Observation and Analysis of the Postoperative Analgesic Effect of Sub-Anaesthetic Dose of Ketamine in Kashin-Beck Disease Patients after Total Knee Arthroplasty

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Introduction. To investigate the clinical application value of subanesthesia ketamine in analgesia of patients with kaschin-beck disease after total knee replacement.

Methods. This research belongs to a randomized, prospective study, selected in July 2020 to December 2021 in our hospital the kaschin-beck disease in 79 cases of total knee arthroplasty, according to the method of random Numbers table it can be divided into the dosage group (n = 40) and normal group (n = 39), the dose group, by making in small dose ketamine and propofol anesthesia, The normal group received single ketamine general anesthesia. VAS scores were used to compare the pain degree of the two groups immediately after awakening (T0), 2h after awakening (T1), 6h after awakening (T2), 12h after awakening (T3) and 24h after awakening (T4). Changes of hemodynamic parameters before (K1), during (K2) and after (K3) anesthesia were observed in 2 groups. Fentanyl dosage was compared between the two groups within 24 hours after surgery. The incidence of postoperative adverse reactions was compared between the two groups.

Results. Wake up immediate pain in the two groups had no significant differences, as the anesthetic efficacy gradually disappear, two groups of patients with pain levels tend to rise, and in T2 peak, over time the pain of the two groups after T2 are decreased, and the dose groups of VAS score in T1 ~ T4 stage always lower than normal group ($P < 0.05$); Compared with normal group, the changes of intraoperative hemodynamic parameters in subdose group were more stable ($P < 0.05$). The number of postoperative fentanyl analgesia in subdose group was significantly lower than that in normal group ($P < 0.05$). Compared with normal group, the incidence of postoperative adverse reactions in subdose group was significantly lower ($P < 0.05$).

Conclusion. Subdose ketamine in patients with kashin-beck disease undergoing total knee replacement can significantly reduce postoperative pain, reduce the frequency of opioid use, and maintain intraoperative hemodynamic stability while reducing the incidence of postoperative adverse reactions, which has high clinical application value.

Keywords. subanesthetic dose; Ketamine; Total knee replacement; Analgesic effect; Application value

INTRODUCTION

As a surgical method to further improve the function of the knee joint by replacing the bone and cartilage with artificial biomaterials, total knee replacement is mainly used for the treatment of various diseases such as osteoarthritis and rheumatoid arthritis in clinical practice [1-2]. Kashin-beck disease, as a kind of deformed osteoarthropathy commonly occurring in children and adolescents, has not yet been studied to clarify its pathogenesis, and its main clinical characteristics are mainly manifested as the earliest involvement of the joints of the extremities, with symmetric onset, which has a serious impact on the development and daily life of adolescents [3-4]. For symptoms lighter kaschin-beck disease mainly prevention, but for serious kaschin-beck disease has appeared joint deformation must surgery, including total knee arthroplasty as a surgical treatment, in alleviating pain, improve the function of knee joint and restore ability plays an important role in daily life [5-6]. However, as this kind of surgery is a highly invasive surgical method, it will produce severe and difficult to control the pain after surgery, so the use of narcotic drugs during surgery is of great significance for postoperative analgesia [7]. Studies have shown that ketamine as a kind of NMDA receptor antagonist, with propofol compound which can play a better analgesic effect, and reduce the postoperative adverse events, based on the tonggu oh this study selected 79 routine of kaschin-beck disease, total knee arthroplasty with different doses of ketamine in operation, observe the postoperative analgesic effect of concrete and its clinical value.

1. GENERAL INFORMATION AND METHODS

1.1 General Information

This study belongs to a randomized, prospective study, selected in July 2020 to December 2021 in our hospital the kaschin-beck disease in 79 cases of total knee arthroplasty, according to the method of random Numbers table it can be divided into the dosage group (n = 40) and normal group (n = 39), two groups of patients with baseline data contrast are shown in table 1, are comparable (P > 0.05). All the patients included in the study signed informed consent and obtained the right to know and consent about the anesthesia method used in the surgery. The clinical data and general information collected in the study were kept confidential and used only for research purposes, not for other purposes.

Inclusion criteria :(1) it met the relevant standards for total knee replacement in clinical practice [8]; (2) No history of allergy to narcotic drugs used in the study; (3) Complete clinical data and general information; (4) High treatment compliance.

