# Effects of analgesic and antiemetic treatment for postoperative nocturnal sleep deprivation in patients with hemifacial spasm: A prospective preliminary study

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**Research Article**

**Keywords:** Hemifacial spasm, postoperative nocturnal sleep deprivation, analgesic and antiemetic treatment

**Posted Date:** March 16th, 2022

**DOI:** https://doi.org/10.21203/rs.3.rs-1403023/v1

# Abstract

Poor sleep combined with the stress of surgery negatively influences postoperative recovery. Thus far, information is quite limited regarding the sleep quality of patients with hemifacial spasm (HFS) after microvascular decompression (MVD) surgery. This study aimed to investigate the prevalence and causal factors of postoperative nocturnal sleep deprivation (PONSD) in patients with HFS after MVD surgery, and to assess the therapeutic effect of interventions targeted to the main causal factors. Thirty patients with HFS (control group) were interviewed. Data were collected on the self-reported night sleep quality and main causal factors of PONSD after MVD surgery. A separate intervention group of 18 patients with HFS received treatment after MVD surgery that was targeted to these causal factors, and the therapeutic effects were assessed. The main causes of PONSD for patients in the control group were pain, nausea, and emesis. An analgesic and antiemetic treatment reduced fragmented sleep, but also reduced effective sleep. For patients with HFS, the main causes of nocturnal sleep deprivation after MVD surgery were pain, nausea, and emesis, related to the effects of surgery. Analgesic and antiemetic treatment did not satisfactorily improve the quality of sleep for these patient.


# Introduction

Sleep is a condition of partial unconsciousness, characterized by reductions in responsiveness, motor activity, and metabolism, from which an individual can be aroused by stimulation.[1] It is well known that a normal sleep pattern is important to maintain and recover mind and body.[2] Sleep deprivation is defined as inadequate total sleep, which impairs attention, memory, learning, and decision-making. The effects of sleep deprivation in surgical patients are potentially dangerous.[3] Sleep deprivation leads to repletion of cellular glycogen stores and oxidant production, and promotes the generation of pro-inflammatory cytokines, all of which contribute to poor postoperative recovery.[3,4] Most patients after major surgery experience pronounced impairment in their sleep architecture and quality.[5] Poor sleep combined with the stress of surgery negatively influences postoperative restoration, while good sleep quality reduces pain and fatigue.[6]

Postoperative sleep deprivation is commonly underestimated and ignored by most physicians.[7] However, early recovery after craniotomy has been given new research attention, focused specifically on the postoperative sleep of patients after neurosurgery. Studies thus far have concerned patients who underwent craniotomy for intracranial tumor resection and aneurysm clipping,[7–10] while information is quite limited regarding the sleep quality of patients with hemifacial spasm (HFS) after microvascular decompression (MVD) surgery.

The present study investigated the prevalence and causes of postoperative nocturnal sleep deprivation (PONSD) in patients with HFS after MVD surgery. The main causes of PONSD were self-reported by a control group of 30 patients. The therapeutic effect of interventions targeted to the identified causal factors were assessed in 18 patients.

# Methods

## Patients

The Ethics Committee of the hospital approved this prospective study, which was conducted in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. Forty-eight patients with HFS selected for MVD surgery from February 2016 to July 2017 were included. Patients with facial nerve lesions, demyelination, or space-occupying lesions near the brainstem were not considered for MVD or this study.

The inclusion criteria for enrollment included willingness to provide written informed consent, and ability to complete the sleep assessment questionnaires. Patients with any of the following were excluded: history of chronic sleep disturbance; taking sleep medication; current disorders or stress that might disturb normal sleep patterns; or requiring postoperative therapy in the intensive care unit.

The outcomes after MVD were rated excellent (spasm-free), good (occasional spasm, but improved degree and frequency), or poor (no relief).

