Original Article

Does Smoking Affect the Onset Time of Sensory Blocks or the Duration of Motor Blocks in Parturient Women? A Randomized Controlled Trial

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Received: 08-Aug-2022;
Revision: 05-Sep-2022;
Accepted: 27-Sep-2022;
Published: 20-Dec-2022

ABSTRACT

Background: In general, smoking or exposure to secondhand smoke is still common worldwide, and the rate of smoking in women of childbearing age is gradually increasing. Cesarean section rates have been increasing in recent years, and anesthesia guidelines recommend regional anesthesia for cesarean sections. Since nicotine and local anesthetics have different effects on ligand-gated ion channels, smoking may affect spinal anesthesia in pregnant women. **Aim:** The aim of this study was to investigate the effects of smoking on spinal anesthesia, which is applied for cesarean sections in pregnant women. **Patients and Methods:** After approval from the institution's ethics committee, 100 pregnant women were divided into two groups: current smokers (Group S, smoker) (n = 50) and lifelong nonsmokers (Group NS, nonsmoker) (n = 50). The dose of local anesthetic was adjusted according to the height of each patient. After free cerebrospinal fluid flow was observed, all patients were given 20 μμg of fentanyl in 0.05 mg/cm hyperbaric 0.5% bupivacaine within 10 seconds. The onset of sensory and motor block, the duration of sensory and motor block, and the visual analogue scale (VAS) score were monitored. **Results:** Data from 100 parturient women were investigated. Even though the median time required for the onset of sensory block to occur was significantly higher in Group S (P = 0.019), the duration of motor block was found to be shorter (P = 0.003); however, the duration of sensory block was similar in both groups (P = 0.771). VAS scores were significantly higher in Group S (P = 0.001). **Conclusions:** In conclusion, the pregnant women who smoked had longer motor block onset times, shorter motor block durations, higher VAS scores, and lower patient satisfaction levels.

KEYWORDS: *Cesarean section, effectiveness of spinal anesthesia, pregnant women, smoking*

INTRODUCTION

Smoking habits have been an important public health issue. The prevalence rate of smoking any form of tobacco among women of childbearing age is gradually increasing,[1] and smoking or exposure to secondhand smoke is still a common condition worldwide.[2-4]

Cesarean section rates have been increasing in Turkey, and both developed and developing countries.[5] Anesthesia guidelines recommend regional anesthesia for cesarean delivery.[6] Tobacco smoke contains more than 7,000 chemical toxins, including nicotine,[7] which cause many diseases by damaging almost all organ systems.[8,9]

Access this article online

Quick Response Code:

Website: www.njcponline.com

DOI: 10.4103/njcp.njcp_527_22

Nicotine clearly exerts pharmacological and analgesic effects by interacting with nicotinic acetylcholine receptors (nAChRs), which are widely distributed in the central and peripheral nervous systems. Many anesthetic medications, cigarette smoke, and local anesthetic agents act by either modulating or inhibiting nAChR functions.[10,11] After smoking, nicotine diffuses readily

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How to cite this article: Güneş HY, Çalışkan DK, Sakar HA, Yüzkat N. Does smoking affect the onset time of sensory blocks or the duration of motor blocks in parturient women? A randomized controlled trial. Niger J Clin Pract 2022;25:2039-45.

into brain tissues and binds to nAChRs, which are ligand-gated ion channels. When nicotine binds outside the ligand-gated ion channel, the channel opens, allowing the entry of cations such as sodium and calcium.[12] Local anesthetics cross the neural cell membrane and bind to the α subunit of voltage-gated sodium channels. As the sodium channels are blocked, sodium ions cannot influx into cells. Thus, nerve cells cannot generate and conduct nerve impulses, thereby halting the transmission of the advancing wave of depolarization down the length of the nerve. This situation results in sensory and motor blocks.[13] A previous study reported that by opening sodium channels, nicotine allows sodium to enter; therefore, smokers need higher local anesthetic doses to achieve effective anesthesia than nonsmokers.[14]

As the effects of nicotine and local anesthetics on ligand-gated ion channels are different, smoking may affect spinal anesthesia in pregnant women. Thus, our aim in this study was to investigate whether smoking also affects regional anesthesia, particularly spinal anesthesia, in pregnant women.

