

## Research Article

# Plasmapheresis Effect on Respiratory Condition and Acidosis in Unstable Complex Patients with Pelvic and Long Bone Fracture

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## Abstract

**Background and Objective:** After head trauma, pelvic fracture is the most common cause of death in multiple trauma patients. In cases with stable hemodynamic, sepsis or multi-organ failure is the cause of mortality. There are many efforts to improve these patients status. It seems that plasmapheresis by reducing inflammatory response could improve these patients status. The aim of current study is to evaluate the role of plasmapheresis on improving respiratory condition and acidosis in trauma patients with unstable complex pelvic fracture and long bones. **Methodology:** In this clinical trial, 12 patients (11 men and 1 woman) 30-60 years old with unstable complex pelvic fracture and long bones admitted to surgery ICU were evaluated. All patients received plasmapheresis and the plasmapheresis was repeated if needed. Atrial blood gas and hemodynamic findings before and after plasmapheresis were evaluated. Also, mortality and duration of hospital stay was recorded. **Results:** Thirty four sessions of plasmapheresis were performed in 12 patients. After plasmapheresis, systolic blood pressure was significantly increased ( $p = 0.02$ ) and hear rate was significantly decreased ( $p = 0.001$ ). Also, following plasmapheresis, oxygen saturation and blood pH were both increased ( $p < 0.001$  in both). The decrease in  $CO_2$  ( $p = 0.25$ ) and increase in  $HCO_3$  ( $p = 0.22$ ) was not significant. Mean ICU stay was  $16.83 \pm 5.70$  days and mean hospital stay was  $19.50 \pm 6.04$  days. There were three (25%) deaths. **Conclusion:** Plasmapheresis in patients with unstable complex pelvic fracture could improve acidosis and respiratory condition and so be effective in improving these patients condition.

**Key words:** Pelvic fracture, plasmapheresis, respiratory function, acidosis

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**Competing Interest:** The authors have declared that no competing interest exists.

**Data Availability:** All relevant data are within the paper and its supporting information files.

## INTRODUCTION

Trauma is a common cause of death and disability in young population in developed countries. In recent years, significant development is seen in dealing with traumatic patients including quick transfer of traumatic patient, on time resuscitation, special care and treatment of wounds. Pelvic fracture is the most common cause of death in multiple trauma patients after head trauma<sup>1,2</sup>.

Pelvic fractures usually occur after a car accident or a fall from a height and it is accompanied with fracture of other bones and injuries of other body tissues and viscera<sup>3-5</sup>. The main reason of death in patients with hip fracture is uncontrolled and uncontrollable bleeding and the main reason in cases of delayed death is pelvic or generalized sepsis and also multi-organ failure<sup>6,7</sup>.

There are many different causes that can lead to multi-organ failure such as infectious outcomes. It is suggested that inflammatory response of body to trauma induced stress can lead to failure of various organs and death through inflammatory cytokines production<sup>8-12</sup>. There are different mechanisms that inflammatory mediators can lead to organ failure. One of these mechanisms is increased capillary permeability which affects lungs more than all and leads to acute respiratory distress which is one of the main causes of death in traumatic patients<sup>10,12</sup>. Since the inflammatory response plays an important role in the serious consequences of trauma, interference and inhibition of inflammation can have a significant role in management of traumatic patients<sup>13</sup>.

There is a high risk of death in patients with hip and long bones fracture (33-57%). Since motor vehicles are a major contributor to the injured trauma patients in our country, 80-84% of hip fractures are due to the motor vehicle accidents<sup>14-16</sup>. Now-a-days, severe trauma which involved bone and soft tissue is one of the biggest challenges in medicine. Ninety percent of traumatic injuries are associated with bone fractures. The main reason of death in severe blunt trauma is multiple organ failure<sup>17,18</sup>. This failure can be due to infectious process which can lead to failure in lung and other organs. Additionally, inflammatory response of body that occurs after trauma and extensive injury of bone and soft tissue play a significant role in this organ failure.

According to the studies, inflammatory mediators especially TNF- $\alpha$  increases in first hours after trauma and it is the most important stimulator to start inflammatory process<sup>11,12</sup>. Plasmapheresis can also change the cytokine-anti cytokine pattern<sup>19</sup>.