# Assessment of night-time sleep

Patients typically have poor sleep on the first night in the hospital, due to the discomfort of a novel environment; this is termed the first night effect.[11] The night prior to the MVD operation, it is likely that patients are anxious about their forthcoming surgery and it is assumed that their preoperative sleep is adversely affected. Therefore, in the present study the second night's sleep in the hospital was considered the preoperative (preop), or baseline, sleep. After surgery, the patients' sleep quality was assessed daily according to the sleep quality of the previous night, from postoperative day 1 (postop-1) to postoperative day 3 (postop-3), using the Verran and Snyder-Halpern (VSH) Sleep Scale.

The VSH Sleep Scale scores the subjective sleep quality of hospitalized patients [12] by assessing 2 domains of sleep experience: disturbance, and effectiveness. Disturbance includes sleep latency, mid-sleep waking, soundness of sleep, and movement during sleep. The items under the effectiveness domain relate to rest upon waking, subjective quality of sleep, and total sleep period. Each item of each domain is measured using a 10-cm visual analog scale. When necessary, the authors clarified the questions or helped the patients mark the sleep scale. Attempts that may affect the patient's response were avoided.

Polysomnography is the gold standard to measure sleep objectively.[5] There have been discrepancies between subjective and objective assessments of sleep, but subjective estimates of total sleep time and sleep latency are similar to that of polysomnography.[10] For the present study, polysomnography was deemed too impractical and costly and was not used.

The general causes of disrupted postoperative sleep (environmental, pathophysiological, and psychological) were identified from the literature.[13] Using a table of these itemized causal factors, a control group of 30 patients with HFS (in the surgical wards with 3-bed bays) were interviewed to determine their specific causes of PONSD. Interventions (described below) based on these PONSD factors were administered to 18 additional patients with HFS (intervention group), and these patients were interviewed to assess the effect of the interventions.

# General anesthesia

Induction of general anesthesia was accomplished using midazolam (0.05 mg/kg), sufentanil (3 μg/kg), atracurium (0.2 mg/kg), and etomidate vecuronium (0.1 mg/kg). Three minutes later, tracheal intubation was performed. Anesthesia was maintained with continuous infusions of propofol (4 mg/kg/h), atracurium (0.1 mg/kg/h), and remifentanil (0.1–0.2 μg/kg/min). During the surgery, the infusion rates were continuously adjusted to maintain the bispectral index (BIS monitor; BSM-6501C, Nihon Kohden, Tokyo, Japan) fluctuation between 40 and 60 and to stabilize the mean blood pressure and heart rate. A bolus of 10-mg dexamethasone was given as a routine prophylactic for the prevention of postoperative nausea and vomiting (PONV). When the operation was completed, the patient was taken to the postanesthesia care unit for close monitoring and further management.

# MVD surgery

MVD surgery via posterior fossa craniotomy is the best procedure for patients with HFS[14]. Under general anesthesia, the patient was typically placed in the lateral decubitus position. A craniotomy inferior of the transverse sinus and the medial of the sigmoid sinus was performed to expose the dura. Once identified, the offending vessel was mobilized and separated from the facial nerve root using shredded Teflon implants. At the end of the MVD procedure, the cerebellopontine angle was irrigated, the Teflon implants were verified as immobile, and the dura was closed.[14]

## Postoperative intervention with analgesic and antiemetic treatment using intravenous (IV) patient-controlled analgesia (PCA)

An IV-PCA pump (Apon Medical Technologies, Jiangsu Province, China) was attached to the patients of the intervention group in the postanesthesia care unit. Based on the magnitude of the surgical insult, ketorolac (75 μg/kg/h), sufentanil (0.4 μg/kg/h), and tropisetron (4 μg/kg/h) were administered based on body weight, with 100 mL of normal saline. The dose was pre-programmed at 0.5 mL/15 min with a 0.5-mL bolus available on demand. The lockout interval was set to 15 minutes. Therefore, the total dose of ketorolac, sufentanil, and tropisetron delivered via PCA lasted for 50 hours, to the third postoperative night.

