Observation of the clinical efficacy of esketamine in the treatment of depressive insomnia in patients after shoulder arthroscopy and analysis of its effect on plasma 5-HT content

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Introduction. To investigate the clinic effectiveness and effect on plasma 5-HT levels of esketamine in treating depressive insomnia in postoperative shoulder arthroscopy patients.

Methods. A total of 84 patients with depressive insomnia after shoulder arthroscopy received in our institution from June 2022 to June 2023 as study participants were randomly classified as 2 sets of patients, one set of patients in esketamine group (n=42) received 0.25 mg/kg of esketamine intravenously, while one set of patients in the comparison group (n=42) received an equal amount of saline intravenously. Before and after treatment, peripheral blood was drawn from both groups to detect changes in serum 5-HT levels, and clinical efficacy was also evaluated by PSQI, HAMD, HAMA, and Asberg Side Effects Scale (SERS).

Results.（1）Prior to treatment, no remarkable results of HAMD and HAMA scores of the two sets of patients showed any remarkable discrepancies ($P > 0.05$), following therapy, HAMD as well as HAMA decreased in two sets of patients ($P < 0.05$), which were lower in the esketamine sets compared to the controlled sets ($P < 0.05$).（2）Prior to treatment, no remarkable results of PSQI scores of the two sets of patients showed any remarkable discrepancies ($P > 0.05$), following therapy, PSQI decreased in two sets of patients ($P < 0.05$), which were lower in the esketamine sets compared to the controlled sets ($P < 0.05$).（3）Prior to treatment, no remarkable results of 5-HT level of the two sets of patients showed any remarkable discrepancies ($P > 0.05$), following therapy, 5-HT level increased in two sets of patients ($P < 0.05$), which were higher in the esketamine sets compared to the controlled sets ($P < 0.05$).（4）Following treatment, the aggregate efficacy ratio of the esketamine side of the

group was 95.24% greater as compared to 85.71% in its counterpart (P<0.05). （5）Following therapy, a decrease in SERS was seen in both groups (P<0.05), and it was below that of the controls in the patients in the esketamine group (P<0.05).

Conclusion. Esketamine can significantly reduce PSQI, SERS, HAMD and HAMA scores, increase serum 5-HT content, improve symptoms of anxiety, depression and insomnia, and has few adverse reactions.

Keywords. esketamine; shoulder arthroscopy; depression; insomnia; plasma 5-HT

INTRODUCTION

Anesthesiology science is a very unique and very important interdisciplinary discipline that integrates life sciences and medical sciences for clinical anesthesia, intensive care, analgesia, first aid, emergency care, and assisting surgeons, nurses, and patients in life safety. Through multidisciplinary evidence-based research, we explore ways to reduce postoperative stress, optimize postoperative physiological function, and promote postoperative recovery. Along with the rapid development of national economy and people's demand for humanization, the management of perioperative pain has become an important topic in the field of anesthesia. However, constrained by factors such as human resources, material resources, technology and concepts, perioperative analgesia is still mainly treated with opioids internationally, which not only leads to complications such as nausea and vomiting, itching, constipation, and respiratory depression, but also leads to problems such as patient's hospitalization time, healthcare costs, and sequelae [1,2].

Shoulder arthroscopy (scalp resection) is currently the main clinical treatment for shoulder pain, and although it is minimally invasive, about nearly half of the patients still feel severe pain after surgery, which is mainly characterized by moderate to severe pain and a VAS score of up to 7 at 24 h after surgery, accompanied by delayed recovery [3]. If the anesthesiologist and surgeon give the patient adequate pain relief in the perioperative period, then approximately 10% of patients will develop chronic pain [4]. Especially during prolonged postoperative bed rest, psychiatric problems can be easily induced due to reduced sleep quality, which reduces the quality of life of the

patient and decreases the quality of life of the patient. Although opioid analgesics can effectively reduce postoperative pain, surgical trauma, continuous flushing of the joint cavity, and tissue edema can cause severe pain to patients. Effective pain relief encourages early mobility, accelerates postoperative recovery, and shortens hospitalization days. Existing analgesia for shoulder surgery mainly uses perioperative hyperalgesia, transvenous patient-controlled analgesia (PCIA) and local infiltration, which can relieve pain, but there are still problems such as incomplete analgesia and opioid overdose [5]. In recent years, the combination of opioids with other analgesics has gradually been paid attention by researchers and considered as an effective analgesic strategy, such as the addition of opioids to PCIA can effectively improve the analgesic effect of PCIA. However, its application in the clinic is still controversial, with some scholars arguing that the addition of opioids to PCIA can lead a patient to experience nausea and emesis, constipation, breathing suppression, and other adverse reactions [6]. Other scholars believe that there are obvious synergistic effects when opioids are combined with other analgesics [7]. Therefore, how to reasonably select the anesthesia mode, rationally use analgesic drugs, minimize the dose of opioids, achieve the best analgesic effect and minimize the occurrence as well as the adverse reactions are the urgent questions that need to be resolved in clinical work at present.

