Transient restless legs syndrome after spinal anesthesia

A prospective study

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Abstract—*Objective:* To assess the incidence and time course of new-onset restless legs syndrome (RLS) after spinal anesthesia. *Methods:* A total of 202 consecutive patients undergoing spinal anesthesia for various types of surgery were prospectively evaluated regarding the presence and severity of RLS symptoms 48 to 72 hours post surgery and after 1 week, 1 month, 3 months, and 6 months. A diagnosis of RLS was made according to the criteria of the International RLS Study Group (IRLSSG), and severity was assessed by the IRLSSG severity scale. *Results:* Of 161 patients without any history of RLS, 8.7% developed first-onset RLS after spinal anesthesia. Symptoms were transient, with a mean duration of 33 ± 30 days. Low mean corpuscular volume and mean corpuscular hemoglobin were associated with the occurrence of new-onset RLS after spinal anesthesia. *Conclusions:* Transient RLS can be induced by spinal anesthesia. The mechanisms by which spinal anesthesia can trigger RLS are unclear but may include deficits in spinal sensorimotor integration in susceptible individuals.

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Restless legs syndrome (RLS) has a prevalence of about 10%.[1-4] At least 42% of patients with primary RLS have a positive family history,[5] indicating a genetic basis. Although a linkage for RLS has been reported on chromosome 12, no specific genetic mutations causing RLS have been identified.[6] RLS pathophysiology involves dopaminergic and possibly opioidergic[7] mechanisms as well as alterations of brain iron metabolism. Neurophysiologic studies have shown disinhibition of motor cortex[8] and hyperexcitability of spinal pathways.[9,10] The latter and several other observations argue for a pathogenetic role of dysfunctional spinal cord circuitry in RLS.

RLS has been found to be associated with structural spinal cord pathology, such as transverse myelitis of different etiologies.[11,12] Single case reports describe severe restless legs symptoms as well as periodic limb movements (PLM), PLM-like dyskinesias, or myoclonic events during[13] and at the end[14-16] of spinal anesthesia.

We examined the possible relationship between RLS and spinal anesthesia by assessing the incidence and time course of new-onset RLS after spinal anesthesia in 202 consecutive patients.

Methods. *Patients.* A total of 202 consecutive patients undergoing spinal anesthesia for various types of surgery at the Department of Anesthesiology of the Innsbruck University Hospital between August 2000 and December 2000 were enrolled in the study. Indications for surgery were orthopedic (n = 90; 32 total hip and 42 total knee arthroplasties, 16 minor orthopedic surgeries such as hallux valgus procedures), gynecologic (n = 80; 72 cesarean sections, 3 cervical cerclages, 3 nonmalignant tumor resections, 2 malignant tumor resections), urologic (n = 28; 21 transurethral prostatic resections due to benign hyperplasia, 7 resections of prostatic or vesicular carcinoma), and vascular/reconstructive procedures (n = 4; 3 peripheral arterial bypass procedures, 1 skin graft).

Spinal anesthesia. Lumbar puncture was performed at the L3-4 intervertebral space. Through a 22-gauge sharp or a 25-gauge pencil point needle, the anesthetic agent was injected into the subarachnoid space by single shot. Anesthetic agents used were bupivacaine 4% (n = 179, mean dose 13.5 ± 2.9 mg) and mepivacaine 0.5% (n = 23, 80 mg single dose). Both are amide local anesthetics and act via blockade of neuronal sodium channels.

Mepivacaine was administered in a 10% glucose solution, bupivacaine without any adjuvant. The 72 patients who underwent cesarean section received bupivacaine together with fentanyl 15 mcg. Vasoconstrictors were not added.

Study design. For the duration of recruitment (5 months) one of the authors (B.F.) regularly contacted the anesthesiologists responsible for the orthopedic, gynecologic, urologic, and reconstructive surgeries of the day, thereby identifying all consecutive patients undergoing surgery in spinal anesthesia.