## Statistical analysis

The clinical data were subjected to a standard statistical analysis using SPSS software version 22. The numerical variables, as mean ± standard deviation, were compared through repeated measures analysis of variance (ANOVA) between the control and intervention groups, and with Student's *t*-test for the demographic data. For intra-group comparisons, the least significant difference (LSD-t) test was used. Nominal variables are shown as number and percentage, i.e., as n (%), and compared with the results of the chi-squared test. A 2-tailed $P$ value < 0.05 was considered statistically significant.

### Results

## Demographic characteristics

The control and intervention groups were statistically similar with regard to gender ratio, age, and operative time (Table 1). Women patients predominated overall, but the ratio of male-to-female subjects did not differ between the 2 groups ($P = 0.493$). No patients withdrew from the study after they provided written consent. All the MVD operations were performed by the same experienced neurosurgeon. Immediately after the surgeries, there were 44 (91.7%) and 4 (8.3%) patients with, respectively, outcomes that were excellent (no spasms) or good (not spasm-free, but improved in degree and frequency). There was no incidence of neurologic deterioration after any MVD operation.

Table 1
Demographic data of the patients in the control and the intervention groups

| | Control | Intervention | P |
|---|---|---|---|
| Subjects, n | 30 | 18 | |
| Male/female, n | 13/17 | 6/12 | 0.493 |
| Age, y | 47.4 (28–63) | 49.0 (39–66) | 0.556 |
| Operative time, h | 4.2 (3.50–5.75) | 4.2 (3.50–5.00) | 0.815 |

## Postoperative nocturnal sleep disturbance and effectiveness

When compared with the nocturnal sleep they had experienced preoperatively, after the surgery the patients in the control group reported greater wakefulness and tossing and turning at night, shortened sleep duration, extended sleep latency, increased light sleep, and waking unrefreshed (Table 2). From postop day 1 to postop day 3, the score for nocturnal sleep of the patients in the control group gradually but significantly returned to the preoperative baseline levels.

Table 2
VSH Sleep Scale scores of the control and intervention groups

| | | **Sleep disturbance** | | | | **Sleep effectiveness** | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Day | Sleep latency | Awakenings | Soundness | Movement | Rested upon waking | Subjective quality | Total period | Method of waking |
| CG | BL | 31.33 ± 5.36 | 18.83 ± 3.89 | 82.22 ± 2.90 | 18.83 ± 3.21 | 85.50 ± 3.12 | 88.83 ± 2.21 | 85.67 ± 3.03 | 87.83 ± 2.97 |
| | Postop-1 | 79.50 ± 3.48* | 88.33 ± 2.52* | 21.00 ± 4.28* | 78.50 ± 4.12* | 33.17 ± 4.01* | 19.17 ± 4.14* | 27.17 ± 4.23* | 22.83 ± 4.34* |
| | Postop-2 | 61.17 ± 3.18*§ | 66.66 ± 3.20*§ | 40.83 ± 3.54*§ | 73.00 ± 3.31* | 55.67 ± 3.33*§ | 45.50 ± 3.28*§ | 19.50 ± 3.28*§ | 42.00 ± 3.57*§ |
| | Postop-3 | 49.50 ± 3.18*§¶ | 54.50 ± 3.56*§¶ | 50.17 ± 3.38*§¶ | 56.33 ± 3.38*§¶ | 61.50 ± 3.30*§ | 56.67 ± 3.08*§¶ | 59.67 ± 2.89*§¶ | 62.33 ± 2.80*§¶ |
| IG | BL | 18.00 ± 9.28 | 17.50 ± 6.74 | 74.50 ± 5.01 | 24.50 ± 5.56 | 81.00 ± 5.74 | 83.00 ± 3.82 | 84.50 ± 5.26 | 85.00 ± 5.15 |
| | Postop-1 | 57.50 ± 6.03* | 41.00 ± 4.37* | 41.50 ± 7.41* | 34.5 ± 7.14 | 32.00 ± 6.95* | 42.00 ± 7.18* | 35.50 ± 7.32* | 41.00 ± 5.72* |
| | Postop-2 | 55.00 ± 5.51* | 49.50 ± 5.54* | 35.00 ± 6.13* | 44.5 ± 5.72 | 35.00 ± 5.78* | 37.00 ± 5.68* | 38.50 ± 5.68* | 38.50 ± 6.18* |
| | Postop-3 | 55.50 ± 5.50* | 52.50 ± 6.17* | 33.50 ± 5.85* | 53.5 ± 5.85* | 33.00 ± 5.72* | 32.00 ± 5.33* | 33.50 ± 5.00* | 32.50 ± 4.85* |
| | F | 4.009 | 20.562 | 0.204 | 18.449 | 9.716 | 0.888 | 2.685 | 0.8000 |
| | *P* | 0.052 | < 0.001 | 0.654 | < 0.001 | 0.003 | 0.352 | 0.110 | 0.377 |

