ORIGINAL PAPER

Opiate Analgesia Treatment Reduced Early Inflammatory Response After Severe Chest Injuries

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ABSTRACT

Background: The frequency of severe chest injuries are increased. Their high morbidity is followed by systemic inflammatory response. The efficacy of pharmacological blockade of the response could prevent complications after chest injures. **Aim**: The aim of the study was to show an inflammatory response level, its prognostic significant and length of hospital stay after chest injures opiate analgesia treatment. **Methods**: Sixty patients from Department of Thoracic Surgery with severe chest injures were included in the prospective study. With respect of non opiate or opiate analgesia treatment, the patients were divided in two groups consisted of 30 patients. As a inflammatory markers, serum values of leukocytes, neutrophils, C-reactive protein (CRP) and fibrinogen in three measurements: at the time of admission, 24hours and 48 hours after admission, were followed. **Results**: Statistically significant differences were found between the examined groups in mean serum values of neutrophils (p=0.026 and p=0.03) in the second and the third measurement, CRP (p=0.05 and 0.25) in the second and the third measurement and leukocytes in the third measurement (p=0.016). 6 patients in group I and 3 in group II had initial stage of pneumonia, 13 patients in group I and 6 in group II had atelectasis and 7 patients from group I and 4 from group II had pleural effusion. The rate of complications was lower in group of patient who were under opiate analgesia treatment but without significant difference. The length of hospital stay for the patients in group I was 7.3±1.15 days and for the patients in group II it was 6.1±0.87 days with statistically significant difference p=0.017. **Conclusion**: The opiate analgesia in patients with severe chest injures reduced level of early inflammatory response, rate of intra hospital complications and length of hospital stay.
Keywords*: severe chest injuries, inflammatory response, opiate analgesia.*

1. INTRODUCTION

This study is designed to show an evaluation of prospectively collected data of all consecutive adult patients admitted to our Department of thoracic surgery after chest injures and opiate analgesia treatment between 1st October 2013 and 31 st March 2014 to analyze development of early inflammatory response. Inadequately controlled pain after severe chest injures may still extend the length of hospital stay and predispose to expensive, time-consuming complications such as pneumonia (1). Experimental and clinical investigations suggested that acute pain causes chronic pain very fast and has impact on long-term neurophysiological changes and quality of life with reduced morbidity and mortality (2). Effective management of pain decreased intra hospital complications incidence, length of hospital stay and chronic pain syndrome occurrence (3). It has been concluded that good

controlled pain management of severe chest injures will improve the outcome with reduced morbidity, need for repeated hospitalization and convalescence, and there is a common consensus that optimal pain relief is a prerequisite for early postoperative recovery (4).

2. MATERIALS AND METHODS

Sixty patients were included consecutively between 1st October 2013 and 31 st March 2014 in prospective study with University Clinical Centre Tuzla Ethical Committee approval. All patients with severe chest injures were admitted to Department of Thoracic Surgery. Radial immunodiffusion method on Dimension RxL- Max Sysmex-Simens device was used to determine serum level of acute phase proteins fibrinogen (1.8 - 3.5 g/L) and CRP (0-3.3 mg/l). Leukocytes and neutrophils cell by cell analyses were performed by The CEL-DYN Ruby system instrument. Patients were divided in two homogeneous groups, 30 patients each, which were of the same age and sex. Non-opiate intermittent analgesia of metamizol sodium was applied to the first group of patients and continuous tramadol hydrochloride opiate analgesia to the second group. All the patients had three measurements: the first - at time of admission, the second - 24 hour after and the third - 48 hours after admission. Metamizol sodium was applied intramuscularly or intravenously, intermittently, in ampules of 5ml which contains 2,5 g. The maximum dose was 10g/24h. Tramadol 50mg/ml solution was administered in ampule which contains 100mg tramadol hydrochloride in 2ml solution (50mg/ml) for injection or infusion. The usual dose was 50mg or 100mg, 4 to 6 hourly by either intramuscular or intravenous routes, maximum 400mg/24h. The patients with polytrauma, diabetes mellitus, systemic chronic diseases and respiratory support were excluded from study.

