

## Comparison of the Effect of Intravenous and Epidural Administration of Fentanyl on Pain Severity and Hemodynamic Status in Patients with Abdominal and Thoracic Trauma

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Article information	Abstract
<p>Article history: Received: 16 July 2011 Accepted: 4 Aug 2011 Available online: 28 Oct 2012 ZJRMS 2013; 15(2): 14-18</p> <p>Keywords: Fentanyl Epidural Pain Mechanical ventilation</p> <p>*Corresponding author at: Fellow of Pediatric Cardiology, Shiraz University of Medical Sciences, Shiraz, Iran E-mail: mehdia50@gmail.com</p>	<p><b>Background:</b> The pain of the chest and abdominal injuries in patients who undergoing mechanical ventilation is controlled by regional or systemic administration of drugs. We designed this study for comparison of effect of intravenous and epidural injection of fentanyl on pain reduction and hemodynamic status in patients with abdominal and thoracic injuries.</p> <p><b>Materials and Methods:</b> In this prospective clinical trial study, we randomly allocate 60 patients aged 16 to 80 years who were undergoing mechanical ventilation due to thoracic or abdominal injuries, to two groups. In B group during first 24 hour of admission pain management was done by epidural infusion of fentanyl and in the next 24 hours, this method was changed to intravenous infusion of fentanyl. In A group, initially method was intravenous and after 24 hours, we changed it to epidural method. We assessed pain score and hemodynamic status at the specific times.</p> <p><b>Results:</b> In both groups after first 2 hours, pain score was significantly lower in intravenous method but after 6 hours, pain score was significantly lower in epidural method. Hemodynamic status in epidural method was significantly more stable than IV method.</p> <p><b>Conclusion:</b> This study showed that for patients who were undergoing mechanical ventilation due to chest or abdominal injuries, intravenous infusion of fentanyl provides more pain relief during first two hours but after six hours epidural method is better than intravenous infusion.</p>

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### Introduction

Pain may cause increased blood coagulability, reduced patient mobility, atelectasis and subsequent pneumonia, most physicians are concerned with reducing severity of pain. Many different reasons for pain in ICU were recognised which including prolonged immobility, using invasive monitoring methods, mechanical ventilation and specific nursing care. Today non-steroidal anti-inflammatory drugs, neuro axial nerve blocks and systemic analgesic drugs are used for pain relief. Narcotics are effective and accessible analgesic drugs with low side effects; they are a good choice for pain controlling. Morphine is used more than other opioids; fentanyl as a synthetic opioid with an effect 100 times more than that of morphine and with no effect on histamine release [1]. Epidural administration of narcotics and local anesthetic is aimed for reducing of pain with preserve of consciousness [1].

Another method of pain controlling is intravenous administration of analgesics that its complications are infection, blood or gas clots embolism, phlebitis and hemodynamic disorders [2]. Thus, electrocardiography and non-invasive monitoring of arterial blood pressure are

mandatory [3]. Different types of rating systems such as visual analog scale, numeric rating scale in conscious patients and behavioral pain scale in patients with decreased level of consciousness are used to assess pain in ICU conscious patients [4].

Previous studies, reported different results of effectiveness of pain controlling of epidural and intravenous administration of analgesics. Result of a study by Murakami et al. indicated that after surgery, intravenous fentanyl analgesia was more safe and effective compared to epidural [5].

In Della Rocca et al. study it was found that after thoracotomy, epidural infusion of morphine lead to better controlling of pain [6]. Study of Movafagha et al. indicated that there was no significant difference in pain relief after chest surgery in both epidural fentanyl and intravenous injection of pethidine. However, epidural technique lead to better respiratory function [7].

In Ali et al. study, simultaneous administration of drugs with local anesthetic through epidural caused more pain relief and better quality of life after surgery of abdomen and chest compared with intravenous opioids [8].

Study of Salengros et al. showed that combined use of epidural catheters and low dose of remifentanyl during surgery reduces pain more in surgical site than high-dose of intravenous remifentanyl [9].

In some studies, it was observed that epidural technique is more effective than intravenous method [10] and in some others there was no significant differences between two methods [11]. Now by considering importance of pain controlling in ICU and controversy between previous studies, we decided to compare intravenous and epidural administration of fentanyl on pain control and hemodynamic stability.