BL, baseline (preoperative); CG, control group; IG, intervention group

Significant differences: * cf. BL; § cf. postop-1; ¶ cf. postop-3.

# Factors affecting postoperative nocturnal sleep of inpatients with HFS

The patients in the control group identified several environmental, pathophysiological, and psychological factors that disturbed their postoperative nocturnal sleep (Table 3). For each disturbing factor, the percentage of patients who considered it a causal factor of PONSD did not differ for each of the first 3 postoperative days. Postoperative pain (POP) was the predominant causal factor, with 93.3, 83.3, and 80% of the patients considering POP the main cause for their disrupted nocturnal sleep on postoperative days 1, 2, and 3, respectively ($P = 0.41$). PONV was the second highest report cause of PONSD, with 70.0, 50.0, and 43.3% ($P = 0.10$) of the patients reporting that it severely disrupted their nocturnal sleep on postoperative days 1, 2, and 3.

Table 3
Causes of PONSD over 3 postoperative days in the control group *

| | Postop-1 | Postop-2 | Postop-3 | χ2 | P |
|---|---|---|---|---|---|
| Environmental | | | | | |
| Nurses attending to other patients | 10.0 | 3.3 | 10.0 | 1.321 | 0.692 |
| Nursing at night | 13.3 | 10.0 | 6.7 | 0.797 | 0.905 |
| Telephones ringing | 6.7 | 23.3 | 6.7 | 4.449 | 0.100 |
| Nurses talking to each other | 6.7 | Nil | Nil | 2.719 | 0.326 |
| Noise from treatment equipment | 6.7 | Nil | Nil | 2.719 | 0.326 |
| Noise from nurses’ shoes | Nil | Nil | Nil | — | — |
| Pathophysiological | | | | | |
| Postoperative pain | 93.3 | 83.3 | 80.0 | 2.40 | 0.413 |
| Nausea and vomiting | 70.0 | 50.0 | 43.3 | 4.659 | 0.1 |
| Dizziness | 50.0 | 50.0 | 50.0 | — | — |
| Limb pain | 20.0 | 13.3 | 13.3 | 0.698 | 0.815 |
| Stomachache | 6.7 | 13.3 | 6.7 | 1.057 | 0.722 |
| Having to take medicine | 6.7 | 16.7 | 13.3 | 1.482 | 0.611 |
| Psychological | | | | | |
| Worries about illness | 60.0 | 43.3 | 46.7 | 0.867 | 0.393 |
| Boredom | 46.7 | 70.0 | 70.0 | 4.632 | 0.099 |
| Missing relatives | 76.7 | 70.0 | 66.7 | 0.757 | 0.685 |
| Not being in control of oneself | 16.7 | 13.3 | 20.0 | 0.48 | 0.787 |
| *Reported as percentage of 30 patients | | | | | |