Statistical analysis

The continues variables were expressed as mean ± standard deviation (SD). Non-parametric methods were used for all comparisons of meteorological parameters. Data were compared by the Wilcoxon signed -rank test so that value of p<0.05 was considered significant in all tests.

3. RESULTS

After the administration of analgesia, mean neutrophils serum levels were lower in the examined group, to which opiate analgesia was administered, in the second and third measurement with statistically significant difference (p=0.026 and p=0.03) as seen in Table 1.

The dynamics of decreasing neutrophils serum values was slower among the patients in the controlled group.

In the second measurement mean serum values in the controlled group were 5.42±1.36 and in the examined group they were 3.92±1.56, with statistically significant difference p=0.05. In the third measurement mean CRP serum values were 4.8±0.78 in the controlled group whereas in the examined group they were 3.6±0.69 with the statistically significant difference p=0.025. In the controlled group, during the second measurement, patients showed increased CRP serum values compared to

MEASUREMENT	I	II	III
GROUP I	5.61 ± 1.50	4.45 ± 0.88	4.27 ± 0.95
GROUP II	6.10 ± 1.59	3.76 ± 0.90	3.77 ± 0.54
	p= 0.16	p = 0.026	p =0.03

Table 1. Mean serum ±SD neutrophiles values (109 /L) in two groups. p= 0.16 p = 0.026 p =0.03

MEASUREMENT	I	II	III
GROUP I	4.6 ± 1.90	5. 42 ± 1.36	4.8 ± 0.78
GROUP II	4.3 ± 2.18	3.92 ± 1.56	3.6 ± 0.69
	p= 0.31	p=0.05	p=0.025

Table 2. Mean serum ±SD CRP (mg/L) values in two groups. p= 0.31 p=0.05 p=0.025

MEASUREMENT	I	II	III
GROUP I	3.33 ± 0.48	3.28 ± 0.46	3.7 ± 0.63
GROUP II	3.10 ± 0.73	3.25 ± 0.55	3.4 ± 0.65
	p= 0.25	p= 0.82	p= 0.06

Table 3. Mean serum ±SD fibrinogen values (g/L) in two groups. p= 0.25 p= 0.82 p= 0.06

MEASUREMENT	I	II	III
GROUP I	7.9 ± 1.46	6.2 ± 0.86	5.47 ± 0.90
GROUP II	8.4 ± 1.50	5.9 ± 0.79	4.75 ± 0.77
	p= 0.18	p= 0.23	p= 0.016

Table 4. Mean serum ±SD leucocytes values (109 /L) in two groups. p= 0.18 p= 0.23 p= 0.016

the initial value, while CRP serum value in the examined group were continually decreasing during each of three measurements in the 48-hour period. CRP serum values in both groups during all measurements were above the referential serum values with tendency of returning within the normal range of values (Table 2).

During the measurements in both groups of patients, mean serum values of fibrinogen have increased compared to the initial measurement, having in mind that the level of increase was much higher in group I. During each measurement serum values of fibrinogen were within referential values (Table 3).

In the third measurement serum values of leukocytes in the controlled group were 5.47±0.90 and in the examined group they were 4.75±0.77 with statistically significant difference p=0.016

During the measurements, leukocyte serum values were decreasing compared to the initial values, taking into consideration that the values were lower in the examined group of patients compared to the initial values, than in the controlled group of patients. In all measure-

ments mean serum values were within reverential range of values. Of the total number of patients, 17 patients or 28.3% had fractures of one or two ribs and 13 patients or 21.6% had fractures of three or more ribs. In the group of patients administered by metamizole (group I/controlled group) were 9 patients or 30% who had up to 2 fractures of ribs whereas 8 patients or 26.6% were in the group administered by tramadol (group II/examined group). 27 patients (45%) after X-ray and CT diagnostics had pulmonary parenchyma contusions of different degree.