The role of plasmapheresis in regulation of immune system includes modification of T-cells function, shifting to Th2 and suppression of IL2 and INF- $\gamma$  production<sup>20-23</sup>.

It was shown in many studies and case reports that plasmapheresis had an important role in improvement of acidosis and finally the patient's prognosis<sup>24-26</sup>.

Due to the significant role of inflammatory response in traumatic patients and effects of plasmapheresis in reduction of inflammatory mediators, it seems to be possible to improve general condition of patients with use of plasmapheresis and decrease of inflammatory response. There is no accessible study to evaluate this hypothesis. The aim of this study is to evaluate the effects of plasmapheresis in improvement of respiratory condition and acidosis as a part of the process of improving the management of trauma patients with complex and unstable fracture of hip and long bones.

## MATERIALS AND METHODS

This clinical trial to No. IRCT 2014082718946N1 has been registered in Iran's clinical trials registering center to the address "www.irct.ir".

Since no similar studies had been done, 12 cases were selected randomly with simple random sampling method. These 12 cases were chosen among patients between 15-65 years with complex unstable hip or long bones fracture who were referred to the hospital during the year of 2014 and hospitalized in ICU ward.

Inclusion criteria were having 15-65 years old, complex unstable hip or long bones fracture, indication for hospitalization in ICU, having respiratory distress and tachypnea, low oxygen saturation and acidosis.

Exclusion criteria were history of renal failure, low consciousness level (GCS<8) at admission, history of angioplasty, history of chronic lung disease such as chronic obstructive pulmonary disease and asthma, the need for surgical intervention and unstable hemodynamic.

Surgery and pelvic pack if there were indications for them and routine treatments for all patients were done according to surgery references. In critically ill patients (who had tachycardia, low blood pressure, low oxygen saturation and acidosis) despite surgical interventions who had normal hemoglobin and hematocrit and in the absence of clinical symptoms of active bleeding, plasmapheresis was performed. So, selection of patients done based on diagnosed as ill and no need for surgery.

Hospitalized patients with unstable complex hip fracture in ICU ward were evaluated in terms of respiratory status such as arterial blood gases, respiratory rate, presence of respiratory

distress and patient's attachment to ventilator at 6 am every day. Plasmapheresis was performed 2 h after these evaluations. The same tests were done at the end of plasmapheresis. Plasmapheresis was continued until the patient's status was not changed or hemodynamic status was not deteriorated.

Plasmapheresis was performed with veno-venous access method. Heparin with dose of 200-300 U kg<sup>-1</sup> was used as anticoagulant. Two liters of patient's plasma was replaced with 4 U of Fresh Frozen Plasma (FFP) in every session of plasmapheresis.

The most common complication of plasmapheresis is allergic reactions and the most dangerous one is anaphylactic reaction. In cases with this reaction subcutaneous epinephrine 1 mg kg<sup>-1</sup> was injected every 20-30 min up to 3 times. Aminophylline 16 mg kg<sup>-1</sup> was administered to relieve spasms. Plasmapheresis was continued until the patient had discharge indication from ICU ward in terms of respiratory status and acidosis. All patients were monitored in terms of coagulation tests, cardiovascular function, level of consciousness daily and 2 h after plasmapheresis.

So, effect of plasmapheresis on cardiovascular and respiratory function in patients with complex unstable hip fracture was evaluated. The number of hospitalized days in hospital (ICU or surgery ward) was calculated.

**Statistical analysis:** Descriptive methods such as frequency, percentage, Mean ± Standard Deviation were used in order to statistical analysis. Wilcoxon parameter was used to compare quantitative variables before and after the intervention. All analysis was done with SPSS 17. The p<0.05 was considered significant.

## RESULTS

In this study, plasmapheresis was done on 12 patients with complex unstable hip and long bones fracture. Patients

were in the range of 30-60 years. All the patients were men except one of them. The most common cause of severe trauma was accidents. Basic findings of the patients were shown in Table 1. Generally, 34 times of plasmapheresis were done for all 12 patients.