For postoperative days 1, 2, and 3, patients in the control group considered that moderate or mild disruption in night sleep was due to the following: homesickness (76.7, 70.0, and 66.7%, $P = 0.69$); worries about illness (60.0, 43.3, and 46.7%, $P = 0.39$); dizziness (50.0, 50.0, and 50.0%); boredom (46.7, 70.0, and 70.0%, $P = 0.10$); limb pain (20, 13.3, and 13.3%, $P = 0.82$); activity of the nursing staff (13.3, 10, and 6.7, $P = 0.91$); stomachache (6.7, 13.3, and 6.7%, $P = 0.72$); and ringing telephones (6.7, 23.3, and 6.7%, $P = 0.10$).

# Effect of analgesic and antiemetic therapy on PONSD after MVD surgery

On postoperative days 1 and 2, the patients in the intervention group reported significantly less fragmented sleep (i.e., less mid-sleep waking and movement during sleep), than did the control group (Fig. 1; Table 2). On postoperative days 2 and 3, compared with the control group, the intervention group felt significantly more exhausted upon waking (reflected by lower scores for restfulness upon waking). From postoperative days 1 to 3, there were no differences in night sleep quality observed by patients in the intervention group, that is, with no improvement in sleep fragmentation (mid-sleep waking and movements), duration, latency, or depth.

# Discussion

To the best of our knowledge, this study was the first to assess the characteristics of postoperative sleep quality in patients with HFS after MVD surgery during the early postoperative period. The patients were in the general surgical wards, and it was found that their nocturnal sleep after MVD surgery was severely disturbed relative to their preoperative (baseline) nocturnal sleep in the hospital. POP and PONV were verified as the main causes of the patients' PONSD. The administration of analgesic and antiemetic treatment using sufentanil, ketorolac, and tropisetron through IV-PCA reduced fragmented sleep, but patients felt more exhausted upon waking.

The patients experienced significant PONSD during the first 3 postoperative days compared with their preoperative baseline, with more mid-sleep waking and movements, shorter sleep duration, extended sleep latency, and decreased sleep depth. Several studies have shown that patients after craniotomy have disrupted sleep, from the early postoperative period to more than one year after surgery. For example, patients with acromegaly after transsphenoidal surgery had worse subjective sleep quality in the first 3 postoperative months, compared with patients with nonfunctioning pituitary adenomas.[8] Huang et al.[9] reported that the sleep quality of patients who underwent a glioma resection more than one year previously was worse than that of normal adults. Arık et al.[7] found that patients in the neurosurgical intensive care unit who had received elective open-brain surgery experienced reduced sleep quality during the first 3 postoperative days. In addition, patients who underwent a craniotomy for pineocytoma had disturbed sleep latency and duration during a follow-up of 10.7 to 52.1 months, compared with patients after lumbar discectomy.[10]

In the present study, the patients in the control group considered POP to be the main cause of PONSD in the early postoperative period. This is consistent with previous findings.[3] It was reported that subjects with chronic pain are 17 times more likely to suffer from sleep disturbance compared with pain-free individuals.[15] MVD is a posterior fossa surgery that tends to cause greater intensive pain than supratentorial surgery.[16] In the present study, the second most prevalent cause of PONSD was PONV, afflicting 70.0% of the HFS patients, who stated that it severely disrupted their nocturnal sleep on the first postoperative day. A similar rate of PONV was reported in patients within 24 hours after MVD surgery, despite the use of intraoperative prophylactic ondansetron.[17]

In the present study, the patients of the control group also suffered moderate or mild sleep impairment due to emotional reasons, such as worries about illness, missing relatives or homesickness, and boredom. However, the intensity of POP and PONV overwhelmed the effect of the emotional factors in disrupting nocturnal sleep. Our present results are not in accord with the findings of a questionnaire study conducted more than one month after surgery by Zhang et al.,[8] whose patients had acromegaly, in whom disturbed sleep quality was associated with emotional problems (e.g., anxiety, depression, and disease stigma).