Patients may experience depression and insomnia after shoulder arthroscopy, which can seriously affect their quality of life. As patients are bedridden for a long period of time after shoulder arthroscopy, their emotions and sleep quality are affected. It can cause adverse emotions as anxieties and dejection, which could affect sleeping performance; moreover, pain can also lead to insomnia [8]. At present, the treatment modalities for depression and insomnia in patients after shoulder arthroscopy mainly include medication, psychotherapy and nursing interventions. Pharmacotherapy includes antidepressants, anxiolytics, antipsychotics, etc., while psychotherapy mainly includes cognitive behavioral therapy and relaxation training [9]. Studies have shown that the symptoms of depression and insomnia in patients after shoulder arthroscopy are similar to those in patients with preoperative sleep disorders, and sleep disorders

not only reduce the quality of sleep, but also increase the risk of anxiety and depression [10]. According to statistics, the incidence of depression and insomnia in patients after shoulder arthroscopy is 30%~50% and 20%~40%, respectively [11], and both of these conditions are more common after shoulder arthroscopy, so how to improve the depressive and sleeplessness conditions and the life qualities of the passengers is currently a hotspot in the studies of anesthesiologists. It has been found that patients with preoperative sleep disorders also have a much larger prevalence of postoperative anxious and depressed moods [12]. In addition, it has been found that the symptoms of depression and insomnia in patients after shoulder arthroscopy are similar to those in patients with preoperative sleep disorders [13]. Arthroscopic surgery is currently one of the main methods of treating joint diseases. The joint capsule is filled with abundant blood vessels and nerves, and after arthroscopic surgical treatment, the damaged synovium, cartilage and ligaments and other tissues cause dilation of local blood vessels, increased permeability of blood vessels, edema of local tissues, and increased leukocytes in vivo, which act on the peripheral nerve pain receptors and thus trigger pain. This leads to a higher incidence of postoperative complications (delayed recovery of muscle strength, prolonged joint stiffness, etc.). Therefore, effective analgesia in the early postoperative period has become urgent to reduce resting and motor pain scores and to promote postoperative recovery [14]. 5-hydroxytryptamine (5- HT) is a major type of neural transmitter, which can adjust the body's mood and sleep condition.When 5- HT level increases, it can improve the patient's sleep quality and reduce the patient's depression; on the contrary, when the 5-HT level decreases, it will aggravate the patient's depression [15]. A previous research has demonstrated a regulatory action of 5- HT on depression, which can exert its neuromodulatory effect by affecting the pathways of 5- HT synthesis, release and metabolism [16]. 5- HT exerts its neuromodulatory effect by increasing the activity of monoamine oxidase (MAO) in the brain; in addition, it can also increase the activity of the enzyme 5- HT synthase (5-HT3). An important link in the 5- HT pathway associated with depression is MAO-B. Studies have shown that MAO-B inhibitors reduce depressive symptoms [17]. The mechanism of depression and insomnia in

postoperative patients after shoulder arthroscopy is unclear, but it may be related to postoperative patient pain, prolonged bed rest, high surgical trauma, and anxiety and depression.5- HT improves sleep and is associated with motor, learning, and memory functions, with 5- HT receptor agonists being effective in improving sleep [18].

Currently, there are many treatment modalities for depression and insomnia in patients after shoulder arthroscopy, but with varying efficacy and many side effects. Previous studies have found that ketamine has good therapeutic effects on both insomnia and depression, but whether it improves depression and insomnia in patients after shoulder arthroscopy remains controversial. Esketamine is a novel ketamine analog whose mechanism of action is different from other ketamine by blocking the 5-hydroxytryptamine transporter, thereby inhibiting the reuptake of 5-hydroxytryptamine, and thus inhibiting the release of the neurotransmitter 5-hydroxytryptamine, which in turn is an important neurotransmitter in one of the major components of the mesolimbic systems and has a modulating influence on sleep [19]. Meanwhile, esketamine is safe, efficient, and rapidly acting, and it is effective for all types of depression and insomnia [17]. Therefore, the purpose of this investigation to observe the effects of escrivastigmine in patients after shoulder arthroscopic surgery and its influence on plasma 5- HT levels.