Methods

This prospective, randomized controlled observational study was approved by the ethics committee (2019/18) of Van Training and Research Hospital. All enrolled patients provided written informed consent.

The study was conducted with 100 patients from September 2019 to July 2020. Patients with an American Society of Anesthesiologists (ASA) status of class I–II, aged between 18 and 45 years, and scheduled to undergo spinal anesthesia for elective cesarean section were included in this study.

The exclusion criteria included the requirement of emergency cesarean section for delivery; ASA class ≥ III; a contraindication for spinal anesthesia; multiple gestations; placental abnormalities such as placental abruption, placenta previa, or adherent placenta; allergy to local anesthetics; height <150 cm; coagulation disorders; and refusal of spinal anesthesia.

In this study, all pregnant women were divided into two groups: Current smokers (group S; n = 50) and lifelong nonsmokers (group NS; n = 50). Group S had smoked for an average of 6–8 hours before the cesarean section. The patients were randomized according to their order of admission to the hospital [Figure 1]. We determined the sample size as follows: In the study, the duration of the motor block (minutes) was considered a primary characteristic. According to previous studies,[15,16] the standard deviation for motor block duration ranged from 12 to 22. Thus, in this study, a standard deviation of 17 was used. In addition, for the 0.05 types, the I error rate, the Z value, and the effect size were assumed to be 1.96 and 5, respectively. On the basis of this information and in accordance with the equation for sample size calculation, the minimum sample size was 45. Therefore, we determined the appropriate number of samples to be 50.

Upon arrival in the operating room, noninvasive blood pressure (BP) monitoring, electrocardiography, and continuous pulse oximetry were commenced, and baseline values were recorded. After the insertion of an intravenous line, all patients were preloaded with a balanced crystalloid solution (8 ml/kg) for 10 minutes before spinal anesthesia was applied. The spinal anesthesia technique was applied with the patients in the sitting position, using a 25-gauge Quincke spinal needle at the L_3–L_4/L_4–L_5 level. The local anesthetic dose was adjusted according to the patient's height (0.05 mg/cm).[17] After free cerebrospinal fluid flow was observed, all patients were given 20 μg fentanyl (0.4 ml; Fentanyl 0.05 mg/ml, Johnson and Johnson, Istanbul, Turkey) in 0.05 mg/cm 0.5% hyperbaric bupivacaine (Marcain Spinal Heavy, AstraZeneca PLC, Istanbul, Turkey) over 10 seconds. The patients were immediately turned to a supine position and tilted to the left by 15°–20° to minimize aortocaval compression. The block height required for a cesarean section was determined by sensory and motor block assessments. The onset and duration of the sensory blockade after the intrathecal administration of local anesthetics were evaluated using a cold-hot test. The onset and duration of motor blockade were evaluated on the basis of the modified Bromage motor blockade score. In this study, the onset of sensory block was defined as the time from the intrathecal injection to the time sensory blockade was achieved at the T12 or higher dermatome level. Sensory block duration was defined as the time of sensory block regression to L1 from the maximum sensory block level. The onset of motor block was defined as the time from intrathecal injection until a modified Bromage scale score of 1 or higher was achieved (modified Bromage scale score: 0 = no motor block [free movement of the legs and feet], 1 = unable to raise the extended leg, able to move the knees and feet, 2 = unable to flex knee but able to move feet, and 3 = complete motor block of the lower limbs (unable to move the legs or feet). Motor block duration was defined as the time of regression until a modified Bromage scale score of 0 was achieved.[18]

After intrathecal local anesthetic administration, hemodynamic parameters and SpO_2 values were recorded at the first (T1), second (T2), third (T3), fourth (T4), fifth (T5), 10th (T6), 15th (T7), 20th (T8), 25th (T9), and 30th minutes (T10). The surgical procedure was started

when the block height required for cesarean section was achieved (T4–T6 dermatome level). All patients were given oxygen at a flow rate of 3 L/min with a face mask. After delivery of the newborn and removal of the placenta, 20 IU of synthetic oxytocin was infused in 1,000 ml of crystalloid fluid. If needed, 0.2 mg of methylergonovine was administered intramuscularly. Patients with discomfort during peritoneal irritation were sedated with fentanyl (50 µg) and/or propofol, and the medications used were recorded. Metoclopramide (10 mg) and ranitidine (50 mg) were administered intravenously to patients with complaints of nausea and vomiting.

