

## Effectiveness and safety review by using ropivacaine and bupivacaine in patients with spinal anesthesia: a meta-analysis

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**Abstract: Objective:** To evaluate the effectiveness and safety of ropivacaine in spinal anesthesia. **Methods:** Methods: We electronically searched the Chinese academic journals database (1990-2012) and medline (1990-2012). **Results:** The meta-analysis included 6 trials from 82 studies, a total of 215 patients were included in the analysis. The results of meta-analyses showed that the motor-block time to complete block of ropivacaine was significantly shorter than that of bupivacaine (WMD=1.22 min, 95%CI (0.41, 2.02), P=0.02). The motor-block time to complete recovery of ropivacaine was significantly shorter than that of bupivacaine for cesarean delivery in spinal anesthesia (SMD=-66.59, 95%CI (-72.88, -60.30), P=0.004). **Conclusion:** Equivalent doses of ropivacaine and bupivacaine provide similar analgesia in spinal anesthesia for cesarean delivery. However, haemodynamics in spinal anesthesia with ropivacaine fluctuate lighter than with bupivacaine. Ropivacaine is suitable for spinal anesthesia in low—abdominal operations.

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**Key words:** Ropivacaine; Bupivacaine; Spinal anesthesia; Meta-analysis

### 1. Introduction

All methods of lumbar anesthesia are chose to using bupivacaine with strong efficiency of anesthesia in operation at present. Haemodynamics change obviously during anesthesia and motor block recovery slowly after taking bupivacaine. But the disadvantages of bupivacaine is that once excessive medicine entered into central nervous system and heart with toxicity to cycle, this could lead to ventricular arrhythmias and difficult recovery. Epidural anesthesia with ropivacaine is laevorotatory isomer of bupivacaine, its structure is similar to bupivacaine, toxic reaction is lower than bupivacaine obviously, especially cardiotoxicity.(Morton et al., 1997) And low concentration of ropivacaine benefit fetus in tolerating for its character of separating sensation and motion.(Rosenberg et al.,1986) Ropivacaine with clinical concentrations and dosage, the same as bupivacaine, could also be used in lumbar anesthesia safely. The study adopted the method of system assessment to evaluate anesthetic effect and safety of ropivacaine on under hypogastrium by lumbar nesthesia, in the mean while, compare the anesthesia effect with bupivacaine.

### 2. Materials and Methods

#### 2.1 Inclusion criteria

① Research type: randomized controlled trial (RCT); ② Research object: divided ASA into I and II; ③ Intervention measures: The method of

anesthesia was spinal anesthesia, the experimental group received ropivacaine and the controlled group received bupivacaine.

#### 2.2 Exclusion criteria

① Patients suffered hemopathy and those with the history of hereditary diabetes mellitus; ② patients with cardiopulmonary disease; ③ patients with pregnancy-induced hypertension syndrome; ④ deformity of spine; ⑤ suspected fetal, deformity, fetal distress, and polyembryony; ⑥ time of operation was long and assistant epidural administration was required; ⑦ surgery of non supine position; ⑧ failed to puncture subarachnoid space.

#### 2.3 Determinative indicators of curative effect

The main evaluation indicators: the time of entirety motor block of ropivacaine, healing time of motor block; the secondary evaluation indicators: the rate of hypotension, the incidence of decreased heart rate.

#### 2.4 Document retrieval

2.4.1 Database: the English database retrieval, including PubMed (1999-2008), Cochrane library (2000-1008), OVID (1999-2008), EBSCO database (1999-2008). And MEDLINE, ERIC, Academic Source, Hixtory Reference Center, MasterFILE Premier, Newspaper Source, Professional Development Collegian were included in the EBSCO database. And the Chinese database retrieval, including full-text database of CNKI (1999-2008), which include full-text database of Chinese Ph. D. Thesis and outstanding Master Thesis, CJFD

(Chinese journal full-text database), CCND, Cbfd, CYFD, SCSd, SOSD, CCD (Chinese Citation Database), CYBD and Chinese journal net database.

#### 2.4.2 Search strategy

We adopted network of computer to search subject headings. The key search words of “ropivacaine, bupivacaine, spinal anesthesia, Meta-analysis” were used in Chinese and English respectively. The limited time of the searching was from 1990 to 2012. And we searched the literatures closely related to ropivacaine applied to spinal anesthesia by reading title and abstract. And if we could not get full text of SDOL, we would contact with authors to ask for.

