Phantom limb syndrome induced by combined spinal and epidural anesthesia in patients undergoing elective open gynecological surgery

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Abstract

Background: During regional anesthesia, including combined spinal and epidural anesthesia (CSEA), patients may develop a perceptual alteration of limb position known as phantom limb syndrome (PLS). We aimed to identify factors that influence the PLS onset, to explore whether PLS predisposes to other postoperative symptoms, and to document the relationship between PLS and sensorimotor impairment during recovery.

Methods: Psychological questionnaires for anxiety and depression were completed beforehand, then multimodal tests of sensory and motor function, especially tests of proprioception, were performed regularly afterward. Two hundred participants undergoing elective gynecological surgery under CSEA reported their experiences of PLS and other symptoms using Likert rating scales.

Results: Prolonged preoperative fasting (odds ratio (OR) 2.34; 95% confidence intervals (CI) 1.21–4.52), and surgical history (OR 2.56; 95% CI 1.16–5.62) predisposed to PLS, but patients with more extensive anesthetic histories may be at lower risk (OR 0.57; 95% CI 0.31–1.08). Furthermore, significant correlations were observed between the recovery from PLS and the perception of joint movement within the deafferented area (R = 0.82, P < .01) and motor functions (R = 0.68). PLS increases the chance of experiencing postoperative fatigue, physical discomfort, and emotional upset.

Conclusion: This study is the first to have identified the risk factors for PLS, assessed the relationship between PLS and postoperative sensorimotor impairment, and its influence on postoperative complications.

Abbreviations: CI = confidence intervals, CSEA = combined spinal and epidural anesthesia, OR = odds ratio, PLS = phantom limb syndrome.

Keywords: combined spinal and epidural anesthesia, phantom limb syndrome, postoperative recovery, sensorimotor impairment

1. Introduction

Regional anesthetic techniques are rapidly evolving, and offer several important advantages over general anesthesia for complex patients or for certain surgical procedures. Combined spinal and epidural anesthesia (CSEA), one regional anesthetic technique, combines the rapidity, density, and reliability of a spinal block with the flexibility of continuous epidural anesthesia to extend the duration of analgesia.\textsuperscript{[1]} CSEA is gaining popularity for patients undergoing major surgery below the umbilicus who require prolonged and effective postoperative analgesia, such as hip arthroplasty, hysterectomy, and Cesarean section.\textsuperscript{[2,3]} However, during and after CSEA, patients frequently report a series of abnormal sensations, especially a perceptual alteration of limb position.\textsuperscript{[4]}

The above-mentioned abnormal sensations have been named, perhaps incorrectly, phantom limb syndrome (PLS).\textsuperscript{[5]} as they are reminiscent of the symptoms reported by amputees who still report sensations in their missing limb. PLS is seldom serious nor is it life threatening. Nevertheless, it can be unpleasant and distressing to patients, lengthen the time to recovery and resumption of normal activity, and, in some cases, may increase the intensity of other postoperative symptoms and complications. Therefore, PLS is of importance to all anesthetists and might also be a useful model to study the cortical representation of body schema.\textsuperscript{[6]} Recently, a model has suggested the involvement of an alteration of proprioception and motor functions in the origin of PLS, assisting in the understanding of the phantom limb phenomenon during the onset of brachial plexus block.\textsuperscript{[7]} Kinaesthetic illusions may result from changes in neuronal activity and/or topographic reorganization within the somatosensory cortex. Most studies of PLS during regional anesthesia have concentrated mainly on its onset.\textsuperscript{[5,6]}

This study aims to describe further the phenomenology of PLS induced by CSEA, especially during the recovery period, to explore the preoperative risk factors for the development of PLS, to describe the influence of PLS on postoperative complications
and adverse experiences, and to elucidate the temporal relationship between the sensorimotor impairment and recovery from phantom limb syndrome postoperatively. Our hypotheses were that the development of PLS was influenced by psychological factors before surgery and the physiological status of patients, that PLS could aggravate postoperative side effects, and that the recovery of proprioception could accelerate its disappearance. Proprioception includes arthrokinesis, a sense of joint kinesthesia;[7] and pallaesthesia, a sense of vibration that is usually evaluated using tuning forks.[8,9] To address these questions, we subjected participants to preoperative psychological tests for anxiety and depression, and performed multimodal sensory testing and assessment of motor function regularly after surgery. Participants reported the extent of their experiences of PLS and other postoperative symptoms by means of Likert rating scales.[10]

2. Materials and methods

2.1. Subjects

Of the 245 patients enrolled in the study, 20 patients did not meet the inclusion criteria and 25 were excluded because of alterations in the anesthetic technique or surgical procedure. As a result, a total of 200 consecutive patients were studied. Written informed consent was obtained from the participants. The study was an investigator-initiated, prospective, observational study and was approved by the ethics committee of the Second Affiliated Hospital of Harbin Medical University, China, and was registered in the Chinese Clinical Trial Registry (ChiCTR-TRC-11001344).