Patients were first contacted between 48 and 72 hours post surgery and, for all patients consenting to participate, a detailed medical history including prior RLS symptoms as well as current and previous drug exposure was obtained. Data regarding dose and type of anesthetics, position during surgery, and type of surgery were obtained from the anesthesiologic surgery protocol. The presence or

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absence of RLS was assessed using the minimal criteria of the International Restless Legs Syndrome Study Group (IRLSSG).[17] When RLS criteria were met the RLS severity scale was also applied.[18] The IRLSSG severity scale consists of 10 items assessing subjective severity of RLS-related complaints on a scale from 0 to 4, with a maximum score of 40. The scale has recently been validated in a large population.[18] Blood biochemical variables were taken from the patients' case notes and included hemogram before and after surgery, creatinine, urea, iron, ferritin, and transferrin. Serum iron levels were available only for a minority of patients and were therefore not included for further analysis.

Seven days after anesthesia, the second contact was made personally or by telephone. A third interview was performed after 1 month. Patients still reporting RLS symptoms at month 1 were interviewed again after 3 and 6 months. All interviews were performed by a physician trained in the diagnosis and assessment of RLS (B.F.). After discharge from the hospital, the interviews were conducted by telephone.

All patients who had experienced new-onset RLS after spinal anesthesia were reinterviewed after a minimum of 17 months (up to 21 months) post surgery regarding possible recurrence of RLS symptoms.

Statistics. Results are reported as means and SD or 95% confidence intervals. Patients were divided into two groups based on their previous RLS history (negative RLS history, n = 161; and positive RLS history, n = 41). Because of the small number of patients with a positive RLS history, logistic regression analysis was performed in the negative RLS history group only to detect any differences between patients who developed RLS after spinal anesthesia (n = 14) and patients who remained free of RLS symptoms (n = 147). Differences were evaluated univariately for age, sex, type and dose of anesthetic agent (mepivacaine and bupivacaine; doses calculated separately for each), pregnancy, and blood biochemical variables. Calculations of sensitivity and specificity at different cutoff points of mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) were performed, using optimal cutoff values determined by receiver operating characteristics (ROC) curve analysis. The positive predictive values (PPV) were calculated for the optimal cutoff value in the ROC curve according to the Bayesian formula.

SPSS 10.0 for Windows (Chicago, IL) was used for all statistical analyses. p Values < 0.05 were considered to indicate statistical significance.

Results. A total of 202 consecutive patients (58 men, 144 women, mean age 53 ± 20.2 years) contacted agreed to participate and were included in the study. Of the 144 women, 75 were pregnant (37% of the sample). Forty-one patients had pre-existent RLS (20.3%) according to IRLSSG criteria (17 of 75 [22.7%] pregnant women, 19 of 69 [27.5%] nonpregnant women, 5 of 58 [8.6%] men).

In 161 patients there was no evidence of pre-existing RLS symptoms. Of these, 14 (8.7%) developed RLS after spinal anesthesia (3 of 58 [5.2%] pregnant women, 8 of 50 [16%] nonpregnant women, 3 of 53 [5.7%] men). The onset of RLS symptoms occurred a mean of 7.3 days (95% CI 4.0 to 10.6) after spinal anesthesia. In one patient, new onset RLS symptoms started immediately when the effect of spinal anesthesia was waning; another one first noticed RLS symptoms 18 days after surgery. Mean scores of the IRLSSG severity scale[18] were 15.6 ± 6.3 (range 7 to 27). RLS was transitory in all 14 patients with a mean duration of 33 days (95% CI 15.4 to 50.4). The time course of RLS after spinal anesthesia is shown in the figure.

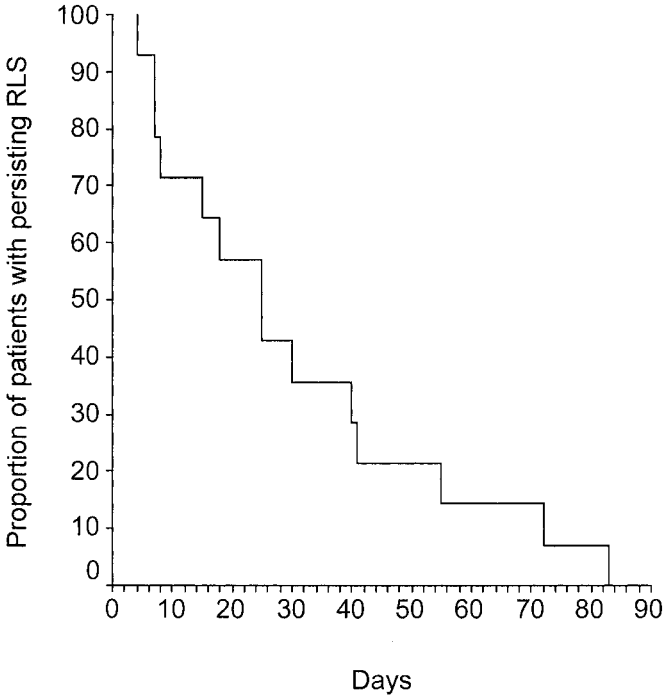

Figure. Kaplan-Meier plot illustrates duration of new-onset restless legs syndrome (RLS) after spinal anesthesia.