Systolic blood pressure was increased and heart rate was decreased significantly. Changes in diastolic blood pressure and respiratory rate were not significant. Table 2 shows hemodynamic changes before and after plasmapheresis.

Oxygen saturation was increased significantly after plasmapheresis (p<0.001). Figure 1 shows oxygen saturation before and after plasmapheresis. Overall, there was improvement in oxygen saturation after plasmapheresis in 75% of cases.

After plasmapheresis, pH was significantly increased (p<0.001). Indeed, acidosis was corrected in majority of cases. Fig. 2 shows pH before and after plasmapheresis. The pH improvement was seen in 69.44% of cases.

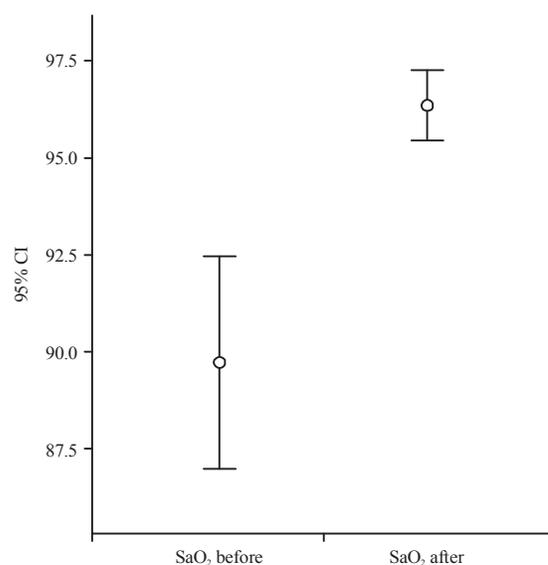


Fig. 1: Changes of oxygen saturation before and after plasmapheresis

Table 1: Basic findings of evaluated patients

Gender	Age	Reason of trauma	Type of fractures
Male	41	Falling from height	Fracture of inferior and superior ramus and left clavicle
Male	45	Road accident	Right sacroiliac diastasis and right inferior ramus fracture
Male	56	Road accident	Pubis symphysis and right iliac diastasis and left lower limb fracture
Male	35	Road accident	Pelvic fracture, amputation of left lower limb
Female	53	Road accident	Bilateral superior and inferior ramus fracture, sacroiliac diastasis and left femur fracture
Male	34	Road accident	Multiple rib and double forearm fractures
Male	37	Falling from height	Right humerus and femur fracture
Male	36	Vehicle rollover	Bilateral ramus fracture, fracture of left sacrum and tibia and multiple bilateral rib fractures
Male	42	Falling from height	Right acetabulum and neck of femur fractures and multiple rib fractures
Male	30	Road accident	Multiple rib and left femur fracture
Male	40	Vehicle rollover	Right acetabulum and iliac fracture

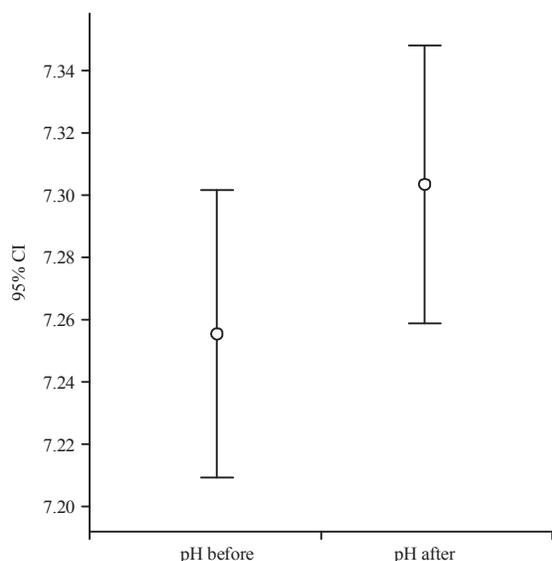


Fig. 2: pH changes before and after plasmapheresis

Table 2: Hemodynamic changes before and after plasmapheresis

Hemodynamic changes	Before plasmapheresis	After plasmapheresis	p-value
Systolic blood pressure	124.64±18.70	130.88±17.37	0.02
Diastolic blood pressure	79.50±15.55	79.61±12.56	0.80
Heart rate	121.09±21.53	112.90±17.87	0.001
Respiratory rate	16.57±4.44	15.42±3.54	0.21

The mean level of CO<sub>2</sub> was 42.26±8.67 before plasmapheresis and 40.4±8.28 after that. Despite decrease in CO<sub>2</sub> level after plasmapheresis, the difference was not significant (p = 0.25). Improvement of CO<sub>2</sub> level was seen in 47.22% of cases.