The inclusion criteria were as follows: age between 18 and 55 years; the American Society of Anesthesiologists physical status I or II; body mass index 18 to 30 kg m\(^{-2}\); an estimated operation duration of less than 2 hours, and the ability to speak and read Mandarin (because the study documents were written in Mandarin). The exclusion criteria were: the existence of a neurological or psychiatric disease that could influence the objectivity of patients’ reporting of the outcome measures; the contraindications for CSEA; a history of allergic reactions to local anesthetics; and known or suspected drug or alcohol dependency. Standard monitoring was applied to all patients undergoing CSEA. All patients were anesthetized using the same needle-through-needle technique.[11]

2.2. The study procedure

On the morning of surgery, several tests were performed to assess the psychological status of participants in a 30-minute session within an hour of surgery. The extent of anxiety and depression were measured using the State-Trait Anxiety Inventory (STAI)[12] and the Center for Epidemiologic Studies Depression Scale (CES-D Scale).[13] The STAI is a 40-item questionnaire that provides measures of trait (20 items) and state (20 items) anxiety, where higher scores indicate greater anxiety levels. The 20-item CES-D Scale is a short self-report scale that measures symptoms of depression in the general population. On arrival at the operating room, continuous monitoring of electrocardiogram, noninvasive arterial pressure (NIBP), and pulse oximetry (SpO\(_2\)) were initiated. During surgery, Ringer solution (10 mL kg\(^{-1}\)) was administered intravenously, and additional fluids were only administered to replace intraoperative fluid losses. CSE was inserted at the L2 to L3 or L3 to L4 interspace with a 27G pencil-point needle, with the patient in the lateral position, preferably with a median approach. A hyperbaric solution of 0.5% bupivacaine hydrochloride (2.5–3.0 mL, depending on the patient) was injected intrathecally. The patient was placed in the supine position immediately following placement of the epidural catheter.

Sensory function testing (analgesia to pinprick and cold pack) and motor block were assessed every 5 minutes until patients met the requirements for surgery. Adequate motor block was assessed as modified Bromage scale 3 (inability to flex ankle).[14] Patients were excluded from the study if the CSE failed. Patients’ spontaneous reports of perceptual distortions were recorded, before they were prompted and encouraged to describe their sensations throughout the rest of the study period.[15,16] Hypotension, defined as a decrease in systolic pressure 30% from baseline, was treated with intravenous ephedrine 6 mg as often as needed. Epidural dosage (2% lidocaine) was adjusted according to the surgical requirements by the anesthetist.

The following sensory and motor function tests were conducted immediately after surgery and then every 30 minutes for 4 hours: the sensation of pain elicited by pinprick, touch by 10 g nylon yarn, cold and heat by Tip-Therm Thermal Sensitivity Tester (Arno Barthelmes, Zella-Mehlis, Germany); the accuracy of proprioception assessed by arthrokinesis (perception of the mobilization of a joint within the deafferented area) and pallaesthesia (perception of vibration applied at the level of a joint using a tuning fork within the deafferented area); and voluntary movement (modified Bromage scale 3). Also, participants’ subjective experiences of pain intensity, fatigue, nausea, physical discomfort, emotional upset, and PLS were assessed every 30 minutes after surgery for 4 hours.[17] At postoperative follow-up visits 24 and 48 hours after surgery, patients were also asked to report the occurrence of any additional symptoms, for example, bleeding, drowsiness, dizziness, headache, and backache. Patients were instructed to grade all symptoms numerically on a 5-point Likert scale as nonexistent, mild, moderate, severe, or particularly severe.

2.3. Statistical analysis

All statistical analyses were performed by Statistics Analysis System, version 9.1.3. Sample size calculation was based on the number of independent variables in Logistic regression analysis, at least 10 times of it. Descriptive statistics using median (range) and mean (standard deviation) were used when appropriate. Univariate unconditional logistic regression and multiple stepwise regression analysis (the standard of entry and rejection were both 0.1) were performed to assess the independent contribution of the risk factors for PLS during regional anesthesia. The odds ratio (OR) of each factor was calculated. The 5-point scales of the traditional adverse reactions were analyzed with repeated measures ANOVA. A value of \(P < .05\) was considered statistically significant. The duration of PLS was the dependent variable, and the duration of sensorimotor impairment was the independent variable. Spearman correlation coefficients were calculated as appropriate. The extent of the influence on the dependent variable was evaluated by means of a standardized regression coefficient.

