

Received: 2022.11.10

Accepted: 2022.12.21

Available online: 2023.01.09

Published: 2023.02.10

Effect of Acupoint Therapies on Postoperative Sleep Quality: A Narrative Review

Authors' Contribution:

Study Design A

Data Collection B

Statistical Analysis C

Data Interpretation D

Manuscript Preparation E

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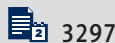
Financial support: None declared

Conflict of interest: None declared

Several studies have reported that sleep quality often decreases in patients after surgery, especially in elderly patients, which seriously affects postoperative prognosis and outcomes, inducing diseases such as postoperative delirium, long-term chronic pain, and potentially fatal cardiovascular events. With the popularization of comfortable medicine, medical workers pay more attention to the postoperative sleep quality of patients. The causes underlying the decrease in postoperative sleep quality may include postoperative pain, the severity of surgical trauma and stress, perioperative anxiety and depression, and postoperative complications. Patients with insomnia often use acupoint therapies as a safe and effective alternative to drugs. Acupoint therapies are among the oldest medical therapies of Traditional Chinese Medicine and are gradually gaining recognition among medical workers worldwide. Various types of acupoint stimulation methods such as transcutaneous electrical acupoint stimulation (TEAS), acupressure, acupuncture, and electroacupuncture can change the brain's local electrical activity, inhibit the central nervous system, and achieve deep sedation through stimulating the related acupoints, which provides a novel idea and basis for improvement in factors affecting postoperative sleep quality. This review explores the mechanism of acupoint therapies from several aspects of affecting the sleep quality of patients after surgery and its clinical results. We found that acupoint therapies effectively improve sleep quality and alleviate the postoperative complications of patients, and we emphasize the importance of acupoint therapies to guide future research and clinical practice. Large-scale, multicenter studies are needed to determine the optimal duration, frequency, and timing of acupoint stimulation for improving postoperative sleep quality.

Keywords: **Acupuncture Points • Acupuncture Therapy • Postoperative Period • Sleep Quality**

Full-text PDF: <https://www.medscimonit.com/abstract/index/idArt/938920>



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Background

Adequate sleep is essential to physical and mental health. Sleep and circadian rhythm disorders often occur in elderly patients after surgery, characterized by sleep fragmentation, decreased deep non-rapid eye movement (NREM) sleep, the initial decrease and subsequent rebound increase in rapid eye movement (REM) sleep, and daytime sleepiness [1,2]. More than 40% of patients reported sleep problems during the first night after surgery and these problems continued for several days [3]. Studies have found that decreased postoperative sleep quality is harmful to recovery and can lead to negative outcomes such as altered pain perception, cognitive impairment (such as delirium and Alzheimer disease), metabolic derangements, mood disturbances, and proinflammatory changes [4-7]. Vlisides Pet et al [8] indicated that 20-50% of elderly patients have postoperative delirium after major surgery, which is a predictor of mortality and prolonged intensive care unit or hospital stay. Long-term postoperative cognitive dysfunction is also a significant economic burden [9]. Recent evidence has shown that acupoint stimulation is related to increased postoperative sleep quality, and sleep improvement can improve postoperative outcome. Here, we review the evidence regarding the causes of decreased postoperative sleep quality, and the effect of acupoint stimulation on postoperative sleep quality in surgical patients.