## Materials and Methods

Target population of this study was patients who were admitted to intensive care unit of Shahid Bahonar Hospital and were under mechanical ventilation from October 2009 to September 2010 because of trauma of chest and abdomen. This study was performed after its approval by the Ethics Committee of the Research Center of Kerman University of Medical Sciences with ethic code of 125/89 k and receiving Iran clinical research code (IRCT201012205426N1). This study is a single blind randomized controlled clinical experiment in which interviewer who measured degree of pain and hemodynamic status of patients was not aware of pain control method.

In this study, 60 patients with their legal written consent by caretaker were investigated in 2 groups each of which included 30 patients. They classified sequentially A and B groups for randomization. Exclusion criteria included: Individuals with less than 16 years old and over 80 years old, BMI more than 30, instability and spinal cord injury, renal and liver failure, heart and pulmonary disease, diabetes, high blood pressure, shock, adult respiratory distress syndrome, massive transfusion, addiction history and contraindications of epidural catheter. Because of numerous confounding factors in ICU and for full integration of patients, it was decided that all patients experience both methods in order to each individual patient to be compared with himself over time. Moreover, in order to eliminate effect of time passage on pain intensity, first epidural procedure was used in group A and next intravenous method was applied in group B.

In group A in the first 24 hours intravenous fentanyl was administered and then for they received epidural fentanyl for 24 hours with insertion of epidural catheter placement at T11-L1 level. In Group B, epidural fentanyl was injected in the first 24 hours and then intravenous fentanyl

injected in next 24 hours. Amount of intravenous fentanyl was 2 µg/kg of body weight and amount of administrated epidural fentanyl was 1 µg/kg of body weight of with a solution of 5-10 µg/ml [1] concentration set by infusion pump at a speed of 5 ml. Interval of these two methods of intravenous fentanyl and epidural injection was 24 hours to metabolize and excrete remained drugs.

During this period, intravenous morphine in rate of 0.01 to 15.0 mg/kg was administered every 1 to 2 hours if necessary. Degrees of pain, Blood pressure and heart rate were measured and recorded at 0, 2, 6, 24, 50, 54 and 72 hours. VAS criterion was used to measure pain severity; electrocardiography was used to measure heart rate and non-invasive cuff method used to measure blood pressure. Moreover, to ensure adequate heart rate before this experiment, central venous pressure maintained at water level of 10 cm of water in order to protect hemodynamic status against intravascular volume deficiency.

Patients information was collected based on a research forms and analyzed statistically by SPSS-16 software. Central mean and standard deviation (Mean±SD) were used to provide descriptive results. Repeated measure ANOVA test was used to compare all variables (pain score, heart rate, blood pressure) in 3 time groups (0, 2 and 50) (0, 6 and 54) (0, 24 and 72). Results of this test provided in both crude and adjusted forms for age and sex variables. *p*-value less than 0.05 was considered significant. As it can be seen in diagrams, two groups are compared in each studied periods (0 to 72) using *t*-test.

**Table 1.** Demographic data in both groups of A and B

Group	Gender		Age (year)
	Male	Female	
A	70	30	34.9
B	60	40	41.2

**Table 2.** Comparison of pain severity at different hours between epidural and intravenous methods

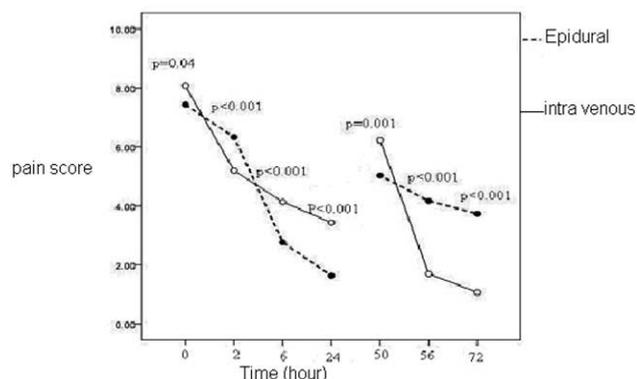
Group	Time (hour)	pain severity in two methods		<i>p</i> -Value
		Intra venous	Epidural	
A	2	5.03±0.99	6.33±1.02	0.0009
	6	4.1±1.08	2.76±1.04	0.0007
	24	3.7±0.90	1.6±0.99	0.0005
B	2	5.2±0.99	6.2±1.5	0.0008
	6	4.1±0.97	1.7±0.95	0.0002
	24	3.4±1.04	1.06±0.98	0.0005