3. Results

3.1. Main characteristics of the patients

Two hundred patients undergoing elective abdominal gynecological surgery under CSEA were prospectively enrolled in the study. Their general characteristics were shown in Table 1.
3.2. Factors influencing PLS during CSEA

We included 16 factors from the 5 major outcomes as the categorical variable in the univariate logistic regression (Table 2). The influence of these factors on PLS was assessed by unconditional logistic regression analysis. The most influential risk factor identified by univariate logistic regression was preoperative fasting time (OR 2.10; 95% confidence intervals (CI) 1.11–3.98). No statistically significant difference was found for any of the other risk factors.

As indicated in Table 2, multiple logistic regression analyses showed that there was a trend toward an increased risk of developing PLS if patients had a more extensive surgical history (OR 2.56; 95% CI 1.16–5.62), and the relationship between preoperative fasting time and increased risk of PLS was still

| Table 1 |
| Main characteristics of the patients (N=200). |

| Age, y | N=200 | N=200 |
|-------|-------|-------|
| Weight, kg | 62 (8.9) | 62 (8.9) |
| Height, cm | 162 (4.5) | 162 (4.5) |
| BMI, kg/m² | 24 (3.1) | 24 (3.1) |
| Duration of surgery, min | 48 (15–120) | 48 (15–120) |
| Puncture interspace | L2–3: 171 | L3–4: 29 |

The values are expressed as mean (range) or mean (SD).

| Table 2 |
| Logistic regression of risk factors (univariate and multiple) of PLS for the 2 groups of patients. |

| Case load performance status (count) | Without PLS | With PLS | OR | 95% CI | P value |
|-------------------------------------|-------------|----------|----|--------|---------|
| Age 18–28 29–40 41–48 49–55 | 3 40 37 10 | 12 37 46 15 | 0.972 | 0.687–1.376 | .05 |
| BMI <18.5 18.5–23.9 24.0–27.9 ≥28 | 5 46 31 8 | 5 49 38 11 | 1.295 | 0.898–1.868 | .05 |
| Psychological states CES-D <15 16–19 ≥20 | 67 10 15 | 72 15 23 | 1.97 | .495–7.849 | .05 |
| SAI <47 ≥47 | 54 31 | 58 38 | 1.80 | .608–5.316 | .05 |
| TAI ≤49 >49 | 87 3 | 103 7 | 1.46 | .405–5.147 | .05 |
| Society States mode of payment Self-paying medical insurance | 24 66 | 26 84 | 1.175 | 0.618–2.323 | .05 |
| Education level primary school junior high school senior high school university and above | 8 26 26 31 | 11 26 44 11 | 1.019 | 0.757–1.371 | .05 |
| Medical history Surgical history None Once Twice and above | 54 32 4 | 59 37 14 | 1.417 | 0.916–2.192 | .05 |
| Anesthesia history None SA GA Both | 56 24 7 3 | 65 33 7 5 | 1.069 | 0.759–1.522 | .05 |
| History of disease Without With | 76 14 | 91 19 | 1.133 | 0.533–2.410 | .05 |
| Preoperative fasting time <12 h ≥12 h | 31 14 | 22 19 | 2.102 | 1.110–3.979 | .0225 |
| Intraoperative conditions (Mean±SD) Single dose of SA (mg) Injection speed of SA, mL/s The time of maximum motor block, min Operating time, min Intraoperative epidural supplement, mL | 13.42±0.96 0.079±0.045 7.73±4.11 46.3±17.87 3.23±4.77 | 13.47±0.90 0.077±0.023 8.53±4.39 46.84±20.64 3.02±4.31 | 1.063 | 0.267 <0.001 <0.001 | .05 .05 .05 |
| Multiple logistic regression of risk factors Standardized estimate | 0.3400 0.2076 0.3177 | 0.785 1.006 0.989 | 1.376 1.129 1.002 | 1.348 1.438 1.053 | .05 .05 .05 |
| P value Surgical history Anesthesia history Preoperative fasting time | 0.0847 | 0.0792 | 0.0213 | .05 .05 .05 |

Results are given as number of patients or mean ± SD.