Normal Sleep Patterns

Sleep is a vital physiological state that exists in all organisms with neurons and glial networks. It is characterized by decreased consciousness, relative inhibition of sensory activity, inhibition of almost all voluntary muscle activity, and reduced interaction with the surrounding environment [10]. The normal range of sleep duration for adults is 6-10 h, with the majority of the individuals sleeping the recommended 7- to 9-h range, with an average sleep duration of 8 h [11]. In humans, sleep is classified as 2 exclusive states – non-rapid eye movement (NREM) sleep and rapid eye movement (REM) sleep – whose occurrence is driven by a cyclic organization. NREM sleep is further subdivided into the following stages: N1, N2, and N3, with N3 being designated as slow-wave sleep (SWS). REM sleep accounts for 20-25% of total sleep duration in adults. Typically, a person enters NREM sleep and experiences a sequence of “descending” stages and then an “ascent” (indicating greater brain activity) and enters REM sleep. These cycles repeat every 90-120 min. Owing to these cyclic shifts in sleep stages, SWS or N3 is skewed towards the beginning of the night, while REM sleep is typically skewed towards the end of the night [12]. The characteristics of sleep are relatively stable for a particular individual; however, the sleep duration and architecture vary according to age, individual habits, sleep schedules,

and environmental constraints. Sleep structure changes with age. Compared with young people, older people have shorter sleep time, more frequent wake-up, and reduced N3 sleep duration, and tend to get up early [13].

Causes of Declined Postoperative Sleep Quality

Various environmental, social, psychological, and pathological factors can disturb sleep. These sleep disturbances can be sorted into 3 categories: insufficient duration, improper timing, and decreased quality. A large amount of clinical evidence has shown that patients often experience significant decline in sleep quality immediately after surgery, especially major surgery. Sleep efficacy is the percentage of time in bed actually spent sleeping. When sleep efficacy is reduced, sleep architecture, which is the structural organization of sleep into its various stages, is disturbed. Polysomnographic manifestations of decreased sleep quality usually include severe sleep deprivation, sleep fragmentation, and reduced or loss of SWS and REM sleep at night after surgery [14]. A study by Chung et al [15] showed the following symptoms among surgical patients: 1) low sleep efficiency for 1-7 nights after surgery, which then gradually increases during subsequent nights, 2) REM sleep was the least on the first night after surgery, partially recovered to normal at the third night, and returned to the baseline level on either the fifth or seventh night, and 3) the proportion of N2 sleep increased significantly on the first and third nights after surgery, reflecting the decrease of REM and N3 sleep on those nights. Rosenberg et al found that postoperative rebound of nocturnal REM sleep can contribute to the development of sleep-disordered breathing and nocturnal episodic hypoxemia [16].

Pain

Although great progress has been made in perioperative care, surgical patients still commonly experience persistent postoperative pain. Some biopsychosocial risk factors have been identified as important predictors of postoperative pain persistence and long-term poor recovery [17]. The prevalence of chronic pain after surgery ranges from 10-40% [18] and patients with chronic pain exhibit decreased sleep quality (10-36%) [19], such as frequent sleep-stage shifts, increased nocturnal awakenings, and decreased N3 or REM sleep [20]. The relationship of pain with short sleep duration or insomnia has been characterized extensively. It is widely accepted that the relationship between sleep and pain is bidirectional, with pain disrupting sleep and sleep disturbances also being a strong and reliable predictor of pain [2]. For example, it was reported that less than 6 h of sleep per night is associated with more severe pain the following day [21], and lower

sleep efficiency is a significant predictor of pain severity after breast surgery [22]. Lack of sleep, both in quantity and in quality, predicts pain in the next 3 years [23]. The following possible underlying mechanisms have been identified in animal experiments: (1) The analgesic effects of endogenous and exogenous opioids depend on the undisturbed sleep structure or sleep continuity. Sleep deprivation may lead to the inhibition of opioid protein synthesis [24] and/or reduced affinity of m- and d-opioid receptors [25]. (2) After 96 h of REM sleep deprivation, the levels of 5-hydroxytryptamine (5-HT) and 5-hydroxyindoleacetic acid in different brain regions were decreased. REM sleep deprivation or continuous sleep interruption in general render the serotonin system functionally could not to support the pain inhibition induced by opioid activation [26]. (3) Other neurotransmitter systems (especially norepinephrine) [27] and neuroimmune factors (especially interleukins) are also affected by sleep deprivation and involved in the regulation of pain. Thus, improving sleep quality appears to reduce pain symptoms [28]. Correspondingly, the treatment of pain can also improve sleep quality.