**Table 3.** Comparison of HR average at different hours between epidural and intravenous methods in both groups of A and B

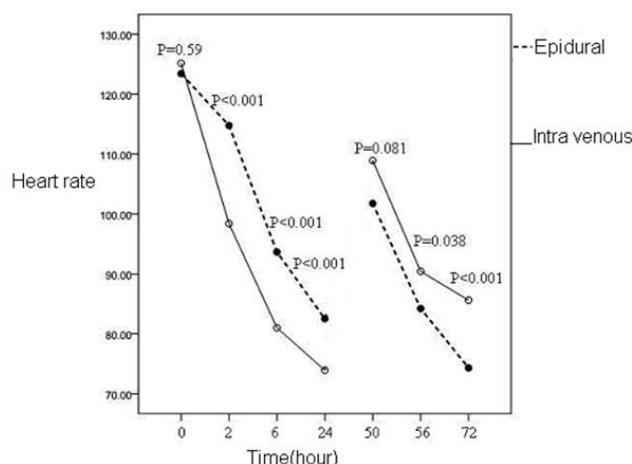
Group	Time (hour)	Mean arterial pressure(MAP) in two methods		<i>p</i> -Value
		Intra venous	Epidural	
A	2	114.7±15.4	101.7±19.7	0.0006
	6	93.6±12.2	84.2±13.4	0.0009
	24	82.5±9.1	74.3±11.9	0.0009
B	2	98.6±15.2	109.1±10.7	0.0007
	6	81.1±8.1	90.4±8.3	0.0009
	24	73.9±6.2	85.6±6.4	0.0009

**Table 4.** Comparison of mean arterial pressure in A and B groups comparison with methods of fentanyl and intravenous methods with injection of fentanyl into the epidural catheter at 0, 2, 6 and 24 hours

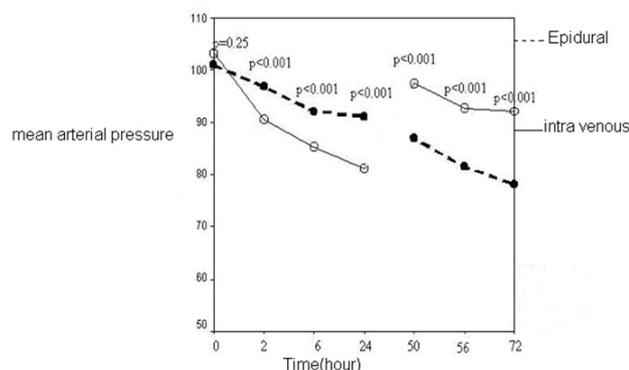
Group	Time (hour)	Mean arterial pressure(MAP) in two methods		p-Value
		Intra venous	Epidural	
A	2	86.9±7.2	96.8±6.7	0.0007
	6	81.5±6.1	92.1±5.8	0.0008
	24	78.1±5.7	91.1±4.3	0.0006
B	2	90.4±4.1	97.3±3.2	0.0009
	6	90.4±4.1	98.3±2.2	0.0009
	24	81.1±4.2	92.2±3.8	0.0008



**Figure 1.** Comparison of average of pain severity in two epidural and intravenous methods



**Figure 2.** Comparison of HR at different hours between epidural and intravenous methods



**Figure 3.** Comparison of mean arterial pressure at different times between A and B group with two methods of fentanyl and intravenous injection

## Results

Number of men in group A was 21 (70%) and 9 women were in this group (30%). 18 men (60%) and 12 women (40%) were in group B. Age average of group A was 41.2 and for group B it was 34.9 (Table 1).

1- Degree of pain severity (PS): Average pain intensity at different times in both groups was evaluated and it was found that both groups, either crude or justified, had a significant decrease in second hour with intravenous epidural methods compared to time zero ( $p=0.003$ ). However, in the 6th and 24 hours, least pain in the epidural was observed that statistically significant ( $p=0.0002$ ,  $p=0.0005$ ), but there was no significant relationship between reduction reduced pain intensity and age or sex of patients (Table 2).

2- Heart rate: Heart rate of patients on their arrival, 2nd, 6th and 24 hours after injection in both groups (either crude or justified) were measured and it was found that there is a significant decrease in heart rate with intravenous injection of fentanyl compared to epidural method and before injections ( $p=0.0007$ ,  $p=0.0009$ ,  $p=0.0009$ ), but this reduction was not significantly associated with age and sex (Table 3).