Exclusion criteria :(1) accompanied by mental diseases, unable to achieve good communication with researchers; (2) coagulopathy; (3) congenital immune dysfunction; (4) patients with dysfunction of major organs such as heart, liver and kidney.

Table1 The baseline data

	Subdose group（*n*=40）	Normal group（*n*=39）	t/x^2	*P*
Age(years)	25.10±4.95	23.72±4.48	1.300	0.198
Gender			0.318	0.573
Man	21（52.50%）	18（46.15%）		
Woman	19（47.50%）	21（53.85%）		
BMI（kg/m^2）	23.99±1.11	24.10±1.07	-0.451	0.653
Level of education			0.949	0.622
Primary and below	5（12.50%）	4（10.26%）		
Junior to Senior High	27（67.50%）	30（76.92%）		
University and above	8（20.00%）	5（12.82%）		

1.2 Methods

1.2.1 Method of anesthesia

Subjects in both groups were required to abstain from food and water for 6h before surgery. After receiving the same routine examination, scopolamine was intramuscular injected at a dose of 0.01-0.02 mg/kg 30min before surgery, and routine ecg monitoring was established after entering the operating room. The subdose group received intravenous induction of propofol at a dose of 10-15mg /kg before surgery, and maintained intraoperative anesthesia with 1-2mg /kg ketamine and 1.5-2mg /kg propofol. The normal group was given an acute intravenous injection of ketamine at a dose of 2mg/kg before the operation, and 0.5-1mg /kg ketamine was injected intermittently at an interval of about 10min for each patient's intraoperative reaction to maintain intraoperative anesthesia. The dosage of anesthesia was appropriately adjusted in both groups according to patients' intraoperative response to stimulation, and the administration was stopped 10min before surgery. During this period, hemodynamic parameters and vital signs of the subjects were closely monitored. Fentanyl can be used for postoperative analgesia if patients have unbearable pain, and the frequency of fentanyl use in each group was recorded.

1.2.2 VAS score

This scale is mainly used to evaluate the pain degree of patients. The specific operation is to draw a line with a length of 10cm on the paper, with one end marked as 0, indicating no pain. The other end is marked with a 10, indicating extreme pain, and patients are asked to mark on a straight line according to their own perception of pain. Scores ≤3 indicate mild pain and tolerable; A score of 4-6 indicates that the pain has affected sleep but is still tolerable. A score of ≥7 indicates pain that is unbearable and interferes with daily life.

1.3 Technical Roadmap

See Figure 1 for details:

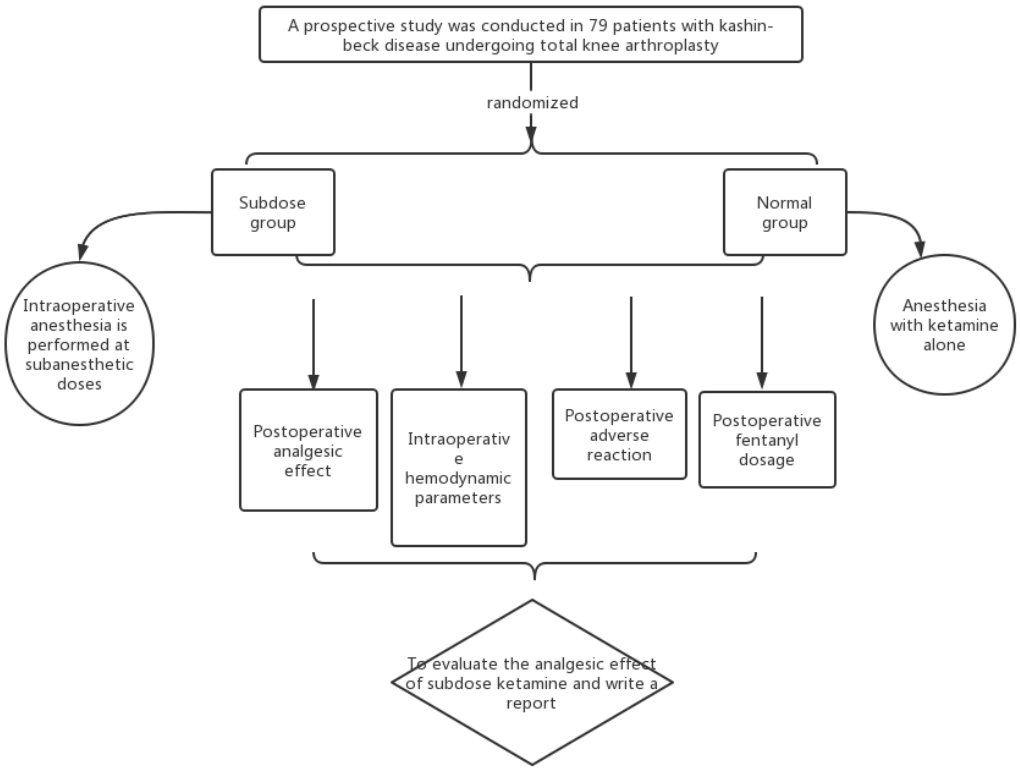

Figure 1 Technology Roadmap

1.4 Statistical Processing

SPSS 25.0 statistical software was used for data analysis. (1) Measurement data: If the data followed the normal distribution and homogeneity of variance after the normality test, it was represented by mean ± standard deviation. Paired sample T was used to test within the group, and variance comparison was used between the groups. Repeated measurement anOVA was used at each time point within the group, and spherical test was performed. (2) Count data: Descriptive statistical analysis was conducted by percentage, and x^2 test was performed. All the above data showed significant differences with $P < 0.05$.

2.RESULTS

2.1 Observe the changes of pain in different time periods after awakening

Results show that the awakening in immediate pain in the two groups had no significant difference, but with the anesthetic efficacy gradually disappear, two groups of patients' pain levels tend to rise, and in the T2 peak, but the dose level of pain, between T1 and T2 were lower than normal group ($P < 0.05$), T2 over time after two group, all the pain of fall, VAS score of the subdose group was still lower than that of the normal group at T3~T4 stage ($P < 0.05$), as shown in Table 2 and Figure 2.

Table 2 VAS score changes

Group	*n*	T0	T1	T2	T3	T4
Subdose group	40	2.63±1.08	4.30±1.22*	4.93±1.51$^{*\#}$	3.88±1.31$^{*\#\&}$	2.10±0.87$^{*\#\&\%}$
Normal group	39	2.49±1.05	5.82±1.17*	7.03±1.44$^{*\#}$	4.51±0.99$^{*\#\&}$	2.54±1.05$^{\#\&\%}$
t		0.576	-5.649	-6.324	-2.437	-2.025
P		0.566	＜0.001	＜0.001	0.017	0.046

Note: "*" means that compared with T0, *P < 0.05; "#" indicates that compared with T1, #P < 0.05; "&" means that compared with T2, &P < 0.05; "%" means %P < 0.05 compared with T3.

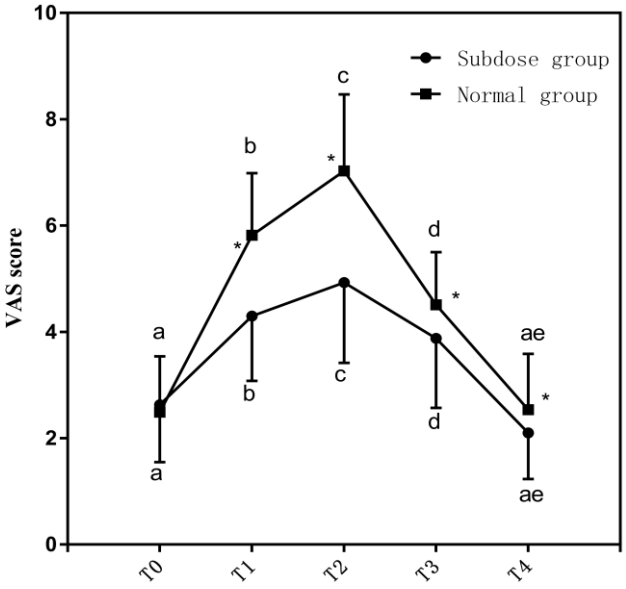

Figure 2 VAS score changes

Note: "a、b、c、d、e" in Figure respectively means that if the same letter is shared between groups, P > 0.05 at different time points; "*" indicates that P < 0.05 between the two groups compared at the same point

2.2 Comparison of intraoperative hemodynamic parameters at each time

MAP changes at each intraoperative time point were shown in Table 3 and Figure 3, and HR changes were shown in Table 4 and Figure 4. The results showed that the intraoperative hemodynamic parameters of the subdose group were more stable than those of the normal group ($P < 0.05$).

