

Original Research Article

Effects of different doses of ropivacaine on postoperative analgesia, incidence of complications and stress factors in patients undergoing total knee arthroplasty

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Abstract

Purpose: To study the influence of various doses of ropivacaine (Ropi) on postoperative analgesia, incidence of complications and stress factors in patients undergoing total knee arthroplasty (TKA).

Methods: One hundred and fifty (150) patients who received TKA treatment in Ganzhou Hospital of Traditional Chinese Medicine from January 2017 to January 2019 were randomly assigned to low-dose Ropi (0.15 %, group A), medium-dose Ropi (0.20 %, group B) and high-dose Ropi (0.30 %, group C), with 50 patients in each group. Changes in visual analogue scale (VAS) scores, MMSE scores, cognitive dysfunction, serum cortisol (Cor) and adverse reactions were determined before and after surgery.

Results: Compared with group A, scores on rest visual analogue scale (RVAS) and passive visual analogue scale (PVAS) were significantly higher in low-dose and high-dose Ropi groups 24 and 48 h postoperatively ($p < 0.05$). Serum Cor levels in low-dose Ropi-treated patients were significantly lower than those in the other groups at 24 and 48 h after surgery ($p < 0.05$). The MMSE scores at 48 and 72 h after surgery were significantly higher in low-dose Ropi-treated patients than in the other 2 groups. The number of patients with cognitive impairment after surgery (POCD) was significantly higher in groups B and C than in A ($p < 0.05$).

Conclusion: Low-dose Ropi exerts significant analgesic effect on elderly patients undergoing TKA, and improves their cognitive function without increasing stress response. Therefore, it should be further investigated on a larger scale for its potential as a candidate analgesic for patients after TKA.

Keywords: Ropivacaine, Total knee arthroplasty, Postoperative analgesia, Stress factors

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INTRODUCTION

Data have shown that with increase in the population of the aged, the proportion of people aged 65 and above in the total population of

China increased from over 7 to 90 % from 2000 to 2010 [1]. Femoral neck fracture and knee arthritis are amongst the frequently-occurring diseases in the elderly, and they have a negative impact on the daily lives of patients, thereby

reducing their quality of life [2]. Total knee arthroplasty (TKA), an important surgery for repairing knee injuries, has been widely used in clinics in recent years. This surgical technique not only solves serious knee diseases, but also corrects knee deformities caused by various factors, and restores knee function [3].

For now, the traditional analgesic methods in clinical practice include oral drug analgesia, intravenous analgesia, epidural analgesia and local nerve block analgesia [4]. Compared with other anesthesia methods, nerve block is safely used for patients with coagulation dysfunction and postoperative anticoagulation therapy, although its motor block effect easily makes patients to experience falls [5]. Ropivacaine (Ropi), a pure levorotatory, long-acting amide local anesthetic, blocks impulse conduction along nerve fibers in the nerve fiber cell membrane by blocking the influx of sodium ions [6]. A study has revealed that low-dose Ropi produced non-progressive motor nerve block [7]. However, there are no studies elucidating the specific dose of Ropi for use in TKA.

Therefore, the present research was carried out to study the effect of different doses of Ropi anesthesia on postoperative analgesia, incidence of complications and stress factors in patients undergoing TKA, so as to provide data for clinical analgesia scheme.

METHODS

Patient data

Patients (150) who received TKA treatment in *Ganzhou Hospital of Traditional Chinese Medicine* from January 2017 to January 2019 were randomly divided into low-, medium- and high-dose Ropi groups (A, B and C), based on random number table method, with 50 patients in each group. This study was approved by the ethics committee of *Ganzhou Hospital of Traditional Chinese Medicine* (approval no. 20161145), and it met the criteria in the Declaration of Helsinki [8]. The subjects or their family members submitted written and signed consents.

Conditions for participation

Subjects of age ≥ 60 years, patients in stages I – III of the American Society of Anesthesiologists (ASA) [9], those with BMI in the range of 18.5 – 23.9 kg/m², and patients who met the indications for TKA, were included in this study.

Exclusion criteria

The excluded patients were those with allergies or intolerance to the study medication, patients with a history of hemorrhagic diseases, abnormal coagulation function, and hepatic or renal insufficiency, subjects with a long history of abuse of analgesic drugs, patients who used adrenaline receptor agonist therapy 1 month before the surgery, and those with hearing impairment or communication disorders.

