Original Article

Distribution of Bupivacaine in Epidural Space

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Abstract

Background: There is no consensus regarding the spread of local anesthesia in thoracic epidural space to obtain regional analgesia or anesthesia. We aimed to determine the distribution of Bupivacaine injected into the thoracic epidural space to evaluate its cranial or caudal spread in patients undergoing epidural anesthesia.

Materials and Methods: In a prospective clinical trial, thirty adults patients (12 males and 18 females) with ASA class I and II, scheduled for elective cholecystectomy under thoracic epidural anesthesia with 0.5% Isobaric Bupivacaine were studied. Clinical and radiological outcomes were evaluated to assess the correlation between the volume of the local anesthetic injected to the thoracic epidural space and the extension of its spread within the epidural space. Immediately after insertion and fixation of epidural catheter, patients were transferred to MRI unit to receive 8 mL of 5% Bupivacaine plus 1 mL Magnevist through the epidural catheter. Then, the patterns of spread were evaluated. Data were obtained prospectively during the procedure.

Results: Mean distribution of bupivacaine in thoracic epidural space was 0.64 level/ml of local anesthetics and the average of spread was 5.21 levels. The mean spread of bupivacaine was more in females (5.5 ± 1.1) than males (4.8 ± 1.1); but the difference was not significant. Unlike Patients' age and weight, the height and body mass index had a significant negative correlation with the distribution of Bupivacaine.

Conclusion: Distribution of Bupivacaine in epidural space in female patients is more than male ones and the tendency of spread is more toward the cephalad direction than caudal.

Keywords: Bupivacaine distribution, Epidural anesthesia, Local Anesthesia, Bupivacaine, Magnevist

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Introduction

Epidural anesthesia is one of the common methods employed to control pain and is indicated for surgical procedures such as thoracic, upper and lower abdominal, cervical, gynecological, urological and lower extremity operations (1, 2). One of the favorable advantages of epidural anesthesia is providing better condition of pain control for several days post operatively (3, 4) by using patient controlled analgesia (PCA). In addition to patient's satisfaction, this method of pain control can prevent the dangerous and intense complications of uncontrolled pain that usually threat patients within the first couple of days after operation. Myocardial infarction causes uncontrolled pain and atelectasis induced by inappropriate ventilation due to postoperative pain is two of the most important complications (5, 6).

During epidural anesthesia, local anesthetic drug acts on the sodium channels on spinal nerves. The sensory and motor blockade is attributed to the direct contact of local anesthetics with the superficial layers of the nerve roots in the spinal cord (7, 8). The distribution of drugs within the epidural space can be influenced by different factors, including the injection volume, rate of infusion, intervertebral foramina status, body position, epidural fat, vascular absorption and the anatomy of a particular species (9–11).

The cranial spread of Methylene blue (MB) into the epidural space studied *in vivo*, and a correlation between the volume administered and the cranial distribution of the dye was observed. Moll and his colleagues studied the distribution of different volumes of MB solution injected into the epidural space in anaesthetized pregnant and non-pregnant sheep. The results showed that the volume of MB injected epidurally into pregnant and non-pregnant sheep correlated directly with its cephalic distribution into the epidural space; and a volume of 0.1 mL/kg or 0.2 mL/kg stained up to the first lumbar segment in pregnant and non-pregnant sheep, respectively. In addition, the results suggested that the volume of drugs administered into the epidural space of the pregnant sheep should be half than in the non-pregnant one (12).

In another study, the spread of labeled blood in epidural space of patients who suffered from severe uncontrollable post spinal postural headaches was detected. In this study, the labeled red blood cells were injected into the patients' epidural space, and in evaluation by imaging techniques using a gamma camera with a parallel-hole collimator, it was found that the blood injected into the epidural space tended to travel more easily upward in a cranial direction. The mean spread of blood was six spinal segments upward and three spinal segments downward (13).

Our study was aimed to evaluate the spread of Bupivacaine in patients who have not any deformity, manipulation or operation in their spinal column. In this study we used the combination of Bupivacaine and the radio-opaque marker Magnevist (gadopentetate dimeglumine) injected in the thoracic epidural space in candidates of cholecystectomy to evaluate the spread of local anesthetic detected by magnetic resonance imaging.

Methods

This prospective clinical trial was conducted in Alzahra University Hospital in Isfahan, Iran. The study protocol was approved by Anesthesiology Department and Ethic Committee of Isfahan Medical University and written informed consent was obtained from each patient.

We studied thirty, ASA I and II adult patients candidates of elective cholecystectomy who had no history of acute or chronic kidney disease, deformity or history of operation in the spinal area and severe hypersensitivity reactions to Magnevist.

Participants were selected by non-probable simple sampling method. The patients were prepared for epidural anesthesia on a side railed table in the room adjacent to the magnetic resonance imaging (MRI) section under full standard monitoring. To achieve appropriate sedation, 50 mg Fentanyl plus 1mg Midazolam was injected intravenously. After sterilizing the patient's thoracic area and determining the space of T7 based on the scapula tip marker, 5cc Lidocaine 1% was injected under the skin area of T7-T8 space.