1 MATERIALS AND METHODS

1.1 Preliminary data

Eighty-four depressive insomnia cases after shoulder arthroscopy treated in the period from June 2022 to June 2023 were chosen as research subjects, which will be randomly classified into 2 sets of patients, one set of patients in ketamine set (n=42) will receive 0.25mg/kg of ketamine intravenously, and the other set of patients in control set (n=42) will receive the same amount of saline intravenously. The number of patients in the esketamine group included 20 males and 22 females, whose ages ranging fro 26 and 59 years, mean ages were (45.87±2.45) years, and disease duration ranging between 1 and 6 years, average duration of the illness was (3.26±1.75) years. The cases of control set patients were 19 and 23 males and females with their age

ranging between 24 and 58 years old, the mean age was (44.85±3.14) and disease duration was ranged between 1 and 6 years, the average length of the case was (3.66±1.40) years. Comparison of the general data of patients with depressive insomnia after shoulder arthroscopy in both groups was not statistically significant ($P > 0.05$).

Inclusion criteria: unilateral shoulder arthroscopy patients who underwent unilateral shoulder arthroscopy under general anesthesia; those who were 18 years of age or older; those who had a HAMD score of greater than 20; those who had a Pittsburgh Sleep Quality Index scale (PSQI) score of greater than 7; those who had not used traditional Chinese or Western medicines for depression and insomnia in the past 1 week; those who had signed the relevant informed consent form; and those who already approved the study by the hospital's Ethics Committee, and the Ethics Committee followed the whole study.

Exclusion criteria: pregnancy; ASA grade 3 and above; weight less than or equal to 40 kg; history of liver disease; allergic reaction to local anesthetics or esketamine; history of dementia; history of alcoholism; history of renal damage; or use of esketamine within 24 hours after surgery; and patients with serious suicidal tendency.

1.2 Blinding and grouping

Patients eligible for the study were numbered in order of admission and each patient was assigned an opaque envelope, each with a corresponding number, which was then given to an anesthesiologist who did not participate in the experiment and who would record the patient's hospitalization number, order of admission, and weight. When it was time to perform the surgery, this nurse anesthetist would look for the corresponding patient according to their hospitalization number, and then take the number out of the corresponding envelope, and if it was a 0, put it in the control group, and if it was left with a 1, then put it in the esketamine group. In the study, the patients, the investigators and the followers were set up to be blinded so that only the nurse anesthetist would know the grouping of the patients and the way the medication was administered. After the follow-up was completed, the nurse anesthetist gave the above information back to the data processor.

1.3 Treatment methods

In this study, it was proposed to compare the HAMD score, HAMA score, PSQI score, SERS score, plasma 5- HT level, and the change in 5- HT between the two groups by dividing 84 patients into the esketamine group and the control group, respectively, using esketamine as the control group.

The study was conducted in a single-blind manner from design to implementation to evaluation; researchers and operators were aware of the group to which the patients belonged, and the patients were able to differentiate between intravenous administration and saline without affecting the effectiveness of the treatment. Escitalopram was administered intravenously by a specialized physician and trained prior to treatment. HAMD, HAMA, and SERS scores were assessed in a double-blind manner, and the patients were not involved in their treatment, ensuring complete confidentiality of patient grouping information. Pre- and post-treatment, testing for 5- HT, routine blood, blood biochemistry, thyroid function, and ECG were done by the Laboratory and Cardiology Department, which did not participate in the treatment.

(1) Preoperative: the researcher and the anesthesiologist came to the patient's ward one day before the operation, explained the experiment and the forms to the patient, and asked the patient to sign the informed consent form. The researcher explained the scales and how to fill them out in detail to the patients, and the patients independently completed the Pittsburgh Sleep Quality Index Scale (PSQI), Hamilton Depression Scale (HAMD), and Hamilton Anxiety Scale (HAMA) in the quiet ward, and the researcher administered questionnaires to the intact patients and scored them, and the general information of the patients (gender, age, education level , height, weight, presence and type of underlying disease, and mode of surgery), while the patient's main vital signs (heart rate, blood pressure) were monitored. Patients were evaluated by the anesthesiologist prior to surgery and scored on ASA, and those who met the inclusion criteria were randomly assigned. The process of randomization of patients in the prearranged order of surgery was done independently by anesthesiologists using a random table calculated by spss23. The fellow in charge of

the scale follow-up was not involved in this process.

