REVIEW

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Improve postoperative sleep: what can we do?

Xian Su and Dong-Xin Wang

Purpose of review
We reviewed evidences regarding occurrence, risk factors, harmful effects, prevention, and management of sleep disturbances in patients after surgery.

Recent findings
Normal sleep is important to maintain physical and mental health. Sleep disturbances frequently occur in patients after surgery. Factors associated with the development of postoperative sleep disturbances include old age, preoperative comorbidity, type of anesthesia, severity of surgical trauma, postoperative pain, environment stress, as well as other factors leading to discomfort of patients. Development of sleep disturbances produces harmful effects on postoperative patients, that is, leading to higher risk of delirium, increased sensitivity to pain, more cardiovascular events, and poorer recovery. Both nonpharmacological and pharmacological measures (such as zolpidem, melatonin, and dexmedetomidine) can be used to improve postoperative sleep. Recent evidences show that sleep promotion may improve patients' outcome, but requires further evidences.

Summary
Sleep disturbances are common in patients after surgery and produce harmful effects on postoperative recovery. Sleep-promotion therapy may be helpful to improve postoperative recovery, but long-term effects deserve further study.

Keywords
outcomes, postoperative complications, sleep disturbances, sleep promotion

INTRODUCTION

Sleep disturbances frequently occur in patients after surgery, and its occurrence is harmful for postoperative recovery [1–5]. Recent evidences show that multiple perioperative factors are related to the development of postoperative sleep disturbances; some of these factors can be properly managed to reduce the severity of sleep disturbances, and sleep promotion may improve postoperative recovery. Here we reviewed evidences regarding occurrence, risk factors, harmful effects, prevention, and management of sleep disturbances in patients after surgery.

NORMAL SLEEP AND SLEEP STRUCTURE

Sleep is a naturally recurring state of mind and body, which is characterized by lowered consciousness, relatively inhibited sensory activity, inhibition of nearly all voluntary muscles, and reduced interactions with surroundings. According to the polysomnographic study results, sleep is divided into nonrapid eye movement (NREM) sleep and rapid eye movement (REM) sleep. NREM sleep can be further divided into stage 1 (N1, also called light sleep, accounting for 5–10% of total sleep in adults), stage 2 (N2, accounting for 45–55% of total sleep in adults), and stage 3 (N3, also called deep sleep or slow wave sleep (SWS), accounting for 15–25% of total sleep in adults). REM sleep accounts for 20–25% of total sleep in adults.

Normal sleep has a significant circadian rhythm and cycles in the order of N1 → N2 → N3 → N2 → REM. In healthy adults, the duration of each cycle lasts approximately 90 min. N3 sleep or SWS is a deep stage and is considered the most restful form of sleep. The sleeper is less responsive to the environment and restores the body. Night terrors, nocturnal enuresis, sleepwalking, and somniloquy

Department of Anesthesiology and Critical Care Medicine, Peking University First Hospital, Beijing, China

Correspondence to Dong-Xin Wang, MD, PhD, Department of Anesthesiology and Critical Care Medicine, Peking University First Hospital, Beijing 100034, China. E-mail: wangdongxin@hotmail.com

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KEY POINTS

- Sleep disturbances frequently occur after surgery, especially major surgery.
- Multiple factors are associated with the occurrence of postoperative sleep disturbances.
- Development of sleep disturbances produces harmful effects on postoperative recovery.
- Both nonpharmacological and pharmacological measures can be used to improve postoperative sleep and may be helpful for postoperative recovery.
- Long-term effects of sleep-promotion therapy deserve further study.

often occur in this stage. During the stage of REM sleep, high-frequency electroencephalographic waves that are similar to a waking state appear, but sleeper is harder to arouse than other stages. Vivid dreams may occur during this stage [6]. Lack of REM sleep impairs the ability to learn complex tasks, and deprivation of REM sleep often results rebound in REM sleep, that is, more REM sleep than usual.

Sleep structure changes across the aging process. Compared with the young, sleep in the elderly tends to show short duration, frequent wake, decreased N3 sleep, and early wake [7]. For healthy older adults of 75 years, normal sleep usually requires a total sleep time of about 6 h; of which, 11, 57, 12, and 20% are the stage N1, N2, N3, and REM sleep, respectively.

SLEEP DISTURBANCES AFTER SURGERY

Patients often develop significant sleep disturbances immediately after surgery, especially major surgery. Polysomnographic manifestations usually include severe sleep deprivation, sleep fragmentation, and decrease or loss of SWS and REM sleep during the night after surgery [1,2,6–9]. Patients may report decreased sleep time, increased numbers of arousals or awakening, lowered sleep quality, and frequent nightmares [10]. During the subsequent postoperative period, sleep structure gradually returns to normal with a REM rebound within 1 week [2].

FACTORS ASSOCIATED WITH POSTOPERATIVE SLEEP DISTURBANCE

Age

Aging is associated with sleep structure changes; furthermore, elderly are more difficult to adjust their sleep to environmental changes [10,11]. In the study of Chung *et al.* [9], higher age is associated with higher apnea–hypopnea index (AHI) and lower sleep efficiency after surgery. Therefore, elderly patients are more prone to develop postoperative sleep disturbances.