Surgical Trauma and Stress

Surgical trauma, stress response, and postoperative pain are the main factors that affect postoperative sleep quality [29]. Lutsey et al [14] demonstrated similar results, showing that major surgery (compared to minor surgery) is related to lower sleep efficiency after surgery. However, minor surgery, such as mastectomy for breast cancer, also produces a small decrease in sleep quality during the night after the operation, and then returns to normal after 2 weeks [30]. Rosenberg-Adamsen et al [31] reported that decreased sleep quality in patients after laparoscopic surgery was less severe, manifesting as decreased N3 sleep but not REM sleep, during the night after surgery; whereas after open surgery, patients had significantly decreased sleep quality manifested as increased N2 sleep, and decreased or lost N3 and REM sleep. In addition, the stress response induced by surgical trauma involves the endocrine metabolic system and inflammatory response, which can last for several days or weeks. Surgical injury followed by a complex stress response is an important cause of postoperative sleep quality decline [32]. The relevant findings are: (1) The inflammatory cytokines tumor necrosis factor (TNF) and interleukin-1 (IL-1) participate in the regulation of sleep. Injection of exogenous TNF or IL-1 can induce all symptoms related to sleep deprivation [33,34]. After administration of IL-1 into the lateral ventricle of rabbits, REM sleep was inhibited, non-REM sleep increased and hyperthermia, which was like that of postoperative patients [35]. (2) Interleukin-6 (IL-6) is also involved in sleep regulation. Preliminary evidence from animal models suggests the intricate contribution of IL-6R signaling to sleep structure [36]. Nocturnal circulating IL-6 levels are associated with the sleep quality; elevated IL-6 levels are associated with sleep interruption, and

low levels were associated with good deep sleep [37]. On investigating sleep architecture, Hong et al found that the IL-6 levels were correlated with waking up more frequently during sleep (WASO), less slow-wave sleep, and reduced sleep efficiency [38]. These findings confirm that the magnitude of the surgical trauma and/or stress response may be key pathogenic factors in decreased postoperative sleep quality.

Anxiety and Depression

Sleep is particularly difficult during hospitalization, considering that the challenges of sleep are multifactorial, hospitalization can cause anxiety and depression in patients due to their health concerns, disturbances from other patients, and an unfamiliar environment. Previous studies have found that patients with persistent anxiety and depression experience disrupted sleep quality such as altered rapid eye movement sleep (REMS) and felt less refreshed after awakening than the non-anxious ones in the first and sixth months after discharge from hospital [39,40]. Recent evidence suggested a bidirectional relationship between psychiatric disorders and sleep disturbances, in which they reinforce each other and share common and overlapping mechanisms. Postoperative sleep is characterized by an initial suppression of rapid eye movement (REM) and slow-wave sleep (SWS). REMS is the main regulator of emotional processes. This fact proves that individuals exposed to traumatic situations usually show fragmentation and reduced time in REMS, and are more likely to develop post-traumatic stress disorder 6 months after trauma [41]. Several studies showed that disturbed sleep can aggravate the consequences that could confer risk of anxiety-related symptoms [42], such as epigenome changes [43], alterations in neuroendocrine function [44], impaired cognitive function [45], and affective dysregulation [46]. Animal studies have suggested that this link is related to the structure of the limbic system due to the following: (1) in sleep-deprived rats, the proliferation of neurons in the dentate gyrus of the hippocampus [47] and the total volume of the hippocampus decreased [48]; (2) sleep-deprived rats also showed increased 5-HT hippocampal turnover [49] with 8 days of sleep restriction decreasing 5-HT_{1A} receptor sensitivity [50], which are 2 well-known depression-related changes; and (3) REM sleep deprivation resulted in increased synthesis and secretion of norepinephrine (NA) in the locus coeruleus [51] and decreased binding capacity of β 1 and β 2 adrenergic receptors in the amygdala and hippocampus (2 brain regions receiving locus coeruleus projection) [52,53].

