

## THE CLINICAL EFFECT AND SAFETY ANALYSIS OF DEZOCINE COMBINED WITH LOW CONCENTRATION ROPIVACAINE IN UPPER LIMB SURGERIES

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### ABSTRACT

**Objective:** To research the clinical effect of Dezocine combined with low concentration Ropivacaine in upper limb surgeries, and analyze its safety.

**Method:** 240 patients who had upper limb surgeries were randomly divided into two groups, research group and control group. Each group had 120 patients. Patients in control group were treated with low concentration Ropivacaine. Patients in research group were treated with low concentration Ropivacaine combined with Dezocine. Difference analysis of the two groups was conducted with anesthesia effect, VAS grading, and adverse reactions.

**Results:** The acting time of anesthesia in research group was significantly shorter than that in control group. The difference had statistical significance ( $P < 0.05$ ). Sensory block and analgesic time in research group were significantly longer than that in control group, and the difference had statistical significance ( $P < 0.05$ ). VAS grading of research group 2h, 4h, 8h after the operation was significantly lower than that in control group, and the difference had statistical significance ( $P < 0.05$ ). The adverse reaction rate in research group (0.83%) was significantly lower than that in control group (13.33%), and the difference had a statistical significance ( $P < 0.05$ ). In addition, patients in both groups did not have retention of urine, skin itch, respiratory depression, or any other severe adverse reaction.

**Conclusion:** mixed solution of Dezocine and low concentration Ropivacaine had a quick anesthetic effect, long anesthesia and analgesic time, low adverse reaction rate and high clinic safety.

**Keywords:** dezocine, ropivacaine, low concentration, brachial plexus nerve block, operation, safety, clinical effect.

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### Introduction

In most cases, the injury in patients' hands was acute injury, with severe pain and configuration change of hands. The patients were generally very nervous with severe stress reactions<sup>(1)</sup>. Therefore, in surgeries including anastomosis of blood vessel and neoplasty of muscle tendon, the anesthesia methods had high standards. The methods should effect quick and well, and had a simple operation and high safety<sup>(2)</sup>. Therefore, this paper researched clinical effect and safety analysis of Dezocine combined

with low concentration Ropivacaine in anesthesia of upper limb surgeries.

### Data and methods

#### General Data

Research objects were 240 patients who were operated with upper limb surgeries between January, 2014 and July, 2016 in our department and with ASA grading between I to II. The 240 patients were divided into two groups with random digits table, each group with 120 patients. One group was

set as control group, the other research group. Inclusion criteria<sup>(3)</sup>:

- 1) with consciousness and ability to express clearly;
- 2) tolerance of the surgeries;
- 3) no participation in other clinical test within one month;
- 4) willing to accept the anesthesia methods and signature of informed consent<sup>(4)</sup>.

Exclusion criteria:

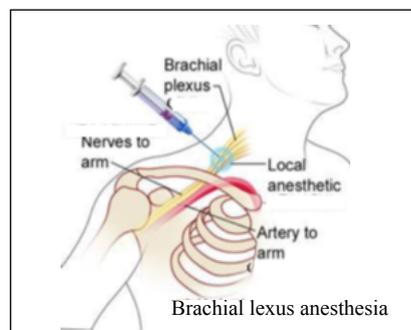
- 1) with drug abuse history;
- 2) with neurogenic diseases;
- 3) with contraindications of brachial plexus nerve block;
- 4) with allergic history of opioid analgesics;
- 5) complicated with heart, liver kidney and other visceral diseases;
- 6) complicated with endocrine system diseases, hematological system diseases, communicable disease, malignancy;
- 7) lack of clinical pathological data.

Control group: male: 68 patients; female: 52 patients. ASA grading: I:62 patients; II:58 patients. The minimum age was 28, the maximum age was 57; the average age was  $41.2 \pm 2.6$ . The minimum weight was 46 kg; the maximum weight was 91kg; the average weight was  $67.1 \pm 5.9$  kg. Fracture with open reduction and the internal fixation: 34 patients; internal fixation removal: 38 patients; lump resection: 13 patients; Flexor Tendon Repair: 24 patients; severed finger replantation: 11 patients; Research group: male: 66 patients; female: 54 patients. ASA grading: I:63 patients; II:57 patients. The minimum age was 27, the maximum age was 58; the average age was  $43.8 \pm 3.3$ . The minimum weight was 45 kg; the maximum weight was 92kg; the average weight was  $68.2 \pm 6.3$  kg. Fracture with open reduction and the internal fixation: 36 patients; internal fixation removal: 37 patients; lump resection: 15 patients; flexor tendon repair: 22 patients; severed finger replantation: 10 patients. Gender, age, weight, classification and grading had no statistic difference ( $P > 0.05$ ).

Therefore, the two groups had comparability. All patients included in this research and their dependents had signed informed consent and were willing to participate in this research and receive follow-up after discharge. The research was reviewed and approved by Medical Ethics Committee of our hospital.