Table 3 MAP（kPa） changes

Group	*n*	K1	K2	K3	*F*	*P*
Subdose group	40	9.22±0.66	9.49±0.64*	9.37±0.62*#	1.845	1.172
Normal group	39	9.22±0.64	9.88±0.66*	9.59±0.63*#	10.109	＜0.001
t		-0.007	-2.668	-1.639		
P		0.994	0.009	0.105		

Note: "*" means that compared with K1, *P < 0.05; "#" indicates that compared with K2, #P < 0.05.

Table 4 HR（times/min）changes

Group	*n*	K1	K2	K3	*F*	*P*
Subdose group	40	119.55±6.05	126.65±7.84*	119.85±5.88#	13.847	＜0.001
Normal group	39	118.92±6.81	141.10±7.29*	133.31±7.35*#	91.217	＜0.001
t		0.433	-8.478	-9.003		
P		0.666	＜0.001	＜0.001		

Note: "*" means that compared with K1, *P < 0.05; "#" indicates that compared with K2, #P < 0.05.

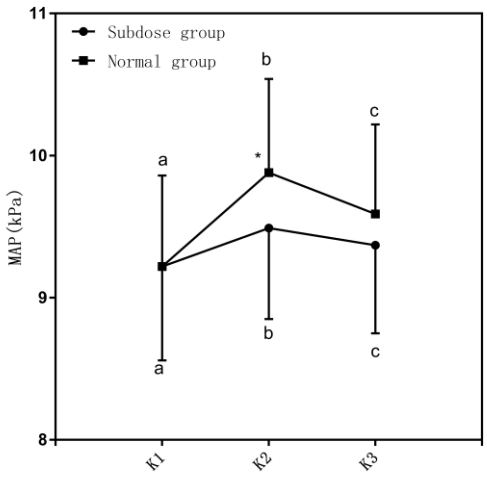

Figure 3 MAP（kPa） changes

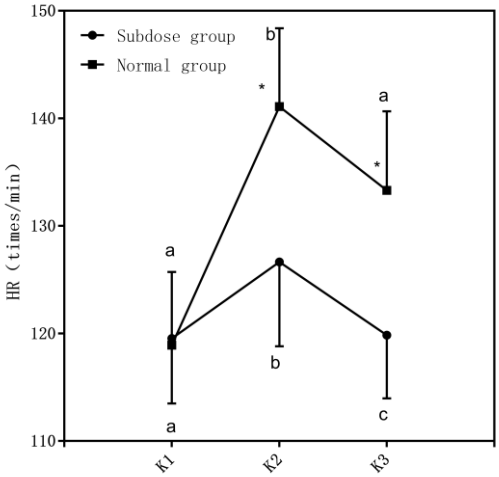

Figure 4 HR（times/min）changes

Note: "a、b、c" in Figure respectively means that if the same letter is shared between groups, P > 0.05 at different time points; "*" indicates that P < 0.05 between the two groups compared at the same point

2.3 Fentanyl use times within 24 hours after operation were compared

During postoperative observation, the frequency of fentanyl use in the subdose group was significantly lower than that in the normal group (P < 0.05), as shown in Table 5 and Figure 5.

Table 5 Number of times fentanyl was used

Group	*n*	Time
Subdose group	40	3.48±1.34
Normal group	39	5.41±1.82
t		-5.398
P		＜0.001

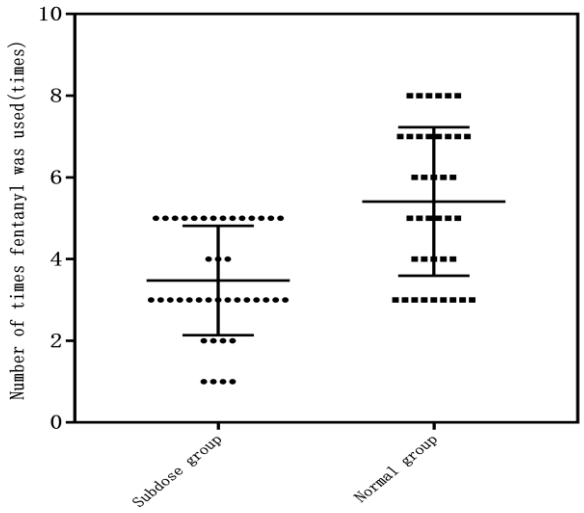

Figure 5 Number of times fentanyl was used

2.4 The incidence of postoperative adverse reactions was compared

Compared with the normal group, the incidence of postoperative adverse reactions was significantly lower in the subdose group ($P < 0.05$), as shown in Table 6.