3- Mean blood pressure: At the beginning of patient admission and during 6th and 24 hours after injection of MAP in both groups (either crude or justified), blood pressure average was measured and it was determined there will be a significant decrease in MAP with intravenous fentanyl injection compared to epidural injection methods ( $p=0.0009$ ,  $p=0.0009$ ,  $p=0.0008$ ). However, this reduction was not significantly associated with age and sex (Table 4).

## Discussion

In this study, we observed that patients who are under mechanical ventilation treatment due to abdominal and chest injuries experienced a significant reduction in pain in early hours of, continuous intravenous infusion of fentanyl compared to epidural method, while after six hours of continuous infusion of fentanyl in thoracic epidural space, quality of pain control with this method is much better than the intravenous method. This result is not consistent with findings of Solek et al. [12]. However, it is consistent with Della Rocca study in which quality of pain control after surgery of chest in epidural technique was better than intravenous infusion [6].

Another finding of this study was that continuous infusion of fentanyl either in IV or epidural space

maintains patient's hemodynamic status but hemodynamic stability is more obvious in epidural method. No valid study has ever been done in this field. Administration of narcotics in epidural space is a common method for pain controlling following surgery in chest and abdomen that is often associated with continuous infusion of local anesthetic such as Markayin [1].

Earlier studies were performed about comparison of intravenous and epidural analgesia. In Della Rocca et al. study it was found that after thoracotomy, epidural infusion of morphine lead to better controlling of pain, shorter hospitalization and less morbidity than intravenous method [6]. Study of Movafagha et al. indicated that there was no significant difference in pain relief after chest surgery in both epidural fentanyl and intravenous injection of pethidine. However, epidural technique lead to better retention of ventilatory function and reduced complications after thoracotomy [7]. In Ali et al. study, simultaneous administration of drugs with local anesthetic through epidural caused more pain relief and better quality of life after surgery of abdomen and chest compared with intravenous opioids [8].

Study of Salengros et al. showed that combined use of epidural catheters and low dose of remifentanyl during surgery reduces pain more in surgical site than high-dose of intravenous remifentanyl [9]. Murakami and colleagues found that the use of intravenous fentanyl reduces pain better than epidural [10]. In Butkovic et al. study, they concluded that pain severity after surgical correction of chest deformity was the same in the patient control analgesia method and intravenous administration fentanyl [11]. Solek et al. study compared continuous epidural analgesia with intravenous infusion of remifentanyl during labor period. In first 2 hours of in epidural method, pain intensity was significantly low but after that they were similar [12].

In Privado MS et al. study, intravenous fentanyl and epidural for analgesia after orthopedic surgery was compared and indicated that both have similar effect on pain, but the need for prescription of complementary drugs of pain inhibitors was lower in epidural method [13]. Previously no comparison is made between intravenous and epidural technique in terms of simultaneous effects on both hemodynamic status and amount of pain relief in patients with chest and abdomen

trauma hospitalized in intensive care unit under mechanical ventilation treatment.

According to above results, it is concluded that due to more rapid effect of intravenous injection of fentanyl in second hour after injection, this method significantly reduces pain compared to epidural method; while after six hours of epidural injection and maximum analgesic effect of this approach, pain in abdomen and chest of patients is dramatically reduced compared to intravenous method. Meanwhile, hemodynamic status of patients in both fentanyl injection methods (intravenous and epidural) was in normal range but patient's condition was better with epidural space injection.

According to results of this study, it seems that it is better to use intravenous and epidural fentanyl methods simultaneously on arrival of ICU patients in T11-L1 space in order to create better analgesia with hemodynamic stability in patients with chest and abdominal injuries. Next, it should be continued during first six hours with intravenous method when patient has more pain to reach the maximum effect of intravenous epidural injection. Then it will be stopped in order to continue epidural method more effectively to relieve pain with better hemodynamic status of patient. Among shortcomings of this study is that there is no classification between chest injury, combined abdominal and chest injuries. However, because comparison of both methods is made in the same patient, effect of trauma type on amount of pain relief and hemodynamic status is reduced as least as possible.

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### Authors' Contributions

All authors had equal role in design, work, statistical analysis and manuscript writing.

### Conflict of Interest

The authors declare no conflict of interest.

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