### Anesthesia methods

Preoperative preparations: double-blind and experienced anesthetist from our hospital conducted anesthesia to patients in two groups 30 minutes before surgeries, both with Atropine Sulfate Injection (Manufacturer: Beijing Double-crane Pharmaceutical Co., Ltd; specification: 0.5mg; registered number of approval: National Medicine Permission Number: H11020766) 0.5mg, intramuscularly. Phenobarbital Sodium Injection (Manufacturer: Tianjin Pharmaceutical Group Xinzheng Co., Ltd; specification: 100 mg; registered number of approval: National Medicine Permission Number: H41025613) 100mg, intramuscularly. When the patients were in the operating room, venous channel was established. Patients were given oxygen, 2L/min, with nasal tube. Heart rate, respiration, blood pressure, mean arterial pressure and saturation oxygen of patients were real-time dynamically monitored. Brachial plexus block: ask the patient to take supine position; Put bolster under the patient's shoulder; Move patient's head to uninjured side and two upper limbs in two sides of trunk; Midclavicular line as a starting point, press to deep; use left hand to brace intermuscular approach; use right hand to insert needle and fix; repeat pumpback to confirm that there is no air, blood, and cerebrospinal fluid. Specific positioning is shown in Figure 1.



**Figure 1:** Brachial plexus block operation positioning.

Control group: 0.375% Ropivacaine Hydrochloride Injection was administrated (Manufacturer: Jiangsu Hengrui Medicine Co., Ltd.; specification: 10 ml: 100 mg; registered number of approval: National Medicine Permission Number: H20060137) 20ml, interscalene injection. Research group: mixed solution of 0.375% Ropivacaine Hydrochloride Injection and Dezocine Injection were administrated (Manufacturer: Yangtze River Pharmaceutical Group Co., Ltd.; specification: 1ml: 5mg; registered number of

approval: National Medicine Permission Number: H20080329; Production certificate number: SU 2007001), 20ml, interscalene injection. Vital signs of patients in two groups were carefully observed. If any discomfort happened, the administration would be stopped immediately and expectant treatment would be carried out. The technical route is shown in Figure 2.

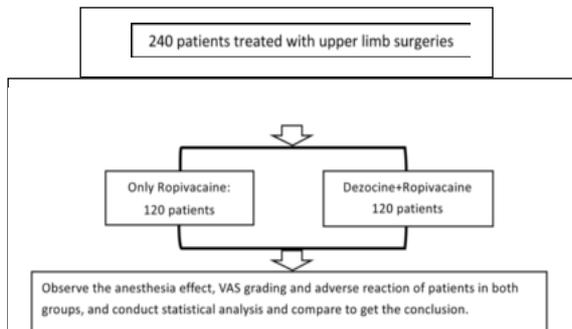


Figure 2: Technical route.

**Observed Value**

Difference analysis of anesthesia effect and Visual analogue scale (VAS) grading (see Figure 3), and adverse reaction between the two groups was conducted.

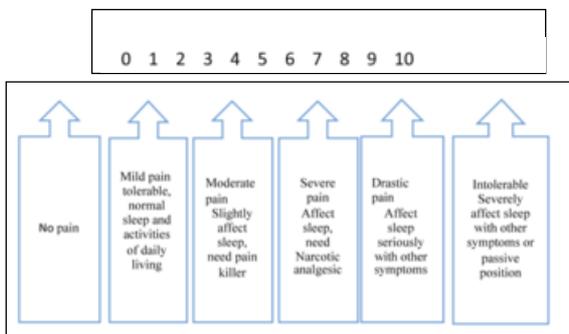


Figure 3: Visual analogue scale.

**Statistical Methods**

Results were studied by statistical analysis with SPSS22.0. Measurement data obeying normal distribution were described by MEAN±SD. Inter-group data were dealt with independent-samples T to test. Skew data was moderately adjusted. Counting data was described by N or rate. Inter group data were dealt with chi-square test. When P < 0.05, the difference had statistical significance; when P > 0.05, the difference had no statistical significance.

**Result**

**Comparison of Anesthesia Effect in Two Groups**

Compared with patients in control group, patients in research group had a significantly shorter anesthesia acting time. The difference between the two groups had statistical significance (P < 0.05). Compared with patients in control group, patients in research group had a significantly longer analgesic lasting time. The difference between the two groups had statistical significance (P < 0.05), see Table 1.

Group	Patients amount	Anesthesia acting time (min)	sensory block lasting time (h)	analgesic lasting time (h)
Control	120	5.71±1.22	5.73±1.01	7.91±1.82
Research	120	3.33±0.99	12.11±2.98	13.78±6.73
t		0.342	0.635	0.762
P		0.027	0	0

Table 1: Comparison of Anesthesia Effect in Two Groups (MEAN±SD) .