Analgesic regimens

Patients were made to fast for 8 h before surgery and were forbidden to drink for more than 4 h. Blood pressure, heart rate and blood oxygen saturation of the patients were measured, and a 16-gauge hypodermic needle was inserted into the forearm vein for normal saline administration. The dose of normal saline was 7 ml/kg/h. Patients in the three groups (A, B and C) were given Ropi anesthesia at doses of 0.15, 0.2 and 0.3 %, respectively. The specific configuration schemes were as follows: using analgesic pump setting, group A was given dexmedetomidine at a dose of 5 μ g/kg, plus sufentanil (2 μ g/kg) and 250 mL of 0.15 % Ropi (1% Ropi + normal saline), at a background flow rate of 4 mL/h. Group B was treated with dexmedetomidine at a dose of 5 μ g/kg, plus sufentanil (2 μ g/kg) and 250 mL of 0.2 % Ropi (1 % Ropi + normal saline), at a background flow rate of 3 mL/h. Group C patients received dexmedetomidine at a dose of 5 μ g/kg, plus sufentanil (2 μ g/kg) and 250 mL of 0.3 % Ropi (1 % Ropi + normal saline), at a background flow rate of 2 mL/h. When the postoperative Visual Analog Scale (VAS) score was > 4 , 50 mg pethidine was injected intramuscularly.

Pain scores

In this study, VAS system was used to score pain in patients. A horizontal line with a length of 10 cm was drawn on paper, with the left end of the horizontal line assigned a value of 0, while the other end was assigned a value of 10: the range of 0 – 10 indicated the degrees of pain. The greater the value, the more severe the pain of the patient. Patients were evaluated at 12, 24 and 48 h post-surgery.

Cortisol (Cor) testing

Venous blood samples of each patient were obtained in the morning prior to surgery as baseline. Then, blood samples were collected 30 min, 24 and 48 h after surgery for measurement of cortisol (Cor) levels. Cells and debris were

removed via centrifugation, and the samples were preserved by refrigerating at -80°C prior to analysis. All measurements were made in the clinical laboratory of the hospital. The Cor levels were determined using electrochemiluminescence immunoassay (ECLIs) on modular analysis Module E170 (Roche Diagnostics Company, Mannheim, Germany), and expressed as nmol/L.

Parameters assessed

Primary endpoints

The VAS scores at 12, 24 and 48 h after surgery were recorded. Moreover, MMSE score was used for determination of cognitive dysfunction before surgery, and at 48 and 72 h after surgery. Changes in serum Cor at 30 min, 24 and 48 h after surgery were analyzed.

Secondary endpoints

The incidence of adverse reactions and postoperative cognitive dysfunction (POCD) were monitored and compared amongst the 3 groups.

Statistical analysis

In this study, images and data analysis were carried out with GraphPad 8 software. Results are expressed as mean \pm standard deviation (SD), and two-group comparison was performed using independent sample *t*-test. Results involving enumeration were recorded as % and analyzed using χ^2 test. Multi-group comparison was done with one-way ANOVA. Analysis of performance at various time intervals was processed with repeated measures ANOVA

(denoted by F). Back testing was done with Bonferroni. Differences were considered statistically significant at $p < 0.05$.

RESULTS

Baseline profile of patients

Comparative analysis of baseline data showed no statistically significant differences amongst the three groups ($p > 0.05$), as presented in Table 1.

Perioperative conditions of patient

Table 2 shows that at the beginning of the study, comparison of anesthesia time, operation time, infusion volume, bleeding volume and urine volume during perioperative period amongst the 3 groups revealed no significant differences.

Changes in VAS scores

There were no significant differences in rest visual analogue scale (RVAS) scores among the three groups at 12 h post-operation, but the RVAS grades in B and C at 24 and 48 h were significantly higher when compared with A ($p < 0.05$). In addition, passive visual analogue scale (PVAS) scores among the three series of patients at 12 h after surgery were comparable, while at 24 and 48 h after surgery, the PVAS scores were higher in groups B and C than in group A ($p < 0.05$). Four, six, and nine patients in the three groups (A, B and C, respectively) underwent analgesic remediation. These data are shown in Table 3.