By using a Tuohy 18G epidural needle and a midline approach through the T7-T8 space, by using one of the techniques of loss of resistance or hanging drop and being certain of the place of needle in the epidural space, 3cc test dose of Lidocaine 2% and Epinephrine 1/200000 was injected in the epidural space and the patient was monitored for two to three minutes. After complete assurance of intact dura and the placement of the needle (by checking patient's heart rate (HR) and lack of motor-sensory block in the lower extremities), the epidural catheter (Gauge 20) was inserted and advanced 3 – 5 cm in epidural space. Then the epidural needle was slowly pulled away from the epidural catheter while care was taken for the catheter not to displace.

After fixing the catheter on the patient's back, patient was quickly transferred to the MRI room and 8cc Bupivacaine 5% isobaric plus 1cc Magnevist (gadopentetate dimeglumine) was injected through the epidural catheter with a rate of 1ml/sec by an anesthesiologist's assistant and then the MRI was done. The MRI was set at 1.5 Tesla. During MRI procedure, the patient was under blood Oxygen saturation (SPO2) monitoring and under direct supervision of the anesthesiologist's assistant.

The extent of contrast spread was determined by calculating numbers of the intervertebral foramina completely covered by contrast medium. The radiologist performed the interpretations of the epidurograms and the spread of contrast medium to the upper and lower segments regarding to the seventh thoracic segment.

Upon completion of MRI, while the patient was under full supervision and cardiovascular and pulmonary monitoring, the patient was transferred to the operating room (OR) within 10 min maximally. HR, systolic and diastolic blood pressor (BP) and mean arterial BP were recorded at 0, 5 and 10 minutes after epidural anesthesia. Then, the MRI cliché was reviewed by the same radiologist and its report recorded.

We also determined patient characteristics such as gender, age, weight, height and body mass index (BMI) to determine differences in spread of local anesthetic in thoracic epidural anesthesia.

Our data was analyzed by using repeated measured design analysis of variance (ANOVA), Pearson correlation coefficient and t-paired test by applying SPSS version 22, Chicago IL, for Windows statistical programs. P values of <0.05 were considered statistically significant.

Results

A total of 24 patients including 18 females (60%) and 12 males (40%) were studied and all of the patients completed the study and were evaluable. The mean of HR at 5 and 10 minutes after thoracic epidural block was significantly lower when compared with the values at the time of 0 ($P<0.001$), but there was no significant difference between mean HR at 5 and 10 minutes after epidural block ($p<0.14$). The mean changes of systolic, diastolic and mean arterial blood pressure at 5 and 10 minutes after thoracic epidural block were also reduced significantly when compared with the values at the time 0.($p<0.001$).

The mean distribution of Bupivacaine in thoracic epidural space was 0.64 level/ml of local anesthetics and the average of spread was 5.21 levels. The mean spread of Bupivacaine was more in females (5.5 ± 1.1) than males (4.8 ± 1.1), but this difference was not significant. The spread of Bupivacaine in the thoracic epidural space in men was 2.2 levels higher and 1.56 levels lower than the injection site (T7 space) and in females these measures were 2.8 levels higher and 1.7 levels lower. A comparison of the spread of local anesthetic in female and male patients is given in Table 1.

It showed that, Bupivacaine was spread in a wider range in females than males; although it was not statistically significant. Moreover, the spread of Bupivacaine in the thoracic epidural space has been more toward cephalad rather than caudal. Table 2 shows the Pearson correlation coefficient between the variables of spread of Bupivacaine in thoracic epidural space and the patients' age, weight, height and BMI. The Pearson correlation test showed a correlation coefficient between age and thoracic epidural local anesthetic spread of -0.03.

Table 1: Distribution of Bupivacaine according to Gender in Epidural Space.

	Females (Mean± SD)	Males (Mean± SD)	P- value
The mean spread of Bupivacaine in the thoracic space	5.5±1.1	4.8± 1.1	0.08
Number of distribution levels higher than the injection site	2.8±1.15	2.2± 0.83	0.1
Number of distribution levels lower than the injection site	1.7± 0.82	1.56± 0.53	0.36

Variables are presented as mean ± SD
P values less than 0.05 indicate statistically significant difference

Table 2: Distribution of Bupivacaine according to Age, Weight, Height and BMI in Epidural Space.

	Pearson Correlation Coefficient	**P- value**
Age (Years)	0.03	0.445
Weight (Kg)	0.2	0.17
Height (Cm)	0.71	<0.001*
BMI (Kg/m2)	0.34	0.05*

*significant difference

We also found a significant inverse relationship between height and Bupivacaine spread in thoracic epidural space (r=-0.71, P<0.001). The average height of our patients was 1.68cm. In the case of BMI, we found a significant positive relationship (r=0.34, P=0.05) between BMI and thoracic spread of Bupivacaine. The spread of Bupivacaine had weak relationship with Patient’s weight with a correlation coefficient of -0.2 and this correlation was not significant.