Nine patients or 15% were diagnosed with initial stage of pneumonia, 6 patients or 20% were from the controlled group and 3 patients or 10% were from the examined group. Atelectasis was diagnosed to 19 patients or 31.6% . In group I there were 13 patients with atelectasis or 43.3% and in group II there were just 6 patients or 20% with diagnosed atelectasis. 11 patients or 18.35% were diagnosed with pleural effusion, 7 patients or 23% from group I and 4 patients or 13.3% from group II. The length of hospital stay for the patients in group I was 7.3±1.15 days and for the patients in group II it was 6.1±0.87 days with statistically significant difference p=0.017.

4. DISCUSSION

Suppressing the pain caused by chest trauma is the primary therapeutic procedure. By reducing the pain, patient has no restrictions in respiratory process and lowering the secretion of inflammation mediators results in lower tissue injury (5). As a result, faster better recovery of the patient is evident and the incidents of chronic pain syndrome occurrence, preventing the patient, after healing, to return to normal everyday life or causing repeated hospitalization or respiratory complications, are much more rare. Uncontrolled pain as a consequence may have increasing mortality and morbidity (1). The releasing of histamine and inflammatory mediators like bradykinin, prostaglandin, neurotransmitters or neutrophils, are conditioned by tissue injuries. The secretion of these mediators activate peripheral nociceptors and by transduction and transmission, nociceptive information are communicated to CNS (6). In acute phase it responds to trauma and stress, initiate the secretion and the increase of serum values of acute phase proteins (7). All inflammatory mediators,at certain point, have protective role, although in the case of massive tissue injuries, their secretion can have harmful impact on the tissue.

Opioids are one of the most frequent options when it comes to the treatment of postoperative and post traumatic pain (8). This agent acts through μ receptors in CNS even though there are proofs of existence of peripheral opioid receptors (9). Analgesic activity of opioids is limited by development of tolerance and secondary effects like nausea, vomiting, sedation and respiratory depression. The advantage of tramadol use as postoperative analgesia is the absence of respiratory depression, systemic toxicity, gastrointestinal motility and low percentage of drug abuse. The administration of tramadol has lowered the number of leukocytes after 24 hours and 48 hours more efficiently than the administration of metamizole sodium (Table 1). Decreasing of CRP serum values during the second measurement (after 24 hours) among the patients in the controlled group after the administration of tramadol was more than evident.

Taking into consideration CRP synthesis during the tissue injury, it is essential to suppress it to avoid more serious tissue injuries and prevent any further complications (10). The administration of tramadol decreased mean CRP serum values more efficiently than the use of metamizole sodium.

The efficiency of tramadol in pain suppression resulted in better respiratory functions and less frequent occurrence of pneumonia. Pneumonia can extend the length of hospital stay and cause other complications to patients with co morbidity (the occurrence of other diseases). In group I, 6 patients (20%) had pneumonia and in group II 3 patients (10%) had pneumonia. Of the total number of patients, 19 patients or 31.6% had atelectasis. In group I 13 patients or 43.3% had atelectasis and in group II just 6 patients or 20% had atelectasis. Therefore, in the group of patients administered by tramadol after the injury,the incidents of atelectasis occurrence were less frequent. Patients administered by tramadol for pain suppression had fewer complications. These patients had shorter period of hospital stay, namely for group I it was 7.3±1.15 days and for group II it was 6.1±0.87 days with statistically significant difference p=0.01.

5. CONCLUSION

The level of early inflammatory response is lower among the patients with severe chest injuries treated with opiate analgesia treatment than those treated with non-opiate analgesia. Considering that tramadol is a semi-synthetic opioid and its efficiency as analgesia is more intense than metamizole sodium, its use in treatments of pain caused by chest trauma has significantly better results in suppressing neutrophils and CRP activation thereby lowering the occurrence of secondary injuries caused by inflammatory mediators to minimum with a lower incidence of complications and shorter hospital stay.

- Conflict of interest: none declared.

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