A decrease in mean arterial pressure (MAP) by >20% from the baseline or to <65 mmHg in the intraoperative period was considered hypotension, and an intravenous bolus of ephedrine (10 mg) was administered. The amount of ephedrine used during the operation was recorded. When the heart rate (HR) decreased to <50 beats/min, it was considered bradycardia, and 0.5 to 0.75 mg atropine was administered intravenously. A decrease in SpO_2 to <90% was considered low peripheral oxygen saturation, and the amount of oxygen given to the patients by face mask was increased to 4–5 L/min.

Side effects such as nausea, vomiting, headache, chest pain, hypotension, and bradycardia were recorded. The patients' satisfaction levels (scored as not satisfied, less satisfied, and very satisfied) were recorded. The time between the beginning of the surgical incision and the last suture to close the skin was recorded as the operation duration. The patients were informed that the visual analogue scale (VAS) would be used to evaluate the pain they felt preoperatively, intraoperatively, and postoperatively (from 0: no pain to 10: extreme pain). In the postoperative period, if the VAS score was ≥4, 1,000 mg of paracetamol was administered intravenously for analgesia.

Statistical analysis

Descriptive statistics are presented as mean, standard deviation, median, minimum, maximum, frequency, and percentage values. The normality of the variables was evaluated with the Kolmogorov-Smirnov test. Independent-samples t-test and Mann-Whitney U test were used in the analyses of the quantitative data in independent groups. Chi-squared test was used in the analyses of the qualitative data in independent groups, and Fisher's test was used when the Chi-squared test conditions were not met. Statistically, the significance level was considered 5%, and the statistical package for the Social Sciences 27.0 software for Windows was used for all statistical computations.

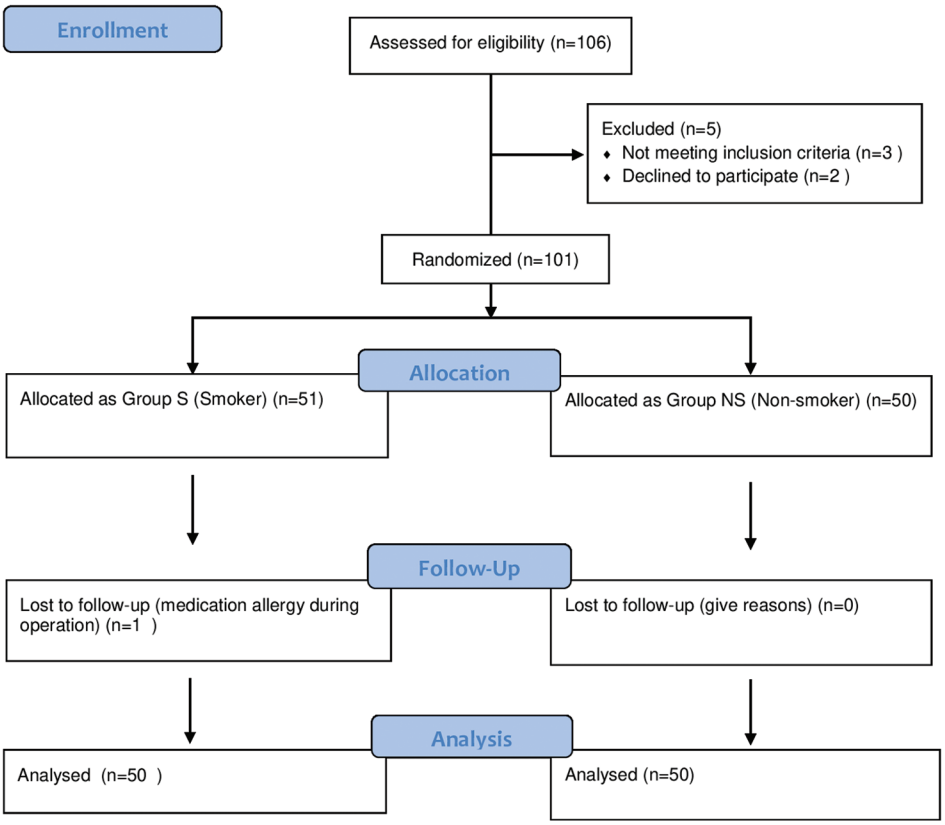

Figure 1: CONSORT diagram

Results

The data from 100 pregnant women were investigated. The demographic data of the groups were similar, and no significant differences were found between the groups [Table 1].