Discussion

The aim of this study was to identify a relationship between the injection volume of Bupivacaine and the degree of its migration during thoracic epidural anesthesia. There are several factors, mentioned in the introduction, that influence the spread of drugs injecting in the epidural space. Our results showed that the mean distribution of Bupivacaine in thoracic epidural space was 0.64 level/ml of local anesthetics and the average of spread was 5.21 levels. We found that the mean spread of Bupivacaine level was more in females (5.5 ± 1.1) than males (4.8 ± 1.1), although this difference was not significant.

According to our findings in order to block one intervertebral level in males 1.88 cc and in females 1.63cc 0.5% isobaric Bupivacaine was required. A number of variables determine how far a local anesthetic will spread after injection into the epidural space. Some variables are regarding the patient and some are extrinsic, depending on variations in technique and the drugs given (14).

Burn et al. reported that it is impossible to predict accurately the level attained after epidural injection of contrast medium. The unpredictable pattern of spread is likely due to anatomical variation of the epidural space (15). Recent reports have indicated that the structure of the epidural space is more complex and variable than ever thought and this intrinsic factor makes the spread of solution in the epidural space unpredictable (16).

Szeinfeld et al, in a study, evaluated the volume and spread of blood injected to the epidural space in patients experienced postural headaches after spinal anesthesia. They injected an average volume of 14.8 cc labeled blood in lumbar epidural space and reported that the mean number of segments of blood spread was nine and the average volume of blood spread per spinal segment was 1.6 cc (13). In our study as well, this value was calculated as 1.88 cc and 1.63cc of 0.5% Isobaric Bupivacaine for males and females, respectively and was almost similar to the former study.

Coombs et al, also injected 18cc blood with 2cc tracer Maglumine (total 20cc) in lumbar epidural space for epidural blood patching and showed that this substance can spread in 5 intervertebral levels; i.e. 4cc blood was needed for each level. This difference might have been due to the fact that, in this study the subjects were women who had been recently given birth. Those, whose spinal column curve, body physiology, absorption and excretion of medicines are affected by pregnancy up to 40 days after childbirth. In addition, the mentioned study was carried out on the lumbar epidural space whereas our study was done on the thoracic epidural space (17). Moreover, in our study we used 0.5% isobaric Bupivacaine while in the previous studies, blood was injected in epidural space. It is obvious that the absorption of 0.5% isobaric Bupivacaine in epidural space is different from blood absorption in this region. On the other hand, in our study, for every one level drop in local anesthetic, 1.6 level rises in the thoracic epidural blood absorption space was seen, but in the study carried out on women after childbirth in lumbar epidural space, 2.5 levels blood absorption was raised for every blood fall level. This difference may be attributed to the difference of the epidural space in studied groups and studied solutions (blood vs. 0.5% isobaric Bupivacaine). In addition, in mentioned studies, there were no reports of differentiation of distribution of any injected solutions in epidural space according to the gender. Moreover, most studies in this regard performed on pregnant or post-childbirth women.

In contrast to the conflicting reports on lumbar epidural anesthesia, the few studies investigating the effects of age on thoracic epidural spread. It suggested that there is a positive correlation between age and spread of blockade, but recently Wink et al, reported that after injection of a fixed loading dose of Ropivacaine at the T3–T4 level, they were unable to demonstrate an effect of age on the maximal number of spinal segments blocked after thoracic epidural anesthesia (18). Similarly, in our study, we demonstrated almost no effect of age on thoracic epidural spread of local anesthetic.

It seems that taller patients require more local anesthetics to establish a certain level of blockade than shorter subjects, but clinical trials evaluating the relationship between height and spread of blockade after epidural administration of local anesthetics are lacking in thoracic epidural anesthesia. In thoracic epidural anesthesia, correlation coefficients from -0.25 (14) to -0.37 (19) have been found between the spread of epidural injected contrast medium and patient height. We also found a significant negative relationship (correlation coefficient of -0.71) between Bupivacaine spread in thoracic epidural space and the height of patients, which is almost similar to the findings of other studies.

Few studies report on the correlation between weight and spread of local anesthetics in thoracic epidural space. Yokoyama, et al, reported that weight was not correlated with epidural spread of contrast in thoracic epidural anesthesia. We also found that spread of Bupivacaine had weak relationship with Patient’s weight (14).

Since a total of 8cc local anesthetic was injected, it could be concluded that to block each level of epidural space 1.6 and 1.88cc 0.5% isobaric Bupivacaine is required in female and male patients respectively. Moreover, the local anesthetic in thoracic epidural space raised 1.38 levels in males and 1.65 levels in females toward cephalic for each one level moving caudally. In the present study, Bupivacaine injection rate was 1cc/sec. which was similar to many other studies; however, in one study where analgesic injection was infused at the rate of 1cc per 3 seconds, the spread of the injected solution for each intervertebral level was reported as 1.96cc. This difference with our results may be due to the injection rate.

Conclusion

In conclusion, our study indicated that the distribution of Bupivacaine in epidural space is more in females than males and the tendency of spread is more toward the cephalad direction than caudal.

Acknowledgment

None.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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