(2) Intraoperatively: One day before surgery, the experimental drug (ketamine hydrochloride) was distributed to the anesthesiologist by a non-participating anesthesiologist, who drew 0.9% sodium chloride solution in a 10 ml syringe, diluted the drug to 10 ml, and labeled it with a white label that reads "investigational drug" and the content (5 mg/ml). The anesthesiologist draws 10 mL of 0.9% sodium chloride saline into a 10 mL vein and white-labels the drug "Study Drug" and the concentration (5 mg/mL). The investigator who dispensed the drug did not participate in this procedure. Under the supervision of the investigator, 5 minutes before induction of anesthesia in the control group, a single dose of 0.9% sodium chloride saline was administered at 0.25 mg/kg, i.e., 0.05 m/kg. patients in the esketamine group received a single intravenous injection of esketamine 5 min before induction of anesthesia, at a dose of 0.25 mg/kg, i.e., 0.05 ml/kg. The same surgical approach was used in the group and the control group. The patient entered the operating room and lay flat on the operating table.The anesthesiologist monitored the patient electrocardiographically, measured blood pressure and axillary temperature.The anesthesiologist turned on the heater and gave the patient continuous heater body surface warming to keep the patient warm during the operation, to prevent postoperative chills due to loss of patient's body temperature during laparoscopic surgery.The patient's body surface was warmed with a heater during the operation. Intraoperative monitoring of four-lead ECG, heart rate, noninvasive cuff blood pressure, finger pulse oximetry, and depth of anesthesia was used, and the anesthesiologist tested the safety of the anesthetic instruments before the initiation of anesthesia and set their respiratory parameters in accordance with the patient's profile, and the anesthesiologist administered the drugs 0.25 mg/kg, midazolam 2-3 mg, and 0.4-0.5 mg of remifentanil for 5 min after the induction of anesthesia. fentanyl, and 5 min later 10 mg/ml isoproterenol plasma-targeted induction (3-5 mg/ml), cis-atracurium (2 mg/kg) by Cisco medical inhalable pump, and 3 min intubation scale of 21-23 cm was given under the mask by anesthesiologist after it was secured in the airway and connected to anesthesia machine to implement ventilation in

PCV-VG mode. The operator covered the whole body with iodophor iodine tablets and started laparoscopic shoulder surgery. Intraoperative depth of anesthesia was maintained at 37-64 and end-expiratory CO2 concentration was 35-40 mmHg. cis-Atracurium was continuously given intraoperatively, gallbladder was removed, sufentanil citrate (0.2-0.4μ g/kg) was administered to prevent postoperative nociceptive hypersensitivity due to remifentanil; and 0.25 mg palonosetron (0.25 mg) was administered intravenously to prevent nausea and vomiting. The investigator should record the patient's vital signs 5 minutes before induction of anesthesia, 5 minutes after induction, at the beginning and end of surgery, and record the time of surgery and time of anesthesia. After surgery, the anesthesiologist will gather the patient and send him/her to the anesthesia recovery unit (PACU) and assess when the patient will be discharged from the hospital in the resuscitation room. The researcher will record the time the patient awakens in the resuscitation room. The patient returns to the hospital and is followed up by the researchers.

(3) Post-operative follow-up: During hospitalization, the researchers assessed by PSQI, HAMD and HAMA, and scored the patient's heart rate and blood pressure. During the follow-up, if the patient has left the hospital, the researcher will call the patient back.

1.4 Plasma 5 -HT specimen collection and testing methods

The 5- HT content was measured by the central research laboratory of our hospital and compared with the control group. Both groups stopped taking drugs on the day of admission, fasted from 20:00 p.m., and took 5 ml of blood from the elbow on an empty stomach at 7:00 a.m. the next morning. It was then placed in two separate cryopreservation of not less than 0.5 ml at -80°C. The samples were collected again on the 28th day after treatment. Competitive enzyme labeling method was applied for detection.