The results on the effectiveness of spinal anesthesia (block onset time and sensory and motor block durations) and VAS scores are shown in Table 2. Even though the median time required for the onset of sensory block was significantly higher in group S (P = 0.019), the motor block duration was shorter (P = 0.003). However, the sensory block duration did not differ between the groups (P = 0.771). The mean

Table 1: Demographic characteristics in groups (mean±SD)

	Group NS		Group S		*P*
	Mean±SD	Median	Mean±SD	Median	
Age (year)	29.7±6.1	30.0	30.5±6.2	31.0	0.478ᵗ
Height (cm)	164.1±5.1	164.0	164.0±5.0	164.0	0.849†
Weight (kg)	72.9±9.8	70.0	76.2±13.6	73.0	0.413†
BMI (kg/m²)	27.0±2.8	26.0	28.2±3.9	26.8	0.149†

Values are mean±standard deviation and medians [interquartile range]. *P<0.05. †Mann–Whitney U-test. ‡Chi-square test. ᵗIndependent sample t-test. SD: standard deviation, BMI: body mass index

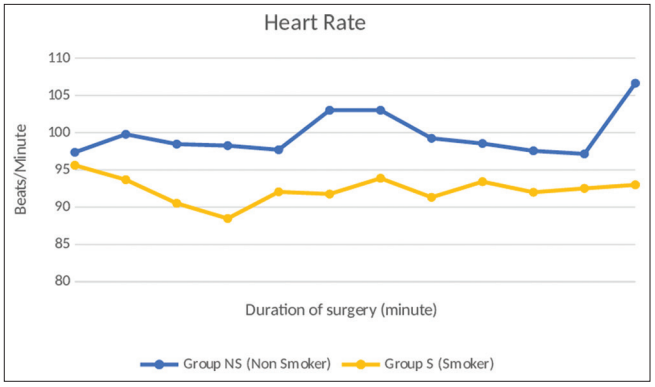

Figure 2: Patient heart rates in groups

Table 2: Efficacy of spinal anesthesia and visual analogue scale (VAS) scores in groups

	Group NS		Group S		*P*
	Mean±SD/*n*%	Median	Mean±SD/*n*%	Median	
Sensory block onset (min.)	3.1±1.0	3.0	4.0±1.9	4.0	0.019*†
Duration of motor block (min.)	167.6±17.7	166.0	153.5±22.3	157.5	0.003*†
Duration of sensory block (min.)	215.9±19.7	212.5	209.6±32.9	215.0	0.771†
Duration of surgery (min.)	33.1±8.7	30.0	32.7±7.1	31.5	0.788†
VAS	1.0±1.2	0.0	2.0±1.8	2.0	0.001*†

Table 3: Additional medication need, cesarean section indications, and side effects data of the groups

	Group NS		Group S		*P*
	Mean±SD/*n*%	Median	Mean±SD/*n*%	Median	
Additional medication need					
Fentanyl (mcg)	7.0±17.5	0.0	14.0±28.6	0.0	0.254†
Propofol (mg)	8.7±20.5	0.0	20.4±41.7	0.0	0.184†
Ephedrine (mg)	7.6±4.9	10.0	9.6±10.3	10.0	0.847†
Indications for C/S					
Old cesarean section	26	52.0%	27	54.0%	0.841‡
Fetal distress	9	18.0%	12	24.0%	0.461‡
Cephalopelvic disproportion	7	14.0%	3	6.0%	0.182‡
Abnormal labor progress	3	6.0%	3	6.0%	1.000‡
Breech presentation	5	10.0%	5	10.0%	1.000‡
Side effects					
Nausea-vomiting					
(−)	27	54.0%	24	48.0%	0.548‡
(+)	23	46.0%	26	52.0%	
Headache					
(−)	39	78.0%	43	86.0%	0.298‡
(+)	11	22.0%	7	14.0%	
Chest pain					
(−)	45	90.0%	43	86.0%	0.538‡
(+)	5	10.0%	7	14.0%	

