counterpart (the Friedman test) was used to evaluate the changes of outcome measures over the time. The line charts were demonstrated with Microsoft Excel 2010. A p-value of ≤0.05 was considered statistically significant.

**Results**

The flow diagram of the study is presented in Figure 2. Accordingly, 16 patients were evaluated at the final analysis.
The characteristic features of patients who met the criteria are presented one by one in details in Table 1. The mean age of the patients was 33 ± 5.5, ranging from 26 to 39 years. The mean body mass index (BMI) of the patients was 26.1 ± 3.6 kg/m². Thirteen (81.3%) out of 16 patients were married. The mean number of gravidity was 1.8 ± 1.3. All patients were sexually active.

The mean baseline VAS score for dysmenorrhoea was 8.6 ± 1. The mean VAS score for dysmenorrhoea significantly improved after the SHP block (p < .001) and did not reveal a significant change over time (p = .37; Figure 3(A)). The mean post-treatment VAS score for CPP revealed no remarkable change over time (p = .18; Figure 3(C)).

The mean overall baseline EHP-5 score was 54.3 ± 18.2 before the intervention and 24.6 ± 13.3 after the intervention. This difference was statistically significant (p < .001). The mean post-treatment EHP-5 demonstrated no significant change over time (p = .37; Figure 3(D)).

Adverse effect

Bruising of the injection site was recorded in two (12.5%) of patients that was spontaneously healed. No major side effects such as infection, nerve damage, and bleeding were seen in the present series.

Discussion

A significant number of patients suffering from chronic pain associated with endometriosis are refractory to the available treatment modalities (Pavone and Bulun 2012; Martınez et al. 2013). Considering the significant impact of this pain on the quality of life of the affected patients, the development of safe and effective treatment for pain control in refractory endometriosis is of considerable importance. Although several attempts have been made in this respect (Pavone and Bulun 2012; Bedaiwy et al. 2017), the search for more efficacious treatment options for refractory endometriosis continues.

In this study, we evaluated the effect of SHP block in the management of endometriosis-associated pain in patients who were resistant to conventional therapies. Based on the results, the SHP block significantly improved the CPP, dysmenorrhoea pain, and dyspareunia. The quality of life of the patients was also significantly improved following the SHP block. The positive effects of the SHP block did not diminish over the six months follow-up of the patients. No major side-effect was detected in any of the patients.

Laparoscopic presacral Neurectomy has been extensively investigated as an effective technique for the treatment of chronic pelvic pain in endometriosis and dysmenorrhoea (Kwok et al. 2001; Soysal et al. 2003). However, laparoscopic...
presacral neurectomy is an elective operation requiring surgical skills and expertise. Moreover, it may be associated with vascular and lymphatic complications due to the vicinity of great vessels and lymphatic channels (Chen and Soong 1997).

In 1990, anaesthesiologists showed that transcutaneous neurolysis of the superior hypogastric plexus is an effective and safe technique in relieving pelvic pain (Plancarte et al. 1990). Subsequently, SHP block has been frequently used for the treatment of pelvic pain in a variety of pathologies, including cancer (de Leon-Casasola et al. 1993; Plancarte et al. 1997; Mishra et al. 2008). However, it has been rarely used for the treatment of pelvic pain in endometriosis.

Wechsler et al. evaluated the use of SHP block with computed tomographic (CT) guidance in the management of chronic pelvic pain in five patients with endometriosis. The

Table 1. Characteristic features of patients with refractory endometriosis who met the study criteria.

<table>
<thead>
<tr>
<th>ID</th>
<th>Age (years)</th>
<th>BMI (kg/m²)</th>
<th>Marriage status</th>
<th>Gravidity</th>
<th>VAS for dysmenorrhoea</th>
<th>VAS for dyspareunia</th>
<th>VAS for CPP</th>
<th>EHP-5 score</th>
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</table>

BMI: body mass index; VAS: visual analogue scale; CPP: chronic pelvic pain; EHP: endometriosis health profile.

Figure 3. Comparison of VAS for dysmenorrhoea (A), VAS for dyspareunia (B), VAS for CPP (C), and EHP-5 score (D) of the patients at different time-points using repeated measure ANOVA or Friedman test.
SHP block resulted in mild pain relief in one patient, considerable pain relief in three patients, and complete pain relief in one patient. One procedure was terminated owing to anaesthetic injection into the peritoneal cavity. No other complication was recorded. They concluded that CT-guided SHP block is an easily performed method with a low rate of complications and can be further assessed to find whether it attenuates chronic pelvic pain in endometriosis (Wechsler et al. 1995). Similar to the study of Wechsler et al., the results of the present study reveals the safety and efficacy of SHP block in pelvic pain associated with endometriosis. Wechsler et al. anticipated pain return within three days as would be expected with a temporary nerve block. However, one patient reported two weeks of pain relief, and another reported one month of pain relief. The pain relief lasted at least 6 months in the present study.

Yang et al. used the SHP block for the treatment of 25 patients with refractory secondary dysmenorrhoea. The pain level was significantly decreased after SHP block (from 7.74 to 2.96). The anxiety level and mental health status were significantly improved as well (Yang et al. 2018). Similarly, the results of the present study revealed the significant improvement of dysmenorrhoea pain following the implication of SHP block (from 8.6 to 2.4).

Altogether, the results of the present study reveal that the SHP block could be used as an effective technique for the management of pain in refractory endometriosis. The effect of the SHP block was not attenuated during 6 months follow-up of the patients. These positive effects led to the significant improvement of the quality of life of the affected patients.

The present study was not without limitations. The main limitation of the study was the absence of the control group. The small number of patients could be regarded as the other limitation of this study. Therefore, future high-quality trials are required to confirm the results of this study.

Conclusion

Preliminary data suggest that SHP block could improve the CPP, dysmenorrhoea pain, and dyspareunia pain in patients with refractory endometriosis, thereby improving the quality of life of the patients. The SHP block is associated with no major adverse effects, as well. Therefore, the SHP block could be regarded as a safe and efficacious method for the treatment of refractory endometriosis in patients who are irresponsible to conventional medical and surgical therapies.

Acknowledgement

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Disclosure statement

The authors have no conflicts of interest in this article.

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