Table 1: Comparison of baseline data (mean \pm SD, n = 50)

Parameter	Group A	Group B	Group C	P-value
Age (years)	64.9 \pm 3.2	66.4 \pm 3.8	65.7 \pm 4.0	0.129
Gender (male/female)	32/18	30/20	28/22	0.717
Height (cm)	164.5 \pm 7.9	166.5 \pm 8.9	163.5 \pm 6.8	0.159
BMI (kg/m ²)	21.4 \pm 1.8	22.1 \pm 1.7	21.9 \pm 1.6	0.110
ASA classification (I-III)	10/38/2	12/35/3	14/33/3	0.866

Table 2: Perioperative conditions of patients in the 3 groups (mean \pm SD, n = 50)

Group	Anesthesia time (min)	Operation time (min)	Infusion volume (mL)	Bleeding volume (mL)	Urine volume (mL)
A	126.3 \pm 21.7	99.8 \pm 21.2	1501.8 \pm 235.7	253.2 \pm 36.7	150.2 \pm 36.7
B	129.8 \pm 22.3	101.3 \pm 19.7	1499.4 \pm 234.6	252.1 \pm 35.8	149.4 \pm 35.4
C	128.9 \pm 20.8	102.6 \pm 20.8	1502.2 \pm 232.5	254.5 \pm 36.0	151.3 \pm 38.5
P-value	0.602	0.657	0.968	0.826	0.865

Table 3: Comparison of RVAS scores and PVAS grades after surgery (points, mean ± SD, n = 50)

Group	12 h	24 h	48 h
RVAS scores			
A	3.1±0.6	2.3±0.3	1.2±0.3
B	3.4±0.5	2.8±0.2*	1.8±0.2*
C	3.3±0.5	2.7±0.3#	1.9±0.3#
PVAS grades			
A	4.2±0.3	3.6±0.5	3.1±0.2
B	4.3±0.4	3.9±0.5*	3.3±0.3*
C	4.1±0.3	3.8±0.5#	3.4±0.3#

*P < 0.05, vs group A; #p < 0.05, vs group A

Changes in serum Cor

As shown in Figure 1, there was significantly lower concentration of serum Cor in group A than in groups B and C at 24 and 48 h after surgery.

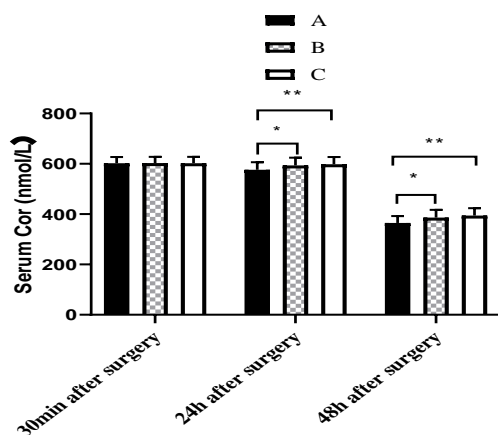


Figure 1: Changes in serum Cor levels in the three groups of patients after surgery. *P < 0.05; **p < 0.05

MMES scores

Figure 2 shows that there were significantly higher MMSE scores at 48 and 72 h after surgery in group A than in groups B and C.

Incidence of adverse reactions

There were no significant differences in symptoms such as nausea, itching, lethargy and chills among the three groups. However, there was significantly higher incidence of POCD in groups B and C than in A. Details of these data are presented in Table 4.

Table 4: Incidence of adverse reactions (mean ± SD, n = 50)

Group	Nausea	Itching	Lethargy	Lethargy	Postoperative cognitive dysfunction
A	4 (8.00%)	5 (10.00%)	1 (2.00%)	1 (2.00%)	6 (12.00%)
B	3 (6.00%)	4 (8.00%)	2 (4.00%)	3 (6.00%)	15 (30.00%)
C	4 (8.00%)	7 (14.00%)	2 (4.00%)	2 (4.00%)	16 (32.00%)
P-value	0.907	0.613	0.813	0.594	0.038