Acupoint Stimulation Improves Factors Affecting Postoperative Sleep Quality

As an adjuvant therapy, acupoint stimulation originated in ancient China, based on the theory of main and collateral

channels. The World Health Organization (WHO) has regarded acupoint stimulation as a beneficial intervention to deal with a wide range of health problems [54]. For the modalities of acupoint stimulation, acupuncture, electroacupuncture, transcutaneous electrical acupoint stimulation (TEAS), and acupressure are widely used in practice. Acupuncture is an integral part of China's health care system. It can be traced back for at least 2500 years and is now widely used to treat various factors that cause disruptions in sleep quality [55]. Electroacupuncture (EA) is a therapy to prevent and treat diseases by provoking and adjusting meridians and collaterals with stimulation by acupuncture inserted into the acupoints with the desired sensation and electrified with micropulse current approaching the bioelectricity of the human body. Studies found that electroacupuncture has significant analgesic and sedative effects, enhancing immune function, and reducing the risk factors of decreased postoperative sleep quality [56,57]. TEAS treat disease through inputting a pulse current of different frequencies, intensities, and waveforms via electrode paste adhering to the skin. Previous studies proved that TEAS has been successfully applied in many different procedures such as reducing postoperative pain [58] and improving postoperative sleep quality [59]. Acupressure is a non-invasive treatment that involves application of pressure on specific parts of the body; hence, different clinical effects can be achieved with the application of acupressure.

Improvement in Anxiety and Depression on Acupoint Stimulation

Preoperative and postoperative anxiety and depression are the main factors associated with decreased postoperative sleep quality. Patients with anxiety or depression may experience prolonged sleep onset latency and waking up frequently in the night, resulting in sleep fragmentation and poor sleep efficiency [60]. Patients with depression usually present with reduced REM sleep latency and prolonged REM sleep early in the night, resulting in an increase in the proportion of REM sleep in general [61]. Improving sleep quality in patients with depression can improve their prognosis. Buchanan et al [62] assessed auricular acupuncture therapy conducted 5 times for 30 min each session over 16 weeks, resulting in anxiety relief in different groups, such as healthy volunteers [63] and post-surgical patients [64]. Shujun and Junli found that with low-frequency stimulation, 10 min of TEAS treatment at EX-HN3 (Yintang) and LI-4 (Hegu) acupoints can effectively improve preoperative anxiety of breast cancer patients [65], and Zhifang et al [66] found that acupuncture at PC-6 (Neiguan) for 30 min at 40-50 Hz can reduce preoperative anxiety and improve sleep in patients undergoing elective orthopedic surgery.

Animal studies have found 3 possible underlying mechanisms. (1) The anti-anxiety effect of acupuncture may be related to

the up-regulation of atrial natriuretic peptide (ANP) expression and the down-regulation of C-type natriuretic peptide (CNP) expression in peripheral adrenal medulla, thus inhibiting the release of corticosterone (CORT) and activity of the hypothalamus-pituitary-adrenal axis (HPA) [67]. (2) Acute restraint stress (ARS) is an emotional stressor that can activate a variety of neurochemical, physiological, endocrine, cognitive, and behavioral responses. Acupuncture can inhibit the increase of amygdaloid norepinephrine (NE) and 3-methoxy-4-hydroxy-phenylglycol (MHPG) brought about by ARS. Acupuncture can also prevent ARS-induced enhancements in the protein and mRNA expressions of tyrosine hydroxylase in the central nucleus of the amygdala (CeA) [68]. (3) Chronic unpredictable stress (CUS) can result in depression-related behavioral deficits in rats and neuroinflammation in the hippocampus, such as increased expression of NLRP3, up-regulation of the level of IL-1 β mRNA and IL-1 β mature protein, and activation of microglia. EA treatment can significantly reduce the depression-like behavior caused by CUS. The antidepressant effect of EA is accompanied by a significant decrease in the expression of certain NLRP3 and mature IL-1 β . Meanwhile, EA treatment can drastically reverse the increased expression of P2X7 receptor, Iba-1, IL-18, TNF α , and IL-6 expression and decrease the glial fibrillary acidic protein (GFAP) expression induced by CUS [69] (Table 1).