#### 2.5 Evaluations of literature quality

2.5.1 **The methods of data extraction:** two evaluators scan title and abstract independently to select related literatures by the way of double-blind. And literatures were included and excluded after finding out related full text. Then cross-check the literatures, at last, discuss or ask for advice of the third evaluators when they disagree with each other. The content of data extraction: ① general information, including number, reviewer, title, author, contact information and the source of original documents; ② general conditions of research, including sample capacity in each group, age, weight, height and the operation duration; ③ intervening measures: puncture of spinal anesthesia; ④ indicators of clinical outcome.

2.5.2 **Evaluations of literature quality:** methodological quality of included studies was evaluated according to methods of literature quality evaluation in 4.2.2 brochure of Cochrane systematic evaluators. And divided the quality of included studies into three levels: A, B and C respectively. MPS-A indicate that literatures according with the four quality criterion above absolutely and the least occurrence of bias, including low bias. MPS-B has moderate possibility of bias, moderate bias, and one or more than one criteria content with the four quality criterions above in part; MPS-C has high possibility of bias, high bias, and one or more than one criteria discontent with criterions above absolutely.

#### 2.6 Statistical methods

RevMan 5.0 software of Cochrane systematic evaluation was adopted to do Meta analysis, count data use OR and 95%CI, and measurement data use MD or SMD and 95%CI. Analyzed clinical and methodology heterogeneity of included studies firstly, following by subgroup analysis of clinical and methodology heterogeneity,

and adopted  $\chi^2$  to test and analyze statistical heterogeneity of results among studies. And fixed effect model was adopted when no statistical heterogeneity existed among studies in subgroup ( $P > 0.05$ ), conversely, random effect model was used when statistical heterogeneity existed among studies ( $P \leq 0.05$ ).

### 3. Results

#### 3.1 Results of document retrieval

Selected 82 related literatures initially, 70 English and 12 Chinese articles, 6 literatures was included finally. (Gautier et al., 1999; Malinovsky et al., 2000; Chung et al., 2001; Oğün et al., 2003; Gautier et al., 2003; Hongbin et al., 2008;) The first chart showed the procedure of literature screening. All the six literature included were about the randomized controlled trials (RCT) of injecting ropivacaine and bupivacaine into subarachnoid space. The patient reported outcomes mainly consist of the whole motor block time of ropivacaine and bupivacaine, healing time of motor block, incidence of hypotension and the comparison of incidence of decreased heart rate. The first table showed the basic information.

#### 3.2 Quality evaluation

Only two studies were randomized controlled trials (RCT), (Gautier et al., 1999; Oğün et al., 2003) and the rest of six included studies were quasi-standard experiments. (Malinovsky et al., 2000; Chung et al., 2001; Gautier et al., 2003; Hongbin et al., 2008) And only two studies referred to specific random methods in aspect of randomized scheme. (Gautier et al., 1999; Oğün et al., 2003) Whether adopted blind method or not, three studies referred to applied method of double blind, (Gautier et al., 1999; Oğün et al., 2003; Gautier et al., 2003) one study adopted single blind. As to the records of “lost to follow up”, (Chung et al., 2001) the six studies did not explain it.

#### 3.3 The results of study

##### 3.3.1 Time of entirely motor block

5 studies reported the time of entirely motor block, and did a Meta analysis of random effect model for statistical heterogeneity existing among studies ( $P = 0.02$ ,  $I^2 = 66\%$ ). The results of significant difference with statistical between two groups prompted that the time of entirely motor block of ropivacaine was longer than that of bupivacaine [WMD=1.22 min, 95%CI (0.41, 2.02),  $P = 0.02$ , Fig 1].

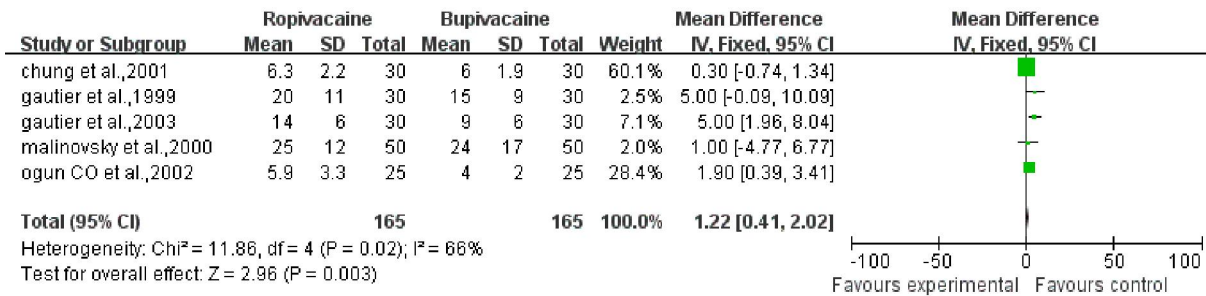


Fig 1. The meta analysis of ropivacaine and bupivacaine for time of entirely motor block.