None of these patients had a positive family history for RLS and 13 were available for follow-up interviews after a mean of 19.2 ± 1.11 (range 17 to 21) months. None of them reported any symptoms suggestive of recurrence of RLS during the period since the previous interview. Post lumbar puncture headaches occurred in 14 of the 202 patients (6.9%). There was no correlation between post lumbar puncture headaches and RLS.

Logistic regression analysis revealed associations between a low MCH and low MCV and the occurrence of first-onset RLS. In new-onset RLS cases, MCV was 8.74 fL, vs 90.8 fL in patients who remained free of RLS (OR 0.855, 95% CI 0.75 to 0.98, $p = 0.014$). MCH was 28.9 pg vs 30.3 pg (OR 0.635, 95% CI 0.45 to 0.90, $p = 0.013$).

The optimal cutoff level with an area under the curve of 0.71 for MCV and 0.72 for MCH to discriminate between new-onset RLS and no RLS after spinal anesthesia was 89.6 fL for MCV (with 75% sensitivity and 63% specificity) and 29.5 pg for MCH (with 58% sensitivity and 70% specificity). The PPV was 16% for both optimal cutoff levels (MCV and MCH), indicating that these are not primary or critical determinants of whether a patient will develop RLS after spinal anesthesia.

No significant correlation was found with other blood biochemical variables (hemoglobin, hematocrit, total erythrocyte count, creatinine, urea) or sex, age, position during surgery, pregnancy, or anesthetic agent or dose.

Discussion. In this prospective study, new-onset RLS was found in 8.7% of patients without any his-

tory of RLS undergoing surgery in spinal anesthesia. Percentages were higher in women than in men, but logistic regression analysis did not corroborate correlations between post spinal anesthesia RLS and sex. The mean delay between spinal anesthesia and RLS was 7.3 days, and symptoms persisted for a mean of 33 days. These findings suggest that transitory RLS is more common than post lumbar puncture headache, which is a well-recognized complication after spinal anesthesia.[19]

The mechanisms of induction of delayed onset RLS by spinal anesthesia are unclear, but may include changes in sensorimotor spinal integration persisting after spinal anesthesia in susceptible individuals. Abnormalities of the spinal flexor reflex have been noted in neurophysiologic studies of patients with idiopathic RLS[9] and a number of reports have described symptomatic RLS in patients with different spinal pathologies.[11,12] Preoperative low MCV and MCH were correlated with postanesthetic RLS in this study, indicating a possibility of iron deficiency as a susceptibility factor.[20]

Previous case reports have described RLS- or PLM-like symptoms occurring toward the end of spinal anesthesia.[14-16] A delayed occurrence of RLS symptoms after the end of anesthesia has not been previously reported. One possible explanation for the delay is the fact that during the postoperative phase most patients received systemic opiate analgesics, which are also an effective treatment for RLS,[21] and might have prevented RLS from becoming manifest earlier.

Because our study did not have a surgical control group undergoing general anesthesia we cannot definitely exclude that bed rest or pain-associated sleep deprivation contributed to the occurrence of RLS. However, there is no evidence in the literature suggesting that these factors by themselves would be sufficient to induce new-onset RLS. It is unlikely that unrecognized RLS had been present in the 14 individuals who developed RLS symptoms after spinal anesthesia, because none of them reported recurrence of RLS over a mean follow-up time period of 19 months after anesthesia.

The RLS prevalence of 20.3% before surgery in our study population is higher than in previous studies.[1-4] The high proportion of pregnant women (37% in our sample) may have contributed to this finding.[22,23] Other service-based studies on RLS have also reported much higher prevalences[24] than community-based studies,[1-4] presumably owing to a higher proportion of cases with symptomatic RLS.

The incidence of spinal anesthesia–associated transitory RLS in this study was higher than that of post lumbar puncture headache. The risk of developing transitory RLS should be discussed with patients undergoing spinal anesthesia.

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