Improvement in Pain by Acupoint Stimulation

Postoperative pain is a common concern during the perioperative period, which can lead to decreased sleep quality, thus prolonging postoperative recovery time. Acupuncture can be an effective adjunctive intervention for postoperative pain by reducing the required doses of analgesics (mainly opioids) and subsequent complications. For high-risk patients, such as patients with chronic obstructive pulmonary disease or obstructive sleep apnea, the use of acupuncture is particularly valuable because these patients may have complications (mainly respiratory depression) due to use analgesics [70]. Asher et al [71] found that auricular acupuncture can be an effective treatment for several types of pain, especially postoperative pain. Postoperative pain can be reduced after acupoint stimulation at PC6 (Neiguan), GB-21 (Jinajing), LU1 (Zhongfu), LI-11 (Quchi), LI-4 (Hegu), TE-3 (Zhongzhu), TE-5 (Waiguan), and the auricular acupuncture points Shenmen, Heart, Lung, Tooth, Mouth, Uterus, Cushion, Thalamus, Hip, Knee, and Forehead [72-74]. EA also has been reported to alleviate pain and raise the pain threshold by about 20-30% in clinical practice [75]. White et al [76] used EA at ST-36 (Zusanli) and LI-4 (Hegu) with low-frequency (2 Hz) and high-frequency (100 Hz) to provoke the release of various types of endorphins (beta-endorphin, met-enkephalin and dynorphin) to combat pain, and a mixed combination of both low and high frequencies releases various opioid peptides and creates a synergetic effect that inhibits pain [76], which can effectively alleviate postoperative

Table 1. Mechanism of acupoint therapies for sleep.

Classification	Mechanism	Subjects	Acupoint	Acupoint intervention	References
Clinical trials	i) Auricular acupuncture can reduce anxiety, improve productivity and well-being	Direct caregivers suffering from violence	5 specific points on the external ear: HT7 (Shenmen), sympathetic autonomic, lung, liver, and kidney	i) 5 sessions within a 16-week period ii) Each session lasted for 30 minutes	Buchanan TM et al [62]
	i) Relieving or eliminating anxiety has obvious effect, which can reduce the stress reaction of patients before operation	Patients with radical mastectomy	EX-HN3 (Yintang) LI-4 (Hegu)	i) The electrode is attached to the acupoint ii) The stimulation intensity was based on the patient's comfort iii) Lasted for 10 minutes	Huang S et al [65]
	i) Reduce the preoperative anxiety level, improve the sleep status ii) slow down the pulse rate of patients with anxiety	Orthopedic patients undergoing elective surgery	PC6 (Neiguan)	i) Acupoint electrode ii) Continuous electrical stimulation of 40-50 Hz iii) Lasted for 30 minutes iv) The daily intervention times were ≤1, and the total intervention times were ≥3	Zhao Z et al [66]
Animal experimental studies	i) The anti-anxiety effect of acupuncture may be related to the up regulation of atrial natriuretic peptide (ANP) expression and the down regulation of C-type natriuretic peptide (CNP) expression in peripheral adrenal medulla, thus inhibiting the release of corticosterone (CORT) and the activity of hypothalamus pituitary adrenal axis (HPA)	Rats with chronic emotional stress anxiety	PC6 (Neiguan) HT7 (Shenmen)	i) Acupuncture time was fixed at 12: 00-14: 00 ii) Oblique needling points 2-3 mm iii) Retaining the needle for 30 min iv) 8 times in total	Yao H et al [67]
	i) Acupuncture could inhibited increases in amygdaloid norepinephrine (NE) and 3-methoxy-4-hydroxy-phenylglycol (MHPG) induced by acute restraint stress (ARS) ii) Acupuncture could also prevent ARS-induced enhancements in the protein and mRNA expressions of tyrosine hydroxylase in the central nucleus of the amygdala (CeA)	Male rats were exposed to acute restraint stress (ARS) for 3 h	PC6(Neiguan), HT7 (Shenmen), or a nonacupoint (tail) located in the tail in a rat	i) Acupuncture, depth 2-3mm ii) 1 min, once a day iii) Last 3 days	Zhao Z et al [68]