### 3.2.2 The healing time of motor block

5 studies reported the healing time of motor block, and did a Meta analysis of random effect model for statistical heterogeneity existing among studies (P<0.00001). And the results of significant difference with statistical between two groups prompted that the healing time of motor block of ropivacaine was shorter than that of bupivacaine [SMD=-66.59, 95%CI (-72.88, -60.30), P=0.004, Fig 2].

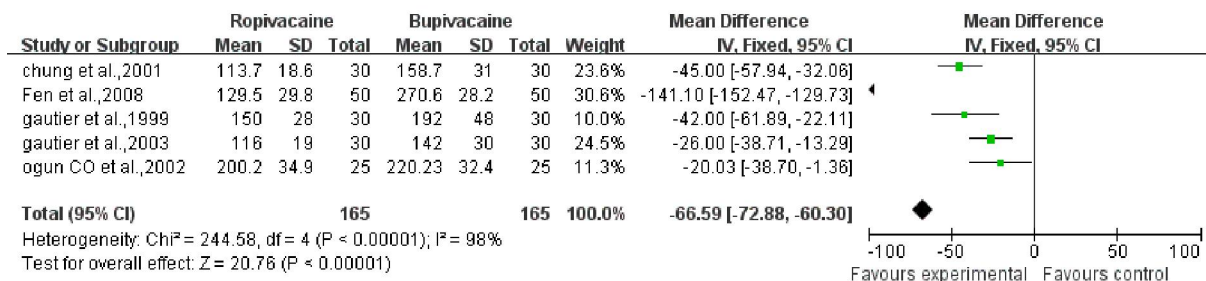


Fig 2. The meta analysis of ropivacaine and bupivacaine for healing time of motor block.

## 4. Discussions

The results of Meta analysis showed that the maximum time of entirely motor block was longer than bupivacaine, but the degree of motor block was lower than bupivacaine, and the healing time of motor block was faster than that of bupivacaine. This might be related to lower fat soluble of ropivacaine. Studies found that fat soluble of ropivacaine was lower than that of bupivacaine by Rosenberg. Ropivacaine with low fat soluble act out the phenomena of sensorimotor dissociative block for it block nerve sheath A fiber more slowly and weakly. And that phenomenon is conducive to keeping kinetic stability of bloodstream, therefore, drop of blood pressure and decreased heart rate were mainly adverse reactions of two groups, yet, the degree of adverse reactions in ropivacaine was slighter than in the group of bupivacaine. On one hand, organism has sufficient compensatory time to adapt to. On the other hand, lower limbs could maintain a certain degree of tension, affecting venous return slightly, blood pressure drop lightly, therefore, hemodynamics change slightly, and the incidence of hypotension and decreased heart rate was lower than bupivacaine distinctly.

Neurovirulence of local anesthetics might induced by local anesthetics acting on bare spinal nerve directly when spinal anesthesia, it manifest as the symptoms of vesicorectal disorder, perineum sensory disorder, lower limbs motor paralysis and myofascial pain, and so on. Some certain factors, which cause neurovirulence of local anesthetics to some extent, including the concentration and dosage of drugs, concentrate in cerebrospinal fluid (CSF), and how long nervous system exposed to local anesthetics, and so on. Ropivacaine with low concentration guarantee the irrigation of placenta and the safety of baby for its slight impact on maternal circulation in lumbar anesthesia. Maternity blood pressure drops after lumbar anesthesia mainly because of angiectasis induced by sympathetic nerve partial blocked, blood volume is not enough relatively and returned blood volume is not enough induced by fetus oppress vena cava of matrix. Block level of ropivacaine rise after lumbar anesthesia, and the longer maximum time of blockade and motor block is benefit to compensatory mechanism of maternal body. In addition, the efficiency of ropivacaine in the group, which was similar to bupivacaine in aspect of lumbar anesthesia, could achieve satisfactory results of analgesia and muscle

relaxant. The results of animal studies showed that ropivacaine did not add toxicity of pregnant animals, and there was no difference between pregnant and non-pregnant sheep in dosage of circulatory failure (12.9mg/kg, 11.6mg/kg respectively), and the dosage was higher than that of bupivacaine, these made the safety of anesthesia improved greatly.

The study indicated that ropivacaine was safe and effective in lumbar anesthesia under hypogastrum. Holding time of sensory nerve block of ropivacaine was similar to that of bupivacaine, but motor nerve block recover rapidly and weak interaction. In conclusion, ropivacaine is an ideal local anesthetic for its simple operation, fast efficiency, definite effect and perfect analgesia.

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