Table 6 Comparison of adverse reactions

Group	*n*	Nausea and vomiting	Agitation during the waking period	Venous thrombosis of lower extremity	Total complications
Subdose group	40	3	2	1	6（15.00%）
Normal group	39	7	4	3	14（35.90%）
x^2					4.561
P					0.033

3. DISCUSSION

Kashin-beck disease (KBD), as a disease type commonly occurring in children and adolescents, is mainly characterized by multi-site symmetry and the earliest involvement of limb joints, which seriously affects the healthy development of

adolescents and causes a serious decline in the quality of life [9]. At present, there has not been a unified conclusion on the pathogenesis of KASHin-beck disease in clinical practice, and the factors affecting the formation of such diseases are mainly environmental factors. Most scholars in the industry believe that selenium deficiency is one of the important environmental factors leading to the occurrence of Kashin-beck disease, because the distribution of such diseases is basically the same in the low-selenium soil zone [10]. Other scholars also believe that eating food contaminated by mold, toxin or organic matter is also associated with the occurrence of this disease, but the specific pathogenesis of this disease has not been clearly explained [11]. The treatment of this disease mainly focuses on prevention, and surgical treatment is necessary for patients with severe joint deformation that cannot be alleviated by drugs. Among them, knee replacement is mainly targeted at patients with severe knee joint involvement resulting in severe osteoarthritis and loss of working ability and living ability [12]. However, since this operation is a highly invasive open surgery, it will cause a strong sense of pain to patients after surgery, so the use of anesthetic drugs during surgery is particularly important. Therefore, in this paper, subanesthetic ketamine was selected for intraoperative anesthesia, and the postoperative analgesic effect was observed.

Results show that the wake up instantly no difference between the two groups of pain, but in the process of efficacy gradually disappear, the pain in two groups are on the rise, and peaked at 6 h after waking up, after the pain relief, in the process of central Asia dose group of VAS score lower than normal group, and the postoperative use of fentanyl dose group was also significantly lower than normal group, It indicates that subanesthetic ketamine has strong analgesic effect after operation. After analysis, the author believes that ketamine, as a derivative of cyclohexidine, is highly lipophilic and its lipid solubility is about 5-10 times that of sodium thiopental. Therefore, ketamine can enter the central nervous system quickly after intravenous injection and exert anesthetic effect within about half a minute [13-14]. The main mechanism of analgesia is through selective inhibition of the medial thalamic nucleus, and has a

certain blocking effect on the upward signal transmission of the spinal cord reticular tract. Therefore, after ketamine application, patients will show decreased somatic pain, but some patients will show indifference [15]. Ketamine can also increase the sympathetic nervous activity at the same time, make blood flow, cardiac output appear different degree of increase, but if intraoperative fade out with ketamine anesthesia excitement excessive can cause cardiovascular system, cause the heart rate, awakening the symptom such as restlessness, this study also shows that, compared with the dose group, The changes of hemodynamic parameters in the normal group were larger, which was consistent with the above research results [16]. Moreover compared two groups of postoperative incidence of adverse reactions, according to the results of the dose group had a significantly lower incidence of postoperative complications, the thorough analysis due to the combined propofol dose group, has a short half-life, smooth induction, has many characteristics, such as inhibition of vomiting, and with the dose of ketamine combined after use can be significantly reduced by ketamine cardiovascular system adverse reactions, Therefore, postoperative nausea and vomiting, agitation during recovery and other side effects can be significantly reduced [17-18].

To sum up the anesthesia of ketamine can play a role of strong analgesia after total knee arthroplasty, and to reduce the use of fentanyl, at the same time can keep patients in intraoperative maintain stable hemodynamics, and reduce postoperative cardiovascular system adverse reactions associated symptoms and agitation, has high clinical value. But as a result of this study belongs to the small sample size, so there is no representative, has the high above and not for the patient on the activity time, degree of knee recovery on record, so this research there are still some shortcomings, can continue to expand in the next step research sample size, and by observing the patients recovery of knee function recovery, The effect of subanesthetic ketamine was further evaluated.

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