Table 1 continued. Mechanism of acupoint therapies for sleep.

Classification	Mechanism	Subjects	Acupoint	Acupoint intervention	References
Animal experimental studies	<p>i) EA 's antidepressant effect was accompanied by markedly decreased expression of certain NLRP3 inflammasome components and matured IL-1β</p> <p>ii) EA treatment can significantly reverse chronic unpredictable stress (CUS) induced increases in P2X7 receptor, Iba-1, IL-18, TNFα and IL-6 expression and decreases in GFAP expression</p>	Rats experiencing chronic unpredictable stress (CUS)	DU20 (Baihui) GB34 (Yanglingquan)	<p>i) EA apparatus (HANS Electronic Apparatus, LH202H, 2/100 Hz, 0.3 mA)</p> <p>ii) 30 min once every day</p> <p>iii) Last 4 weeks</p>	Yue N et al [69]

pain and improve postoperative sleep quality. TEAS in bilateral acupoints of LI-4 (Hegu), PC-6 (Nei guan), SI-3 (Houxi), and SJ-6 (Zhigou) at a frequency of 2/100 Hz for 30 min can effectively alleviate pain in elderly patients undergoing thoracoscopic surgery and promote rapid recovery after the operation [77]. There are 2 possible mechanisms in animal experiments: (1) Acupoint stimulation can reduce the pain of rats with chronic neuropathic pain, which may be related to its actions in down-regulating the levels of HMGB1 and its downstream proinflammatory cytokines TNF- α and IL-1 β in the hippocampus [78]. (2) Acupoint stimulation of PC6 (Neiguan) and LI4 (Hegu) can change the phosphorylation level of NR2B subunit of N-methyl-D-aspartate (NMDA) receptor in C1-C3 segment of spinal cord, up-regulate the expression of 5-HT2AR mRNA and protein, and effectively improve pain threshold and relieve pain [79] (Table 2).

Improvement in Surgical Stress by Acupoint Stimulation

Surgical pressure and inflammation contribute to the development of postoperative complications, resulting in delayed recovery and decreased sleep quality postoperatively. Clinical trials have shown that perioperative stress activates the sympathetic adrenal medullary system and hypothalamus pituitary adrenal axis, leading to the increase of stress hormones and inflammatory cytokines circulation, which are related to organ dysfunction, postoperative infection, and delayed postoperative recovery [80-83]. These surgical stress reactions and trauma are the main factors affecting postoperative sleep, mainly manifested by the initial inhibition of rapid eye movement (REM) and slow-wave sleep (SWS), and then rebound within 1 week after major surgery. There are 2 mechanisms of action: (1) Acupoint stimulation can reduce inflammation and stress response through regulating the expression of Bcl-2/Bax ratio, Caspase-3, IL-1, IL-6, IL-10, TNF- α and other inflammatory factors [84,85]. (2) Acupoint stimulation treatment can restore suppressed lymphocyte proliferation, increase NK cell activity in the spleen by approximately 44%, and significantly

enhance the levels of serum IgM and IgA in postoperative rats with gastric carcinoma, which show that acupoint stimulation can regulate immunity and attenuate anesthesia- and surgery-induced immunosuppression [86,87] (Table 2).