1.5 Observation indicators

Hamilton Depression Scale (HAMD): observe the alteration of each index of HAMD patients after receiving HAMD treatment and the alteration of 7 factors' scores. The comprehensive score can show the disease's seriousness, the heavier the

disease's seriousness, the higher the score. If the score is above 20, the depression is mild or moderate; if the score is above 35, the depression is severe.

Hamilton Anxiety Scale (HAMA): to observe the changes of the scores of Clinical Symptoms and the two index scores of HAMD patients after receiving HAMD treatment. The composite score can reflects the seriousness of the illness, higher the severity of the illness the higher the score. A score of 14 or more without reaching 21 indicates minor degrees of anxiety; those with ratings higher than 21 and lower than 29 are considered moderately anxious; and those with ratings greater than 29 are classified as having a serious disorder of anxiety.

Pittsburgh Sleep Quality Index Rating Scale (PSQI): the PSQI consists of 7 dimensions including sleep quality, sleep duration, hours of sleep, sleep disorders, sleep efficiency, hypnotherapeutic medications, and diurnal functioning, each of which has a score of 0-3, with scores ranging between 0 and 21, giving higher marks and poorer qualities of sleep.

Analysis of adverse events and adverse drug reactions: electrocardiogram, blood routine, blood biochemistry, sex hormones and thyroid function were observed in both groups. Based on this, our study intends to assess the effectiveness of the drug at both clinical and experimental levels, in which the main components of the drug are four aspects, namely headache, sleep disorder, somatic fatigue, vertigo and tremor, which are graded according to a scale of 0-4, and the higher the score, the more serious the adverse effects are.

Efficacy Determination Criteria: Efficacy was assessed based on the rate of HAMD score reduction using [(before treatment scale - after treatment scale)/before treatment scale]×100%. Complete cure: HAMD disease symptom remission rate of 75% or more; Effective: HAMD disease symptom remission rate of 50% or more; Ineffective: HAMD disease symptom remission rate or higher 25% or more; Ineffective: HAMD disease symptom remission rate of <25%.

1.6 Method of statistics

Data from the experiments of this research were analyzed using SPSS 23.0 program for each statistical index. The count data were analyzed by $\chi 2$ testing, and the

measure materials were indicated by average ± std. deviation (x ± s), one-way ANOVA was used for intra-group comparisons, and the t-test for separate samples was used for inter-group differences, and the difference was considered to be statistics meaningful at $P < 0.05$.

2 RESULTS

2.1 Comparison of anxiety and depression scores between patients in the 2 sets of patients

Prior to treatment, no remarkable results of HAMD and HAMA scores of the two sets of patients showed any remarkable discrepancies ($P > 0.05$), following therapy, HAMD as well as HAMA decreased in two sets of patients ($P < 0.05$), which were lower in the esketamine sets compared to the controlled sets ($P < 0.05$). Table 1.

TABLE 1 Analysis on anxiety ,depression ratings of patients in 2 sets of patients (x±s)

Subgroups	HAMD		HAMA	
	Before treatment	After treatment	Before treatment	After treatment
Aceketamine group (n=42)	24.98±3.45	15.48±2.46*	25.84±4.15	10.54±2.63*
Control group (n=42)	24.56±3.68	18.54±2.87*	25.16±4.35	12.63±2.84*
t-value	0.548	3.154	0.964	2.365
P value	0.638	0.036	0.415	0.041

Note: In comparison with the same set of patients prior to therapy, *$P < 0.05$.

2.2 Comparison of sleep quality scores in the 2 sets of patients

Prior to treatment, no remarkable results of PSQI scores of the two sets of patients showed any remarkable discrepancies ($P > 0.05$), following therapy, PSQI decreased in two sets of patients ($P < 0.05$), which were lower in the esketamine sets compared to the controlled sets ($P < 0.05$). Table 2.

TABLE 2 Analysis on PSQI ratings of patients in 2 sets of patients (x±s)

Subgroups	n	Before treatment	After treatment	t-value	P value
Aceketamine group	42	14.85±3.63	5.48±2.31	8.541	0.000
Control group	42	14.33±3.87	7.98±2.64	6.785	0.001
t-value		0.842	2.523		
P value		0.423	0.037		

2.3 Comparison of serum 5-HT between the two groups of patients

Prior to treatment, no remarkable results of 5-HT level of the two sets of patients showed any remarkable discrepancies ($P > 0.05$), following therapy, 5-HT level increased in two sets of patients ($P < 0.05$), which were higher in the esketamine sets compared to the controlled sets ($P < 0.05$). Table 3.