In the present study, to manage POP and PONV effectively and concomitantly assess the effect on sleep quality, the 18 patients in the intervention group received a combination of sufentanil, ketorolac, and tropisetron through IV-PCAs. As the most effective opioid analgesic known, sufentanil is considered appropriate to manage the POP of neurosurgical patients, because it preserves cognitive function and brain relaxation.[18] Ketorolac is a potent IV nonsteroidal anti-inflammatory drug (NSAID), which is necessary to limit the side effects of opioids after craniotomy, while providing patients with effective pain relief.[19] In addition, an antiemetic in combination with analgesics via PCA has been widely accepted as a successful approach toward reducing nausea and vomiting.[20] Tropisetron was chosen in this study due to its ability to decrease PONV in patients with HFS after MVD, as it is recommended as first-line therapy for the prevention of acute nausea and vomiting.[14]

When compared with the control group, on postoperative days 1 and 2 the patients given the intervention (sufentanil, ketorolac, and tropisetron by IV-PCA) experienced less fragmented sleep, due to fewer mid-sleep waking and movements (e.g., tossing and turning). Since the ward's environmental factors were held relatively stable during the 3 nights, and the psychological factors of the 2 groups were similar, this means that the less fragmented sleep of the intervention group was most likely associated with the treatment.

Studies have shown that sleep quality benefits from sufficient control of POP. For example, patients treated with opioid analgesic achieved adequate relief of chronic pain[21] and POP,[22] and significant improvement in sleep quality. Intravenous ketorolac to reduce pain intensity was also associated with improved sleep quality.[23] In the present study, the analgesic and antiemetic effects of the intervention were not directly measured. However, the efficacy of sufentanil and ketorolac for reducing POP after posterior fossa surgery has been documented, as well as the effect of tropisetron on PONV after MVD.[14,19,24]

An unexpected finding of this study was the low scores for feeling rested upon waking that the patients in the intervention group reported on postoperative days 2 and 3. Yet, their sleep quality (reflected by sleep fragmentation, duration, latency, and depth) did not change significantly day-by-day over postoperative days 1 to 3. A previous study reported similar results, that patients after gynecologic surgery treated with opioid via epidural catheter achieved excellent pain control, but also profound sleep impairment.[25] Opioid use has been suggested to cause disrupted sleep and fatigue by influencing sleep hygiene and sleep architecture.[26] Another study showed through polysomnography that IV administration of morphine led to a shift in sleep architecture to lighter stages, by reducing slow-wave and rapid eye movement (REM) sleep; these are generally associated with restorative processes in the body.[27] NSAIDs were reported to increase the number of waking and reduce slow-wave and REM sleep, and sleep efficiency, by inhibiting prostaglandin synthesis, suppressing nighttime melatonin levels, and changing body temperature.[28] Moreover, opioid analgesics are associated with high rates of PONV, which adversely influences postoperative sleep quality.[19]

This study had several limitations. First, this was a non-randomized trial, and the 2 groups were not equal in size. We considered it unethical to randomize patients, because of the invasiveness, cost, and side-effects of the sufentanil, ketorolac, and tropisetron treatment. Patients were apportioned to the groups based on their informed willingness to receive the postoperative treatment. Secondly, this study did not evaluate the effect of the treatment on POP and PONV, and it remains unknown if the patients in the intervention group achieved adequate analgesia or relief from PONV. Third, this was a single-center study, with only 48 patients enrolled. Larger randomized controlled trials are required to verify the outcomes. Fourth, the circadian rhythm and the exact amount of daytime sleep was not investigated. Thus, this study has significant inherent limitations when generalizing the findings.

# Conclusion

Patients with HFS in the general surgical ward suffered severe PONSD after their MVD surgery, and self-reported that POP and PONV were main causes of PONSD. When treated with a combination of ketorolac, sufentanil, and tropisetron through IV-PCP, the patients experienced less fragmented sleep (unwanted nocturnal waking and movements) but felt more exhausted upon waking.