Improvement in Postoperative Complications by Acupoint Stimulation

Surgery, both major and minor, always carries a risk of postoperative complications. Nausea and vomiting are the most common complications of pain within 24 h after surgery in adults [88]. The incidence of postoperative nausea and vomiting is 30%, while that of laparoscopic surgery is 70% [89]. Although self-limiting, postoperative nausea and vomiting (PONV) can lead to severe morbidity, including bleeding, aspiration pneumonia, electrolyte imbalance and torn sutures [90]. Moreover, PONV leads to postoperative sleep disturbance by disruption of gut microbiome diversity [91]. A review showed that PC6 (Neiguan) flows freely with the adverse flow of qi and regulates the digestive system. Therefore, stimulating the PC6 (Neiguan) acupoint is an effective method to prevent PONV, and acupoint pressing is a non-invasive and supplementary method that can be used to stimulate the PC6 (Neiguan) acupoint to prevent PONV after surgery [92]. The acupoint ST36 (Zu Sanli) helps to relax the gastrointestinal tract and improve the body's recovery ability after surgery. Simultaneous stimulation of PC6 (Neiguan) and ST36 (Zusanli) can have a synergistic effect, regulating gastrointestinal function under the action of surgery and anesthetics, which can prevent PONV and accelerate gastrointestinal motility [93]. The acupoint ST36 (Zu Sanli) helps to relax the gastrointestinal tract and improve the body's recovery ability after surgery. Simultaneous stimulation of PC6 (Neiguan) and ST36 (Zusanli) can have a synergistic effect, regulating gastrointestinal function under the action of surgery and anesthetics, which can prevent PONV and accelerate gastrointestinal motility. Animal studies have suggested 3 possible mechanisms: (1) acupoint stimulation can induce release of peripheral opioids to relieve pain and reduce the use of opioids, which can

Table 2. Effect of acupoint stimulation on improvement in factors affecting postoperative sleep quality.

	Classification	Mechanism	Subjects	Acupoint	Acupoint intervention	References
Improvement of pain	Clinical trials	<p>i) Low frequency discrete dense wave stimulation can induce the relaxation of nerve stress</p> <p>ii) High frequency sparse dense wave stimulation has a strong opioid and non opioid mediated analgesic effect on the spinal cord</p> <p>The combination of low frequency and high frequency electroacupuncture stimulation will release a variety of opioid peptides, which has a synergistic effect of inhibiting pain.</p>	Patients with pain points	ST-36 (Zusanli), LI-4 (Hegu)	i) EA, Low frequency: 2 Hz; high frequency: 100 Hz	White A et al [76]
		<p>i) Effectively alleviate pain in elderly patients undergoing thoracoscopic surgery and promote rapid recovery after the operation</p>	Patients undergoing VATS pneumonectomy	LI-4 (Hegu) PC6 (Neiguan) SI-3 (Houxi) SJ-6 (Zhigou)	i) The electric stimulation intensity was 10-15 mA before operation, and 30 mA during operation, and the frequency was 2/00 Hz	Duan Z et al [77]
	Animal experimental studies	<p>i) Acupoints stimulation could relieve pain in chronic neuropathic pain rats, which may be related to its actions in down-regulating the levels of HMGB 1 and its downstream proinflammatory cytokines TNF-α and IL-1 β in the hippocampus</p>	Rats with chronic neuralgia	ST-36 (Zusanli), GB34 (Yanglingquan)	<p>i) EA, The stimulation intensity was increased step by step according to 0.5-1 and 0-1.5 ma</p> <p>ii) Each intensity lasted for 10 min, and the frequency was 2 Hz</p> <p>iii) 30 min, once a day</p> <p>iv) Last 7 days</p>	Wang K et al [78]

Table 2 continued. Effect of acupoint stimulation on improvement in factors affecting postoperative sleep quality.