Values are mean±standard deviation, and median [interquartile range]. *Significant at P<0.05 by ‡Chi-square test. †Mann–Whitney U-test. C/S: cesarean section

Table 4: Spinal anesthesia preferences, patient satisfaction, and educational status data of the groups

	Group NS (*n*%)		Group S (*n*%)		*P*
Spinal anesthesia preferences					
With own request	35	70.0%	38	76.0%	0.499‡
With detailed information	15	30.0%	12	24.0%	
Patient satisfaction					
Not satisfied	1	2.0%	11	22.0%	0.009*‡
Less satisfied	13	26.0%	10	20.0%	
Satisfied	36	72.0%	29	58.0%	
Educational status					
No literacy	21	42.0%	22	44.0%	0.983‡
Primary education	19	38.0%	19	38.0%	
High school	6	12.0%	6	12.0%	
College	4	8.0%	3	6.0%	

Values are *n*%. *Significant at $P<0.05$ by ‡Chi-square test. C/S: cesarean section

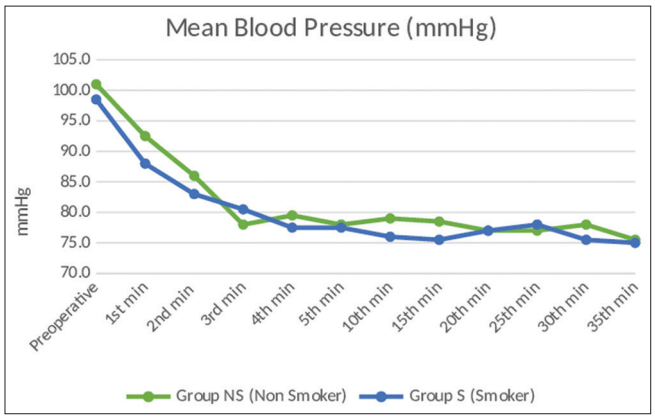

Figure 3: Mean arterial pressure in groups

VAS score in group S was significantly higher than in group NS ($P = 0.001$). The surgery duration was similar between the groups.

No significant differences were found between the groups in terms of the need for additional medication (fentanyl, propofol, and ephedrine), side effects (nausea, vomiting, headache, and chest pain), and spinal anesthesia preferences [Table 3]. The patient satisfaction level was higher in group NS, but the difference was not statistically significant ($P = 0.009$) [Table 4]. The most common indications for cesarean section among the patients were a history of cesarean section or multiple repeat cesarean sections.

The intraoperative HR values in group S were significantly lower than those in group NS ($P < 0.05$; Figure 2). At the 10th and 15th minutes of monitoring, the systolic BPs ($P = 0.020$ and $P = 0.041$, respectively) and diastolic BPs ($P = 0.046$ and $P = 0.027$, respectively) were significantly lower in group S than in group NS [Figure 3]. No significant difference was found between the groups in terms of the BP values measured at other times.

Discussion

The main finding of this study is that group S had longer motor block onset times, shorter motor block durations, lower patient satisfaction levels and HRs, and higher VAS scores than group NS. However, we found that smoking status had no significant effect on the mean BP, sensory block duration, risk of complications, or need for additional medications. We also observed that smoking status did not affect the patients' spinal anesthesia preferences. The literature review conducted for this study revealed that knowledge about whether smoking affects spinal anesthesia in pregnant women is limited.

nAChRs are widely distributed in the central and peripheral nervous systems. Nicotine, an alkaloid, exerts pharmacological and analgesic effects by interacting with nAChRs. Many anesthetic medications, cigarette smoke, and local anesthetic agents act by either modulating or inhibiting nAChR functions. In chronic smokers, tolerance to the effects of nicotine may develop as a result of changes in nAChR quantities or functioning and receptor desensitization due to long-term nicotine exposure.[10] Al-Noori *et al*.[14] investigated the effects of smoking on simple tooth extraction with local anesthesia and found that higher amounts of local anesthetics were needed in patients with toothaches and a history of smoking. A meta-analysis that compared the motor block durations of intrathecally administered ropivacaine and bupivacaine for cesarean section reported that the motor block duration for bupivacaine ranged from 78 to 254 minutes.[19] In our study, the mean motor block duration was 168 minutes in group NS and 154 minutes in group S. The mean motor block onset time was 4 minutes in group S and 3.1 minutes in group NS. nAChR desensitization is known to develop in smokers. Moreover, nicotine, unlike local anesthetics, opens sodium channels. Both conditions may play a role in prolonging the motor block onset time.