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PLS = phantom limb syndrome, OR = odds ratio, 95% CI = 95% confidence intervals, BMI = body mass index, CES-D = Center for Epidemiologic Studies Depression, SAI = state anxiety inventory, TAI = test anxiety inventory, SA = spinal anesthesia, GA = general anesthesia, SD = standard deviation.
evident (OR 2.34; 95% CI 1.21–4.52). Participants with an extensive anaesthetic history appeared to have a reduced risk of PLS (OR 0.57; 95% CI 0.31–1.08).

3.3. The influence of PLS on other adverse reactions in the immediate postoperative setting

Patients were divided into 2 groups, depending on whether they experienced PLS or not. Statistical analysis showed that there was no significant difference between the groups in terms of pain intensity (Fig. 1D) and nausea (Fig. 1A). However, there were clear differences ($P < .01$) between the groups in terms of fatigue (Fig. 1B), physical discomfort (Fig. 1E) and emotional upset (Fig. 1C) at some time points. For emotional upset and physical discomfort, these differences were very substantial at the first 4 time points (Fig. 1C and E).

3.4. Relationship between PLS and sensorimotor impairment during postoperative recovery

The average recovery times of PLS and sensorimotor impairment are shown in Table 3, with PLS duration as the dependent

| Sensorimotor impairment | Pallaesthesia | Arthrokinesis | Motor block | Touch | Pin prick | Cold and heat | PLS |
|-------------------------|--------------|---------------|-------------|-------|-----------|--------------|-----|
| Recovery time, min      | 241.80±46.94 | 208.53±50.03  | 233.62±52.95| 217.30±42.16| 302.57±49.16| 355.39±54.61| 208.44±51.00|
| R value                 | 0.69         | 0.82          | 0.68        | 0.68  | 0.59      | 0.60          |     |

Results are given as mean±SD.

PLS = phantom limb syndrome, $R$ value = Pearson correlation coefficient of the relationship between the average recovery time from PLS and sensorimotor impairment of all patients.
variable and sensorimotor impairment as the independent variable. A significant correlation was observed between recovery from PLS and the perception of joint movement within the deafferented area ($R = 0.82, P < .01$, Table 3, Fig. 2B). Moreover, it also coincided with the impairment of pallaesthesia, measured by a tuning fork within the deafferented area ($R = 0.69, P < .01$, Table 3, Fig. 2A), motor block measured by the modified Bromage scale ($R = 0.68$, Table 3, Fig. 2C), and touch ($R = 0.68$, Table 3, Fig. 2D). A weak but significant correlation was found between the recovery time from PLS and impairment of pinprick sensations ($R = 0.59$, Table 3, Fig. 2E), cold and heat ($R = 0.60$, Table 3, Fig. 2F).

4. Discussion

During regional anesthesia, development of a phantom limb sensation is the most common symptom that emerges from a sequence of abnormal sensations that occur during deafferentation, and, as such, merits special attention. The study of PLS may also afford the opportunity to understand better how the brain constructs a body image, and how this image is continuously updated in response to changing sensory inputs. Illusions of position or movement have been studied separately in amputees, in patients with spinal cord or peripheral nerve lesions, and during regional anesthesia. 

A preliminary understanding of the determinants of PLS has been gained by examining patients’ descriptions of the phantom limb’s final position, the abolition of proprioception and the initial position of the anaesthetized limb in the short time after regional anesthesia. Our study is the first to simultaneously discover the factors that influence the onset of PLS, and to assess the relationship between PLS and sensorimotor impairment during postoperative recovery and the influence of PLS on the incidence of postoperative symptoms during recovery.

However, there are some methodological limitations in this study. The main limitation is that the experience of PLS is based partly on patients’ subjective reports. As patients did not always spontaneously report PLS, direct questioning by the investigator may have influenced their replies. This limitation is difficult to overcome, as it is necessary to draw the patient’s perceptual experience of his or her body out of its “natural obscurity.”

Another limitation is that we were unable to describe the relationship between impairment of sensorimotor function and occurrence of PLS during the onset of deafferentation, as a relatively fast-acting local anaesthetic was used that left insufficient time between the onset of the block and the start of surgery. Therefore, we focused on investigating the factors that
influence the experience of PLS and its impact on other symptoms during the postoperative period.

The incidence of phantom limb pain does not appear to be influenced by the reason for the surgery, the gender, age, marital, or socioeconomic status of the patient. In this study, we found the same for PLS, but that preoperative fasting time, anesthesia history, and surgical history may have some influence. Univariate logistic regression analyses revealed that there is only one statistically significant factor (preoperative fasting time, \( P = .0225 \)). Moreover, sample size is slightly small (N = 200) and the number of risk factors (N = 16) is slightly large. Therefore, the inclusion criteria for multiple stepwise regression analysis was appropriately extended to \( P < .1 \), and the OR value of each factor is calculated. Univariate logistic regression analyses showed that the 2 P values for anesthesia history and surgical history were both greater than 0.05, which may be due to confounding factors. Multiple logistic regression analyses showed that surgical history was considered as a risk factor for PLS (OR 2.56; 95% CI 1.16–5.62; \( P = .0847 \)), and anesthesia history was considered a protective factor for PLS (OR 0.57; 95% CI 0.31–1.08; \( P = .0792 \)). If the sample size is expanded in the future, the P value of both anesthesia history and surgical history may be further reduced to below 0.05.