The mean HCO<sub>3</sub> level was 19.87±5.97 before plasmapheresis and 20.36±5.59 after that. Despite increase in HCO<sub>3</sub> level after plasmapheresis, the difference was significant (p = 0.22). Improvement was seen in 55.55% of cases after plasmapheresis.

The mean PO<sub>2</sub> level was 75.02±20.53 before plasmapheresis and 89.22±18.54 after that. It was significantly increased after treatment (p = 0.009).

The mean FiO<sub>2</sub> level was 64.68±18.48 before plasmapheresis and 60.20±17.01 after that. There was not any significant change in FiO<sub>2</sub> levels before and after treatment (p = 0.15).

The mean period of hospitalization in ICU ward was 16.83±5.70 days with the median of 9. The mean period of hospitalization in surgery ward was 4.16±0.97 days with the median of 4. The mean period of hospitalization was 19.50±6.04 days. There were 3 deaths among 12 patients (25%). There were no death in patients who response to first time of treatment. Indeed, in 3 cases of death, 5 times of

plasmapheresis was done in 2 cases and 4 times were done in one case in which none of them were effective.

## DISCUSSION

Effect of plasmapheresis on patients with complex hip or long bone fractures was evaluated for the first time in this study. Thirty four times of plasmapheresis were done on 12 patients. Respiratory status, general condition and hope to survive of patients were improved with this treatment.

The most common cause of complications occurred after trauma is stress and body inflammatory response and inflammatory cytokines production<sup>8,9</sup>. Increased inflammatory mediators in first hours after trauma was shown<sup>11,12</sup>. So, it seems possible to improve the clinical status of patients through adjustment of the inflammatory response.

Plasmapheresis has a regulatory effect on inflammatory response, cellular and humoral immunity<sup>20-23,27</sup>. It was shown that plasmapheresis can reduce the blood level of inflammatory mediators (18) and control of blood level of immune system stimulatory cytokines<sup>28</sup>.

This is the first study that evaluates the effect of plasmapheresis on the improvement of acidosis and respiratory function of traumatic patients. Results of this study showed that plasmapheresis can improve acidosis and oxygen saturation.

In a case report, it was shown that plasmapheresis can be effective in improvement of acidosis and rapid treatment of acute respiratory distress syndrome<sup>29</sup>.

In another report, one-time treatment with plasmapheresis was accompanied with rapid improvement in hemodynamic status, improvement of lactic acidosis during 24 h and finally complete recovery of the patient<sup>24</sup>.

Complete recovery in terms of arterial gasses and general condition after treatment with plasmapheresis was reported in 3 cases of amitriptyline toxicity<sup>25</sup>.

In previous studies, it was shown that patients with hip and long bone fractures had a high mortality rate (33-57%)<sup>20-22</sup>. In this study mortality rate after appropriate therapy with plasmapheresis was 25%.

Only a single time of treatment with plasmapheresis was effective in 6 patients. In the others, 2-5 times of treatment was done. It was not effective in 3 of patients and so they died.

In previous studies on patients with the guillain-barre syndrome, four times of plasmapheresis were more effective than 2 times in patients without the need for ventilation and in ventilated patients there was no significant difference between 4 and 6 times of plasmapheresis<sup>30</sup>. It seems that times of plasmapheresis depended on clinical status of the patient and his/her diagnosis.

## CONCLUSION FUTURE RECOMMENDATIONS

Plasmapheresis can be effective in improvement of acidosis and respiratory status in patients with unstable complex hip fracture.

According to the results of this study, use of plasmapheresis is recommended in patients who didn't response to routine therapies.

Since this study is the first one in this field, further studies with larger sample size are recommended to achieve better and more accurate results.

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