	Classification	Mechanism	Subjects	Acupoint	Acupoint intervention	References
Improvement of pain	Animal experimental studies	i) Change the phosphorylation level of NR2B subunit of NMDA receptor in C1-C3 segment of spinal cord ii) Up-regulate the expression of 5-HT2AR mRNA and protein	Incision pain in the thyroid region in rats	LI18 (Futu) LI-4 (Hegu) PC6 (Neiguan) ST-36 (Zusanli), GB34 (Yanglingquan)	i) Electroacupuncture, frequency 2 Hz/15 Hz, 30 min, 1 mA in the first 15 min and 2 mA in the last 15 min	Qiao LN et al [79]
Improvement of surgical stress	Clinical trials	i) Acupoints stimulation can reduce inflammation and stress response through regulating the expression of inflammatory factors such as IL-1, IL-6, TNF- α , etc	Patients with Laparoscopic radical resection for colorectal cancer	ST-36 (Zusanli) LI-4 (Hegu) PC6 (Neiguan)	i) Electroacupuncture, frequency 2 Hz, current intensity was no more than 2 mA ii) The duration was from 30 minutes before operation to the end of operation	Guo J et al [84]
	Animal experimental studies	i) Restore suppressed lymphocyte proliferation, increase NK cell activity in the spleen by approximately 44% ii) Enhance the levels of serum IgM and IgA significantly in postoperative rats with gastric carcinoma, regulate immunity and attenuation of anesthesia- and surgery-induced immunosuppression	Liver cancer, gastric cancer and hypodermic tumor rat models were made by implantation of replicated Walker-256 cell strain	ST-36 (Zusanli) LI-4 (Hegu) SP6 (Sanyinjiao)	Electroacupuncture, 2 mA intensity, 2/100 Hz frequency mixing stimulation. once a day, 20 minutes each time Last 15 days	Lai M et al [87]

Table 2 continued. Effect of acupoint stimulation on improvement in factors affecting postoperative sleep quality.

	Classification	Mechanism	Subjects	Acupoint	Acupoint intervention	References
Improvement of postoperative complications	Clinical trials	i) Regulate the digestive system, directly reduce the incidence of postoperative nausea and vomiting	Patients undergoing surgery after anesthesia	PC6 (Neiguan)	i) The acupoints were pressed 6 hour	Yang J et al [92]
		ii) Produce synergistic effect on regulating gastrointestinal function impacted by the surgery and anesthetics to prevent PONV as well as accelerating motility of the gastrointestinal track	Patients undergoing general anesthesia	PC6 (Neiguan) LI-4 (Hegu)	i) All acupunctures were performed by an expert acupuncturist immediately after induction of general anesthesia ii) The needles remained in place until they were removed at the end of the surgery	Alizadeh R et al [93]
	Animal experimental studies	i) Acupoint stimulation could induce release of peripheral opioids to relieve pain and reduce the use of opioid, which may improve postoperative nausea and vomiting ii) Acupoint stimulation can alleviate delayed gastric emptying through CRF type-2 receptors, which mediates the outflow of parasympathetic efferent pathway iii) Sympathetic suppression, preventing presynaptic catecholamines from blocking the release of parasympathetic acetylcholine	Rats			Takahashi T et al [95]

improve postoperative nausea and vomiting [94]. (2) Acupoint stimulation can alleviate delayed gastric emptying through CRF type-2 receptors, which mediates the outflow of parasympathetic efferent pathway [94]. (3) Sympathetic suppression prevents presynaptic catecholamines from blocking the release of parasympathetic acetylcholine [95]. (Table 2)

Conclusions

It is often noticed that sleep quality usually decreases after surgery, especially in elderly patients. Factors related to poor

postoperative sleep quality include postoperative pain, the severity of surgical trauma and stress, perioperative anxiety and depression, and several other factors leading to patient discomfort. Various types of acupoint stimulation methods applied at corresponding acupoints can effectively alleviate postoperative pain, relieve perioperative anxiety and depression, improve the level of neurotransmitters in the body, and regulate the biological clock gene through different mechanisms of action, which can be used to improve postoperative sleep quality and may be helpful for postoperative recovery.

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