To avoid pulmonary aspiration, fasting after midnight has become standard before elective surgery. Preoperative fasting may affect the body's physiological capacity and may impair the experience of PLS during regional anesthesia. Fasting may cause hypoglycaemia, fluid balance disturbance, and may impair recovery. Our results suggest that a long fasting time increases the probability of the occurrence of PLS, but the mechanism responsible is unclear. Previous studies have shown that a long fasting time may cause increased blood viscosity and hypoglycaemia, predisposing patients to blood clots and peripheral nerve dysfunction by interrupting continuous and adequate oxygen and nutrient supply. There is also evidence that increasing neuronal sodium conductance might produce phantom pain in amputees, and it is possible that prolonged preoperative fasting may affect the body’s physiological capacity to control its external fluid and electrolyte balance. As a result, abnormalities of fluid and electrolyte homeostasis may adversely affect organ function, which may increase the chance of developing PLS.

The vividness of phantoms appears to depend on both cortical magnification as well as the subjective vividness of that part in one's body image prior to deafferentation, which would explain why phantoms occurred more frequently in patients who had undergone more operations. The reactivation of preoperative memories in the phantom has been noted before. The influence of previous anaesthetic history is less clear. Patients who received epidural or spinal anesthesia seem to recall significantly less pain in the week after surgery. The degree of the misperception may be connected with the attention paid by patients to the anaesthetized limb before deafferentation, so anaesthetic history may modulate the subsequent vividness of PLS.

Although modern drug regimens are effective in eliminating pain and improving tolerability of procedures, patients still experience pain, discomfort, nausea, fatigue, and emotional upset after surgery. These complications frequently delay recovery, prolong hospitalization, decrease patient satisfaction, and increase costs. Patient satisfaction is a valuable measure of healthcare outcomes. In this study, it appeared that PLS increased the chance of experiencing postoperative fatigue, physical discomfort, and emotional upset. Therefore, if an intervention could be found to reduce the occurrence of PLS, there might also be wider clinical, social, and economic benefits.

The relationship between impairment of sensorimotor function and occurrence of PLS during regional anesthesia has been described before, with the impairment of proprioception (arthrokinesthesia) playing an important role. Perceptual distortions also appear to be not only restricted to the misperception of position, but also involve the misperception of size and shape of the anaesthetized limb, which is related to the blockade of small diameter sensory fibers. These conclusions were drawn by studying the onset of sensorimotor block, whereas we examined the temporal relationship between the impairment of the different sensorimotor functions and recovery from PLS.

The perception of limb position is influenced by afferent signals from skeletal muscle, and a sensation of illusory motion of a stationary limb can be provoked by vibrating a tendon. Other observations support the dynamic, neuroplastic concept that, the last position of a body part which was perceived by the central nervous system before the onset of regional anaesthetic block becomes the imprinted, proprioceptive memory that overrides any existing fixed, universal “body schema.” These observations support the hypothesis that the abolition of proprioception is involved in the genesis of PLS during regional anesthesia.

In this study, the 16 risk factors for PLS was determined after referring to relevant literature and clinical experiences. Since the patients we selected were patients undergoing elective gynecological surgery, the effect of gender on PLS was not taken into account. Thus, gender and even more factors require further investigation.

In conclusion, this study provides the first description of the factors that influence the experience of PLS during CSEA, the impact of PLS on postoperative adverse reactions, and the relationship between PLS and sensorimotor impairment during postoperative recovery. Our results suggest that the occurrence of PLS might be related to the preoperative fasting time, anesthesia history, and surgical history. Because of its negative impact, measures should be taken to address the risk factors that predispose to PLS. Furthermore, we also confirm the involvement of the impairment of proprioception and motor functions in the origin of this phenomenon. PLS has been fully characterized and future studies can now focus on its cerebral correlates, which could pave the way for future clinical and functional brain imaging studies examining the relationship between peripheral anaesthesia and the plasticity of the brain’s body schema. Thereby, modulation of afferent inputs by regional anesthesia could become a new tool in neurorehabilitation.

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