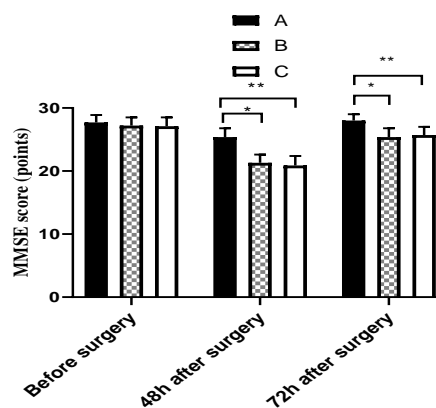


Figure 2: Changes in MMES scores in three groups. *P < 0.05; **p < 0.05

DISCUSSION

Total knee arthroplasty (TKA) is a common replacement surgery in clinical practice, and it is mainly used to treat the elderly. Due to increasing longevity, the population of the elderly in China increases exponentially every year [10]. This study found that low-concentration and high-volume Ropi produced significant analgesic effect on patients undergoing TKA, and alleviated their symptoms of postoperative cognitive dysfunction (POCD). Therefore, low-concentration and high-volume Ropi may become one of the postoperative analgesic schemes for TKA in clinics.

Nerve block analgesia is a vital means of clinical analgesia after TKA, especially for avoiding blood coagulation caused by epidural analgesia [11]. Moreover, it retains the advantages of local block by effectively reducing sympathetic nerve tone and peripheral blood circulation around the wound, as well as preventing formation of peripheral venous thrombosis [12]. However, compared with other anesthesia methods, nerve block analgesia leads to sensory nerve pathway in patients, especially in elderly patients [13].

Ropi, a nerve block analgesic drug used in clinics, is critical in TKA analgesia. However, recent evidence [14] has indicated that different concentrations of Ropi produced different effects

on postoperative analgesia and cognitive function. Based on this, in the present study, collection and analysis of clinical data of TKA patients were carried out to determine the influence of various doses of ropivacaine anesthesia on postoperative analgesia, and incidence of complications and stress factors. This was aimed at providing more data support for subsequent use of Ropi anesthesia in clinical practice.

In this study, VAS scores were used to compare the analgesic effects of three different concentrations and equal doses of Ropi on TKA patients. The comparison identified no difference in RVAS or PVAS at 12 h after surgery, but VAS scores at 24 and 48 h after surgery were higher in B and C than in A. This shows that low-dose Ropi with high volume produced a better analgesic effect in elderly patients following TKA, possibly due to the unique physiological characteristics of the elderly who require lower concentrations of narcotic drugs than normal adults. Since TKA causes great trauma to patients, and since the knee joint is rich in nerve endings, patients feel severe pain after surgery, as well as physical stress responses which are detrimental to their postoperative rehabilitation [15]. Cortisol (Cor), an important marker of stress response and a sensitive indicator of stress responses, is of great significance for maintenance of non-specific defense response [16]. In addition, the influence of different concentrations of Ropi on post-operative stress response of patients after TKA was determined in this study. Comparison of Cor levels after surgery showed that there were no differences in Cor concentration among the three groups at different time points, indicating that the different concentrations of Ropi had no obvious influence on the stress response of patients.

Besides, the cognitive function of patients with different concentrations of Ropi was analyzed. It was found that patients suffered from cognitive dysfunction in different degrees at 48 and 72 h after surgery. This was mainly due to the decreased cerebral blood flow in the elderly patients after surgery, which easily led to postoperative cranial nerve injury. Furthermore, in this study, the MMSE scores of patients decreased less in group A than in groups B and C, which indicated that low-dose and high-volume Ropi had less influence on patients' cognitive function. Moreover, the incidence of POCD in group A was significantly lower than those in groups B and C.

Limitations of this study

There are some limitations in this study. First of all, as a clinical study, the sample size was relatively small. Secondly, since the mechanism by which low-dose and high-volume Ropi improved patients' cognitive function was not determined, there is need for further basic research on this area. Therefore, the results in this research need to be improved through more experiments and larger sample size in future.

CONCLUSION

Low-dose and high-volume Ropi produces significant analgesic effects in the treatment of the elderly undergoing TKA, and improves patients' cognitive function without influencing their stress response. Therefore, Ropi should be further investigated on a larger scale for its potential as a candidate analgesic in patients after TKA.

DECLARATIONS

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Funding

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Ethical approval

This study was approved by the ethics committee of *Ganzhou Hospital of Traditional Chinese Medicine* (approval no. 20161145).

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by the authors named in this article, and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Xiaobo Sun, Yuting Liu and Jian Li conceived and designed the study, and drafted the manuscript. Xiaobo Sun, Yuting Liu, Jian Li and Haihua Liu collected, analyzed and interpreted the experimental data.

Xiaobo Sun and Jian Li revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

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