**Comparison of VAS Grading in Two Groups**

VAS grading of research group 2h, 4h, 8h after the operation was significantly lower than that in control group, and the difference had a statistical significance (P < 0.05). See Table 2.

Group	Patients amount	2h after surgery	4h after surgery	8h after surgery
Control	120	1.91±0.22	2.11±0.98	4.18±1.01
Research	120	1.33±0.99	1.44±0.83	1.67±0.73
t		1.176	2.985	4.208
P		0.032	0.027	0.006

Table 2: Comparison of VAS Grading in Two Groups (MEAN±SD).

**Comparison of Adverse Reaction in Two Groups**

16 patients in control group had adverse reactions. One patient in research group had adverse reactions. All patients with adverse reaction were not specially treated and their symptoms were relieved and had no effect to future treatment. The adverse reaction rate of patients in control group and research group were 13.33% and 0.83%, respectively. Compared with patients in control group, patients in research group had a significantly lower adverse reaction rate. The difference between the two groups had statistical significance (P < 0.05), see Table 3.

Group	Patients' amount	Dizziness	Nausea	Vomiting	Adverse reaction rate
Control	120	7	6	3	13.33%
Research	120	0	1	0	0.83%
$\chi^2$		1.176	2.985	4.208	9.82
P		0.032	0.027	0.006	0

**Table 3:** Comparison of Adverse Reaction in Two Groups (MEAN $\pm$ SD, n%).

## Discussion

The common anesthesia method of upper limb surgery was brachial plexus block. Pain, mental stress and anxiety felt by the patients in or after the surgery were all the reasons of internal environment changes. Endocrine disorder induced irritated responsiveness. ReceptorKin cerebral cortex starts this system protection<sup>(5)</sup>. Currently, opioids were clinically used as blocking enhancer. When combined with narcotics, opioids can significantly prolong the blocking and analgesic time. However, the administration may cause adverse reactions such as nausea, vomiting, dizziness, retention of urine. Once the patient has emotional fluctuation, the administration will affect central nerve and induce adverse reaction<sup>(6)</sup>.

Ropivacaine is a long-term amides and its structure formula is the isomer of (1)-1-propyl-2,6-Piperidine hydrochloride. It is hardly fat-soluble. Molecular weight of its hydrochloric acid hydrates is 329 D, with distribution rate at 141<sup>(7-8)</sup>, with advantages of quick acting time, long effect lasting time, significant anesthesia effect, separate blocking of sensory and motor nerve, and low toxicity to cardiovascular and central nervous system<sup>(9)</sup>.

Therefore, it is frequently used in brachial plexus nerve block. It can block for a long time, inhibiting the normal conduction of sodium ion in neurocytes, and blocking the conduction of pain and nervous excitation. The property of Ropivacaine is unique and can reduce the dosage of opioids. However, the anesthesia with Ropivacaine tends to be incomplete blocking<sup>(10-12)</sup>. Therefore, this paper researched mixed solution of Dezocine and Ropivacaine.

Dezocine is phenyl-morphinan derivative. It is opioid receptor agonist and Opioid receptor antagonists, agonizing Kreceptors while antagonizingureceptors. Comparing with morphine, it had less tolerance and less adverse reactions. In addition, Dezocine had a strong analgesic effect and very slight effect on respiratory depression<sup>(13)</sup>.

Kreceptors mainly exist in cerebral cortex, peripheral sensory neuron and nerve ending, and substantia gelatinosa. Peripheral Kreceptors quickly combine with Dezocine, resulting in strong analgesic effect<sup>(14-15)</sup>. In addition, one reason Dezocine prolongs the analgesic time was probably its slow intrathecal absorption<sup>(16)</sup>. Therefore, this research chose Dezocine as ancillary drug to be Ropivacaine synergist.

The combination of Dezocine and Ropivacaine enhance the drug effect, maintain plasma concentration longer, and prolong analgesic and sensory blocking time<sup>(17)</sup>. When the plasma concentration was 2%, the administration could block the nerve conduction, but increase the adverse reactions<sup>(18)</sup>. Therefore, this research used 0.375% Ropivacaine, largely avoiding adverse reactions.

The result of this research showed that the mixed solution of Dezocine and Ropivacaine acted quickly after the administration. The drug effect lasted long and analgesic effect was also prolonged. The overall effect was significantly better than that in control group ( $P < 0.05$ ). This indicated that Dezocine had a binding site in cornu dorsale medullae spinalis. Through peripheral neurolemma, Dezocine can directly combine with Opioid binding protein, and be transported to cornu dorsale medullae spinalis to have effect<sup>(19)</sup>. In addition, Dezocine can be absorbed into blood through peripheral vessels, joining in blood circulation and irritating the release of endogenous opioid peptides, which has an anti-harm and anti-stimulation effect<sup>(20)</sup>. Therefore, applying Dezocine directly in the selected local nerve to block peripheral nerve has a great blocking effect.

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