The cytochrome P450 enzyme system in the liver plays an important role in the metabolism and easy excretion of drugs from the body.[20] The nicotine and polycyclic aromatic hydrocarbons in cigarette smoke stimulate the cytochrome p450 enzyme system, especially the CYP1A1, CYP1A2, and CYP2E1 isoenzymes. The elimination rates and plasma concentrations of amide-type local anesthetics metabolized by the CYP1A2 and 3A4 isoenzymes in the liver may vary

depending on the cytochrome P450 enzyme level.[21,22] In our study, the motor block duration was shorter in the pregnant women who smoked. This may be due to the rapid decrease in plasma bupivacaine levels induced by the cytochrome P450 enzyme system in these women.

In their study, Aydoğan *et al*.[23] found that exposure to cigarette smoke or passive smoking was associated with increased fentanyl consumption and higher VAS scores in the postoperative period. Smokers have been reported to experience more pain in the postoperative period and tend to develop chronic pain.[24] A retrospective review of patients who underwent coronary artery bypass grafting showed that smokers required 33% more opioids in the first 48 hours after surgery. In addition, women who were smokers needed more opioid analgesia after gynecological surgery than nonsmokers.[10] In our study, the VAS scores of pregnant women who were current smokers were higher than those of lifelong nonsmokers, consistent with reports in the literature.

When a cigarette is smoked, nicotine is easily absorbed through the alveolar membrane, crosses the blood-brain barrier, and enters the cerebral circulation within 20 seconds. It stimulates the nAChR and causes the release of neurotransmitters such as noradrenaline, adrenaline, vasopressin, serotonin, dopamine, and β-endorphin via various secondary messengers.[22] With its sympathomimetic effects, it increases HR, BP, and peripheral vasoconstriction. Nicotine increases oxygen consumption and decreases oxygen delivery. Therefore, it causes hypoxemia in smokers.[25] The oxygen supply-demand balance of the myocardium is adversely affected. However, prolonged exposure to nicotine results in tolerance to many effects of nicotine and decreased stimulant effects.[22] In our study, SpO_2 values did not change significantly according to the smoking status of the patients, and hypoxemia was not observed. We attributed this to the fact that the patients were young and had no comorbidities.

The effects of tobacco consumption on BP and HR may vary, especially in young people. Few studies have reported that tobacco use lowers BP, while others have indicated that it increases BP in adults.[26] Adolescent active smokers have lower BP than nonsmokers or passive smokers.[27,28] Smoking was reported to increase BP in obese adolescents.[29] After excluding factors such as height and body mass index, diastolic BP, mean BP, and HR were found to be lower in adolescents who smoked cigarettes, hookah, or both.[26] Similar studies have determined that BPs were significantly higher in men and women who smoked than nonsmokers.[30] Öztürk *et al*.[31] reported that the mean BP and HR values were higher in active and passive smokers than nonsmokers. In our study, the systolic and diastolic BPs at the 10th and 15th minutes of surgery were significantly lower in the smoking parturients than in the nonsmoking parturients. We think this difference may be due to the tolerance to the sympathomimetic effects of nicotine and the effects of pregnancy-specific hormones and chronic cigarette smoking on the vessel walls.

A previous study reported that smoking significantly increased HR in men but did not make a significant difference in HR in women.[30] In another study, HR was lower in people who smoked cigarettes, hookahs, or both than nonsmokers.[24] In our study, intraoperative HR was significantly lower in the smoking parturients than in the nonsmoking parturients. Our results are consistent with those reported in the literature.

The currently smoking pregnant women included in this study were not classified according to the frequency and duration of their smoking habits. This is considered a limitation of our study. Thus, studies conducted with pregnant women grouped according to their smoking habits are warranted.

Conclusion

In conclusion, the pregnant women who smoked had longer motor block onset times, shorter motor block durations, higher VAS scores, and lower patient satisfaction levels. These results suggest that smoking may change the effectiveness of spinal anesthesia in pregnant women. We believe that different studies are needed on this subject.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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