TABLE The serum 5-HT ratio comparing the 2 sets of subjects (x±s)

Subgroups	n	Before treatment	After treatment	t-value	P value
Aceketamine group	42	103.45±68.48	183.54±84.12	12.540	0.000
Control group	42	104.87±71.63	176.81±74.81	11.871	0.001
t-value		0.974	2.384		
P value		0.382	0.039		

2.4 Comparison of clinical efficacy in the 2 sets of patients

Following treatment, the aggregate efficacy ratio of the esketamine side of the group was 95.24% greater as compared to 85.71% in its counterpart ($P<0.05$). Table 4.

TABLE 4 The clinical effectiveness of the two sets of patients was evaluated in comparison (n,%)

Subgroups	n	Effective Ineffective	Effective	Ineffective	Overall Effective Rate
Aceketamine group	42	23（54.76）	17（40.48）	2（4.76）	40（95.24）
Control group	42	20（47.62）	16（38.10）	6（14.29）	36（85.71）
χ^2-value					2.636
P-value					0.034

2.5 Patients' SERS in the 2 treatment groups

Following therapy, a decrease in SERS was seen in both groups (P<0.05), and it was below that of the controls in the patients in the esketamine group (P<0.05). Please see Table 5.

TABLE 5 The SERS compare in 2 sets of patients (x±s)

Subgroups	n	Before treatment	After treatment	t-value	P value
Aceketamine group	42	11.45±2.65	3.45±0.83	10.565	0.000
Control group	42	11.38±3.14	6.15±0.39	8.453	0.000
t-value		0.716	4.891		
P value		0.408	0.010		

3 DISCUSSION

The drug ketamine has been increasingly researched and ketamine is now being used as a safe anesthetic not only in the operating room but also outside the operating room in various clinical scenarios and its use has expanded considerably.The non-anesthetic use of ketamine as an anesthetic drug with a history of 65 years has been described in the article Non-Anesthetic Applications of Ketamine by Pribish A et al [20]. A ketamine is a nonsselective inhibitor of N-methyl-D atropine (NMDA)

acceptor and is broadly used in medicine being an anesthetic drug; however, ketamine is not just an anesthetic drug possessing anesthesia, sedation, and analgesia, but its mechanism of action leads to a wide range of physiological effects. Ketamine has the same affinity for different NMDA receptor types[21]. NMDA and AMPA are a subgroup of glutamate ionotropic receptors. Among the non-anesthetic uses of ketamine, in addition to the finding that ketamine provides rapid symptomatic relief in depressed subjects as well as rapid elimination of suicidal thoughts in depressed subjects with suicidal ideation, ketamine has been shown to provide relief of acute and acute and chronic pain, likely due to the anti-inflammatory response of ketamine. In patients with intracranial injuries, recent research has revealed that ketamine might exert some neuroprotective properties, a finding that contradicts the traditional claim that ketamine raises intracranial pressure and is not indicated in patients with craniocerebral injuries. Ketamine was also proven to somewhat mitigate relapse rates in alcohol-dependent persons after abstinence from alcohol. As an anomeric version of ketamine, esketamine has been shown to be 3-4 Times less potent as an anesthetic drug than ketamine [22]. The use of esketamine has also been expanded in recent years, not only as an anesthetic for adults, but also routinely as an intensive anesthetic for nerve blocks, and also for pediatric surgery. The pharmacologic effects of ketamine have been explored over the years, and the use of ketamine has also itself being described as valid for the therapy of anxiety and dementia and for improving the mood of the patients [23]. Preoperative use of nasal spray esketamine ketamine has been shown to alleviate separation anxiety and stress in pediatric patients undergoing surgery [24]. clonescu et al. showed that a mono dose IV intake of ketamine had the effect of improving depressive functioning in depressed anxious patient with bipolar spectrum of depression [25]. Although ketamine and esketamine have been shown in numerous studies to have an ameliorative effect on anxiety and depression in patients, the mechanism by which ketamine is anxiolytic and improves mood in patients is still unknown to us. However, we do know that the mode of action of ketamine is different from that of monoamine antidepressants. Traditional antidepressants focus on the monoamine system, with various mechanisms focusing