# Declarations

### Acknowledgements

The authors would like to thank the patients who participated in this study, as well as the health care professionals that supported its conduct.

### Author contribution

Ruizhi Wang and Yuan Shen conceived and designed the study. Wei Lu and Pei Qu completed the questionnaire interview. Wei Lu and Ruizhi Wang wrote the paper. Yuan Shen did statistical analysis. Yuan Shen and Pei Qu reviewed and edited the manuscript.

### Data Availability Statement

All data generated and analyzed during this study are included in the published article.

### Declarations

Informed consent was obtained from patients. Prior approval for the study was obtained from the Ethics Committee of Second Affiliated Hospital of Xi'an Jiaotong University (Shaanxi China).

### Consent for publication

All authors give consent for this manuscript to be published.

### Conflicts of Interest Declaration:

The authors declare that they have no conflict of interest.

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# Figures

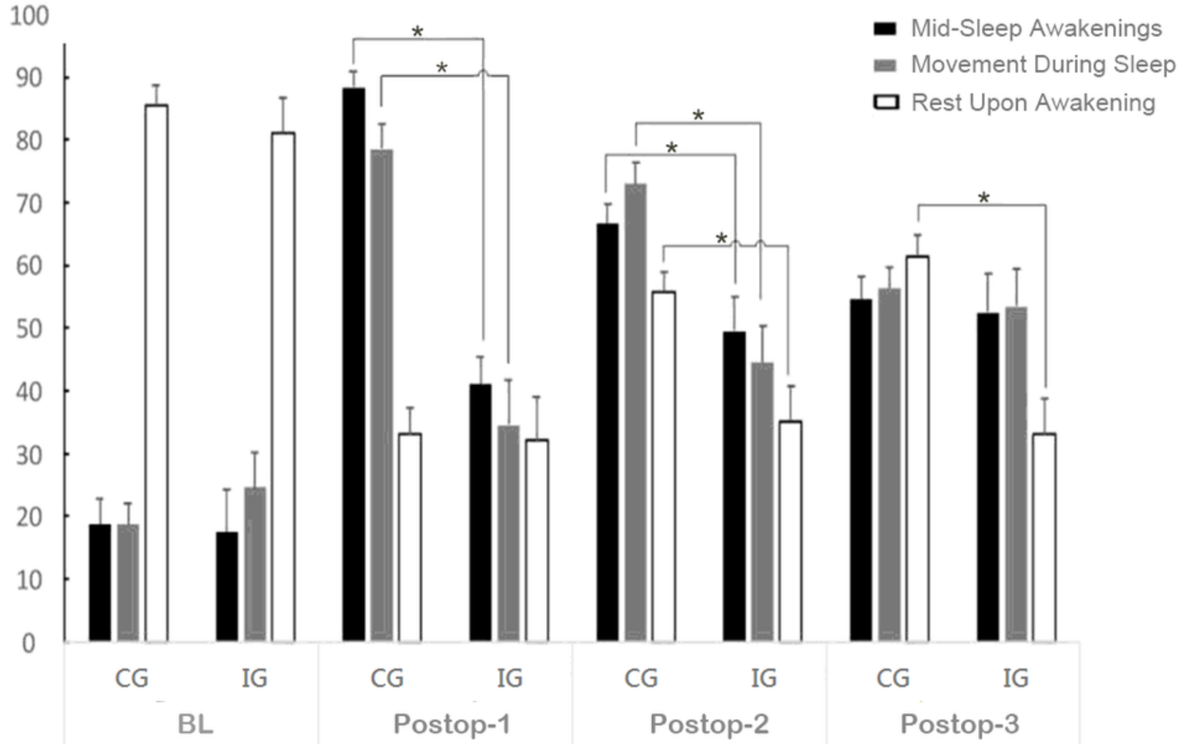


**Figure 1**

Effect of intervention on PONSD in patients with HFS after MVD surgery