Preoperative comorbidity

Patients with preoperative obstructive sleep apnea (OSA) are at increased risk of postoperative sleep disturbances. Studies found that patients with a higher preoperative AHI are predicted to have a higher AHI after surgery [8,9]. Severe preoperative coronary artery disease is also associated with worse sleep quality after surgery. In a small sample size study of Yilmaz *et al.* [12], 52 patients undergoing coronary artery bypass graft surgery were assessed for postoperative sleep quality with Pittsburgh Sleep Quality Index. The results showed that patients with preoperative myocardial infarction had significantly worse sleep quality after surgery, and higher preoperative angina score was an independent predictor of poor sleep quality after surgery. However, effects of other preoperative comorbidity on postoperative sleep quality remain unclear.

Type of anesthesia

Regional anesthesia is helpful to relieve sleep disturbances after surgery. In a randomized controlled trial, 162 women scheduled to undergo fast-track abdominal hysterectomy randomly received either general or spinal anesthesia; the results showed that patients in the spinal anesthesia group experienced less bad sleep in the night after surgery [4]. In a cohort study of 376 surgical patients, regional anesthesia (when compared with general anesthesia) was associated with lower postoperative central apnea index [9]. One possible reason is that regional anesthesia reduced perioperative opioid consumption [4,9]. The impact of opioids on the development of postoperative sleep disturbances is also reported in other studies [2]. However, even when opioids are avoided and pain is well controlled, sleep disturbances still develop after surgery [13,14], indicating the effects of other factors.

Severity of surgical trauma

Sleep disturbances are more severe after major surgery. For example, in patients after open cholecystectomy under general anesthesia, significant sleep disturbances (manifested as increased N2 sleep, and decreased or lost N3 and REM sleep) occurred during the night of surgery [2]; whereas in patients after laparoscopic cholecystectomy under general

anesthesia, sleep disturbances were less severe (manifested as decreased N3 sleep but not REM sleep) during the same night [15]. Chung *et al.* [9] also reported similar results, that is, major surgery (when compared with minor surgery) is associated with lower sleep efficiency after surgery. However, minor surgery such as lumpectomy for breast cancer also produces sleep disturbance in the night after surgery, although less severe, which normalizes after 2 weeks [16].

Postoperative factors

Many postoperative factors are associated with the development of sleep disturbances. Among them pain is possibly the most important one [17▪,18]. However, it is worth to note that opioid analgesia do not improve, but rather worsen postoperative sleep by decreasing REM sleep and increasing AHI [2,9]. Environmental factors including noise and lights in the ward, disturbances from healthcare staff, and disturbances from other patients are also important sleep disturbers [17▪,18]. In the ICU, the noise levels can reach up to 85 dB with alarms and staff conversations [19]. In a general ward, the noise levels can be also as high as 70 dB [20]. Furthermore, various kinds of discomforts, such as needing to use toilet facilities, nausea, anxiety, fever, and others, lead to sleep disturbances as well [17▪].

HARMFUL EFFECTS OF SLEEP DISTURBANCES ON POSTOPERATIVE OUTCOMES

Sleep disturbances and delirium

Sleep disturbances are considered important risk factors of delirium development. In patients undergoing arthroplasty or noncardiac surgery, preoperative sleep disruption was associated with an increased risk of postoperative delirium [21,22▪]. In elderly patients undergoing arthroplasty, preexisting OSA was a significant predictor of postoperative delirium [23]. In veteran patients enrolled in hospice, poor sleep quality was also associated with a high risk of developing delirium [24].

Sleep disturbances and pain

The relationship between sleep and pain is reciprocal; poor sleep also leads to increased sensitivity to pain. Studies of patients hospitalized for burn injury showed that significant temporal relationships exist between sleep, pain, and analgesic medication, that is, a night of poor sleep was followed by a significantly more painful day and higher analgesic intake; furthermore, high levels of pain and analgesic medication during the day were both significant predictors of poor sleep on the following night [25,26]. This is also true for patients with chronic pain [27].

Sleep disturbances and cardiovascular events

Sleep disturbances are associated with increased risk of cardiovascular events in high-risk patients. In a cross-sectional prospective cohort study, 388 patients after percutaneous coronary intervention were assessed for symptoms of disturbed sleep at 1 month and followed-up for at least 4 years for major cardiac events. The results showed a positive relationship between the number of sleep disturbance symptoms and the occurrence of major cardiac events (including cardiogenic death, myocardial infarction, and repeated revascularization). Each additional sleep symptom was associated with a hazard ratio of 1.2 ($P = 0.001$) [5]. As showed in a systematic review, OSA in nonsurgical patients is associated with increased risk of stroke [28].