on the serotonin, norepinephrine, and dopamine systems. However, studies of the pathophysiology of mood disorders suggest that abnormalities in glutamatergic transmission may be implicated in the functional and structural disruption of neural circuits associated with mood regulation [26]. This finding prompted researchers to begin further studies on the role of glutamate N-linked ~D-aspartate (NMDA) reception regulators in the treating depressive disorders [27,28]. Subanesthetic doses of ketamine and esketamine trigger intracellular cascades that induce synaptogenesis and dendrite formation thereby affecting three signaling pathways in the glutamate hypothesis that may be relevant in treating discrimination in depressive disorders, namely, the BDNF (Brain-derived neurotrophic factor) pathway, MMR (Mission Target of Rapamycin (MTOR)) signaling pathway, as well as the AMPA receptor [29].Duman R S et al [27] have found a stimulus-induced effect of ketamine on neuronal plasticity, thereby counteracting the effects of anxiety as well as those of dependency on the depression. The crucial genes of interest in that process being BDNF [30] and MTOR. Ketamine affects the fast excitatory glutamatergic transmission, increases BDNF release, and stimulates synaptogenesis. Ketamine also provided elevated expression of glutamate cotransporters in the rat human hippocampus, particularly EAAT2 as well as EAAT3.Modulation of hippocampal plasticity is another mechanism by which ketamine mediates her anti depressant action, which may be linked to EAAT3's regulation of AMPA receptor transporter and redistribution. It is also possible that the ketamine action mechanism on onset of depression may be related to the mitochondrial network. Ketamine are N-methyl-D-aspartate (NDMN) antagonist with tranquilizing in local system. anxiolytic as well as analgesic effects. Eslicarbazone is the levorotatory form of the racemate of ketamine, and compared with the dextrorotatory form, eslicarbazone has a higher binding affinity towards aspartic acid of N-methyl-D aspartic acid, and only half the dosage can achieve the same effect as ketamine.Wang J [24] et al. intervened in patients undergoing surgery for endometrial carcinoma with different dosages of eslicarbazone and found that the treatment group (eslicarbazone group) had a higher binding affinity for N-methyl-D aspartic acid on the 1st, 2nd, and 3rd days

postoperatively BDNF and 5-HT levels were higher in the s -ketamine higher dose set (0.5 mg/kg) than in the controlled set (P<0.05), with the maximum BDNF level in the s -ketamine upper dose set (0.5 mg/kg) (P<0.05). That means esketamine improves mood of employees probably through expression of BDNF and 5~HT levels.2019 European Association approved the application of esketamine nasal drops spray developed by Johnson & Johnson for refractory . patients with treatment-resistant depression [32]. Given that esketamine differs from conventional antidepressant and mood-improving pathways of action, esketamine is a safe alternative for patients in whom conventional antidepressants (e.g., monoamine antidepressants) are ineffective.

Mental health disorders such as hypertension are characterized by a significant prevalence of depression, a significant relapse risk, and a high rate of suicidality. It has been shown that depression has a high prevalence rate and its pathogenesis is complex, which is mainly characterized by neuroendocrine dysfunction and accompanied by abnormal changes in neurotransmitters, such as changes in content of serotonin 5-hydroxytryptamine (5- HT), non-norepinephrine (NE), as well as dopamine (DA) [33]. The main clinical symptoms of depression are depressed mood, slow thinking, reduced interest, lack of initiative, etc., and they are very prone to self-blame and self-guilt and severe negative emotions. Due to long-term emotional depression, most patients are accompanied by insomnia symptoms, poor sleep quality, and prolonged lack of adequate sleep will exacerbate depressive signs and lower the life quality [15]. Shoulder arthroscopy is a common procedure in shoulder surgery, but because of its traumatic, painful and slow recovery, postoperative patients often suffer from insomnia, which seriously affects the quality of life, and with shoulder arthroscopy, the patients' postoperative recovery time is prolonged, and they may even suffer from depressive symptoms. At present, antidepressant drugs are mostly used in the clinical treatment of depression in postoperative shoulder arthroscopy patients, however, such drugs often bring many adverse reactions, such as drowsiness, fatigue, bradycardia and other symptoms. Therefore, how to improve the sleep quality and alleviate the depressive symptoms of postoperative shoulder arthroscopy patients has become an urgent clinical problem. In addition, patients with depression have

significant autonomic nervous system dysfunction, such as activation of the sympathetic nervous system and vagal hypertonia [34]. In this study, the anxiety and depression symptoms of the patients in the esketamine arm showed marked amelioration, with a difference in terms of improved condition when compared with the controlled arm ($P<0.05$). Insomnia is a component of the depressive symptom cluster, and insomnia is closely related to depression and is one of the prodromal symptoms of depression or a risk factor for recurrence. Among postoperative shoulder arthroscopy patients, depression with insomnia accounts for a high percentage of patients and is prone to pain, anxiety, insomnia and other symptoms, affecting the quality of life. Currently, antidepressant drugs are mostly used for treatment, but some patients still cannot effectively improve insomnia symptoms. This study found that the comparison of 5-HT content between the three sets of data revealed that patients in the three sets had similar 5-HT content before treatment ($P>0.05$), and that both sets of serum 5-HT level showed a significantly greater increase after treatment versus prior to therapy ($P<0.05$), suggesting that aceketamine therapy can increase the serum 5-HT content of patients with insomnia associated with depression, affect the neurotransmitter level, and promote the improvement of depression and the induction of sleep. In addition, studies have shown that the plasma 5-HT content of insomnia patients is markedly decreased than normal, which is related to depressive symptoms and recurrence of depression [35]. 5- HT being a neurotransmitter of extensive biological effects, it has an importance in various physiological processes in the organism. 5- HT, as a neurotransmitter, promotes the excitability of the brain and affects the information transmission between central synapses; it can participate in immune regulation and endocrine regulation through a variety of pathways, etc. [18]; and it is also closely related to immune function. Studies have shown that the 5- HT content is decreased markedly in the insomnia patients' brain, which may constitute a main cause of deployment of factors that lead to depression and insomnia [36]. The main principle mechanism of esketamine therapy for treating insomnia with depressive disorder is to inhibit the 5- HT reuptake of CNS and promote release a neurotransmitter, so as to improve sleeping quality. The present study found ketamine

can improve the sleep quality in patients who suffer from depression with insomnia, improve the depressive status and insomnia patients' symptoms, as well as increase the patients' living quality. In addition, a study comparing the sleep quality of patients in the 2 arms showed that following therapy, the PSQI scale of psilocyamine victims in the estrone group was lower than that of the comparison arm, suggesting that the estrone ketamine therapy can improve the quality of sleep to a certain extent, which may be related to the ability of estrone ketamine to rapidly improve the pain symptoms of the patients, thus improving insomnia [37]. Treatment effect of two groups of patients showed that the HAMD and HAMA scores of patients in both Groups dropped significantly after treatment, and the clinical effectiveness rates of patients in the esketamine group were 95.24%, and 85.71% in the controlled period ($P < 0.05$); the negative effects of patients in both periods revealed that SERS scores were lower than the control group in the esketamine one, with the remarkable discrepancies ($P < 0.05$), and no liver function problems occurred in the control group ($P < 0.05$). And there were no adverse reactions such as liver function abnormality, leukopenia, and elevated blood lipids in the control group, suggesting that acupuncture treatment has fewer side effects and is safer to apply.

4 CONCLUSION

In conclusion, in this study, by comparing the sleep quality, depressive symptom scores and HAMA scores of postoperative depressive insomnia patients after shoulder arthroscopy with those of the control group patients in the pre- and post-treatment periods, the findings indicate that, after therapy, esketamine is able to improve the sleep quality of postoperative patients after shoulder arthroscopy and reduce their depressive symptom scores and HAMA scores, and it is safe with fewer adverse reactions, which makes it a promising application for postoperative depressive insomnia after shoulder arthroscopy. insomnia is promising. This discovery suggests an increasing prevalence of emotional problems among patients undergoing surgical procedures in hospitals, and the importance of paying attention to psychological problems such as anxiety and depression manifested during the perioperative period

and analyzing their causes is needed. In practice, the emotional anxiety and depression of patients are often neglected, and in this context, the study of their anxiety and depression states is of great practical significance for improving the efficacy and safety of the perioperative period. Attention to preoperative emotions, preoperative emotional control, and preoperative administration of necessary medications can help to reduce patients' anxiety and depression. This research will provide a basis for clinical staff (especially anesthesiologists) to rapidly identify postoperative emotional disorders (e.g., anxiety, depression, etc.), for anesthesiologists to apply esketamine to rapidly alleviate patients' anxieties and depressions during the perioperative period, and for anesthesiologists to better control patients' psychological status during the perioperative period.

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