Sleep disturbances and postoperative recovery

Sleep disturbances have significant impacts on the recovery after surgery. In patients after fast-track hysterectomy, poor sleep quality during the first postoperative night was strongly associated with a longer hospital stay [4]. In patients after total knee replacement surgery, sleep disruptions 1 month following surgery was associated with functional limitations 3 months following surgery, indicating the importance of adequate sleep during postsurgical recovery [29]. In patients after kidney transplantation, sleep disorders were common (occurred in 30–62% of patients) and were associated with poorer emotional state and lower quality of life [30–32].

MEASURES TO IMPROVE POSTOPERATIVE SLEEP

Nonpharmacological measures

These include using regional anesthesia whenever possible [4,9], decrease the severity of surgical trauma (perform laparoscopic rather than open-abdominal surgery) [9,15], provide multimodel analgesia (to decrease opioid consumption) [2,17▪,18], and remove ambient stressors during night [17▪]. For patients admitted to the ICU after surgery, managements according to sleep care guidelines, such as maintaining a quiet and dim

environment and decreasing interruptions from care activities at night, improve sleep quality and sleep efficiency [33,34]. A meta-analysis showed that the use of ear plugs and eye mask is also helpful in promoting sleep among patients in ICU [35].

Pharmacological measures

A recent systematic review concluded that there is insufficient evidence to suggest that pharmacotherapy improves the quality or quantity of sleep in hospitalized patients [36▪▪]. The following drugs, however, are recently being used to improve sleep in postoperative patients.

Zolpidem

Zolpidem is a short-acting nonbenzodiazepine compound of the imidazopyridine class that increases the activity of gamma-aminobutyric acid (GABA), an inhibitory neurotransmitter, by binding to $GABA_A$ receptors at the same location as benzodiazepines [37]. In a small sample size study of patients undergoing hip or knee replacement, zolpidem administered one night before and on the first night after surgery improved the feelings of sleep quality and fatigue but not sleep architecture [38].

Melatonin

Melatonin is secreted by the pineal gland, and its secretion regulates and modifies circadian rhythms and sleep [39]. Plasma melatonin levels are decreased after surgery and in hospitalized patients [40]. In a meta-analysis, melatonin given as premedication in adults reduces preoperative anxiety when compared with placebo and is equally effective when compared with midazolam [41]. In a small sample size study of patients undergoing prostatectomy, preoperative melatonin enhanced sleep quality, decreased pain scores and tramadol consumption, but produced sedation during the early postoperative period [42]. For patients after breast cancer surgery, melatonin administration improves sleep quality without producing significant side effects [43–45].

Dexmedetomidine

Dexmedetomidine is a selective α2 adrenoceptor agonist with both sedative and analgesic properties [46]. Unlike other sedative agents, dexmedetomidine exerts its sedative effects through an endogenous sleep-promoting pathway and produces a N2 sleep-like state [47]. In mechanically ventilated ICU patients, nighttime infusion of sedative dose of dexmedetomidine preserved the day–night cycle of sleep and improved the sleep architecture by increasing sleep efficiency and stage N2 sleep [48,49]. In nonmechanically ventilated elderly patients who were admitted to the ICU after surgery, low-dose dexmedetomidine infusion (0.1 μg/kg/h) during the night after surgery prolonged total sleep time, increased N2 (and decreased N1) sleep, and improved subjective sleep quality [50▪].

Effects of sleep promotion on patients' outcomes after surgery

Sleep-promotion is helpful for recovery of postoperative patients. In ICU patients, improving sleep with ear plugs and eye mask reduces the incidence of delirium [35,51▪▪], further demonstrating the correlation between sleep disturbance and delirium development. In a recent large sample size study, 700 patients (≥65 year) who were admitted to ICU after surgery randomly received either low-dose dexmedetomidine infusion (0.1 μg/kg/h) or placebo during the night after surgery. The results showed that low-dose dexmedetomidine infusion decreased the prevalences of delirium on postoperative days 1–3, which was in accordance with the improved subjective sleep quality during the 3 nights of the same period. Low-dose dexmedetomidine infusion also reduces nondelirium complications [52▪▪]. For patients after orthopedic surgery, use of zolpidem reduces postoperative pain, fatigue, and narcotic consumption [53], and improves quality of life [54]. Long-term effects of sleep-promotion therapy remain to be determined.

CONCLUSION

Sleep disturbances frequently occur after surgery, especially major surgery. Factors associated with the occurrence of postoperative sleep disturbances include old age, preoperative comorbidity, type of anesthesia, severity of surgical trauma, postoperative pain, environment stress, as well as other factors leading to discomfort of patients. Development of sleep disturbances produces harmful effects on postoperative patients, that is, higher risk of delirium, increased sensitivity to pain, more cardiovascular events, and poorer recovery. Both nonpharmacological and pharmacological measures can be used to improve postoperative sleep and may be helpful for postoperative recovery. Long-term effects of sleep promotion therapy deserve further study.

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Conflicts of interest

D.-X.W. reports that he has received lecture fees and travel expenses for lectures given at domestic academic meetings from Jiangsu Hengrui Medicine Co., Ltd., China and Yichang Humanwell Pharmaceutical Co Ltd, China. X.S. reports no conflicts of interest.

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