Should we change our approach to resuscitating victims of femoral fracture? A clinical experience in a busy trauma hospital in Shiraz, Iran

Shahram Paydar, Ali Taheri Akerdi, Sadra Nikseresht, Hossein Abdulrahimzadeh-Fard, Leila Shayan, Zahra Ghahramani*, Shahram Bolandparvaz, Hamid Reza Abbasi

Trauma Research Center, Rajaee (Emtiaz) Trauma Hospital, Shiraz University of Medical Sciences, Shiraz, Iran

ABSTRACT

Purpose: Traumatic hemorrhagic shock is a life-threatening event worldwide. Severe brain trauma accompanying femoral fractures can trigger inflammatory responses in the body and increase pre-inflammatory cytokines such as TNF-α, IL-1. The primary treatment in these cases is hydration with crystalloids, which has both benefits and complications. The purpose of this study was to investigate the effects of fluid therapy on the hemodynamics, coagulation profiles, and blood gases in such patients.

Methods: In this cross-sectional study, patients were divided into two groups: femoral fracture group and non-femoral group. The hemodynamic status, coagulation profile, and blood gases of patients in both groups were evaluated upon arrival at the hospital and again 2 h later. Data were analyzed by t-test and ANOVA with repeated data and paired samples t-test.

Results: A total of 681 trauma patients (605 men and 76 women) participated in this study, including 69 (86.3%) men and 11 (13.8%) women in femoral fracture group and 536 men (89.2%) and 65 women (10.8%) in non-femoral group. The laboratory parameters were evaluated in response to the equal amount of crystalloid fluid given upon arrival and 2 h later. Blood gases decreased in the fracture group despite fluid therapy ($p < 0.003$), and the coagulation profile worsened although the change was not statistically significant.

Conclusion: The treatment of multiple-trauma patients with femoral bone fractures should be more concerned with the need for the infusion of vasopressors such as norepinephrine. If there is evidence of clinical shock, excessive crystalloid infusion (limited to 1 L) should be avoided, and blood and blood products should be started as soon as possible.

© 2020 Chinese Medical Association. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction

Shock is defined as “inadequate organ perfusion mode”; hence, fluid therapy is an important component in the rehabilitation of trauma patients along with the establishment of an airway and respiration. Initial hydration in cases of hypovolemic shock should expand intravascular volume, improve arterial mean pressure, improve heart function, provide perfusion, and reduce acidosis, hypothermia, and coagulopathy.

Trauma and hypoperfusion cause various compensatory mechanisms to start in the body, through which catecholamines such as epinephrine, norepinephrine, and dopamine are released. Pain causes a similar response, increases heart rate, and causes tachycardia. With these mechanisms, vasoconstriction occurs and blood is shifted to the vital organs. Reduced blood flow to the organs also causes ischemia, anaerobic metabolism, and increased lactate production. Studies have shown that various injuries such as femoral fractures in brain-injured victims and shock can trigger inflammatory responses in the body and increase pre-inflammatory cytokines such as TNF-α, IL-1 and IL-6. Eventually systemic inflammatory response syndrome (SIRS) occurs. Shock is categorized in four main groups: hypovolemic, cardiogenic, distributive, and obstructive types. Many trauma patients can be classified into these main groups, but some patients exhibit another form of shock known as traumatic shock. Acute respiratory distress syndrome (ARDS), coagulopathy, and multiple organ dysfunction syndrome (MODS) can be consequences of severe shock, delayed treatment of shock, or badly managed shock.1
In trauma, the basis of treatment for hypovolemia is initially fluid therapy with an infusion of 1–2 L of isotonic serum, despite having knowledge of complications such as progressive coagulopathy or reduced oxygen delivery capacity. However, the severity of the damage and the inflammatory process as well as the response of the body to the fluid in the treatment of various traumas are different. In the present study, we investigated the effects of infusion of one to two liters of crystalloids according to the ninth edition of the Advanced Trauma Life Support (ATLS) in trauma patients with and without femoral bone fracture.

**Methods**

After obtaining approval from the Ethics Committee of the Shiraz University of Medical Sciences, patient’s records data were retrospectively studied from the Shahid Rajaee Hospital database, Shiraz Trauma Center on trauma patients aged 16–60 years with multiple traumas from years 2016 and 2017. Patients were divided into two groups: those with and those without femoral bone fractures along with other traumas. Patients transferred from other centers, those with known liver disease, and those with anti-platelet and anticoagulant drug consumption were excluded from the study.

Demographic data, vital signs, blood gas analyses, and coagulation profiles of patients were collected. Patients in both groups were matched in terms of having or not having a femoral bone fracture, abdominal damage and pelvic fractures; the only difference between them was in terms of having or not having a femoral bone fracture. Injury Severity Score (ISS) was used to measure these patients in both groups. ISS has been one of the scoring modalities between them.

After meeting the criteria for participation in the study, 681 trauma patients (605 men and 76 women) were included. Among them, 80 had femoral fracture, including 69 (86.3%) men and 11 (13.8%) women, and 601 did not have femoral fracture, presented as 536 men (89%) and 65 women (10.8%). The mean age of the patients was 31.6 years (Table 1).

**Vital signs**

After the initial treatment of fluids, the average blood pressure in the first 2 h decreased in the femoral fracture group (124.9 ± 125.2 mmHg) and increased in the non-femoral fracture group (120.1–101.7 mmHg) and increased in the non-femoral fracture group. The difference in mean blood pressure between the two groups after the initial treatment was significant ($p < 0.001$). In both groups, fluid therapy reduced the means of respiratory and heart rates in the first 2 h (Table 2).

**Blood gas**

The femoral fracture group had lower pH values in arterial blood gas before and after hydration than the non-fracture group. According to Table 3, the mean pH level and bicarbonate concentration were lower and the base deficit was greater in the fracture group than in the non-fracture group. It seems that hydration with more than 1 L worsened the blood gas variables after 2 h in all traumatized patients.

**Table 1**

Comparison of the patients in two groups in terms of sex, age, amount of fluid intake and level of consciousness.

| Group                  | Gender | Age (years) | GCS score | Fluid intake (mL) |
|------------------------|--------|-------------|-----------|-------------------|
|                        | Male   | Female      |           |                   |
| Femoral fracture       | 69 (86.3) | 11 (13.8) | 33 ± 14  | 12.9 ± 3.3        | 1586 ± 1174 |
| Non-femoral fracture   | 536 (89.2) | 65 (10.8)  | 31.4 ± 13 | 12.5 ± 3.5        | 1476 ± 909  |
| $p$ value              | 0.688  | 0.343       | 0.392     | 0.342             |

Data are expressed as mean ± standard deviation except for “Gender”, which are expressed as n (%). GCS: Glasgow coma scale.

**Table 2**

Vital signs before and 2 h after fluid therapy in two groups, mean ± standard deviation.

| Group                  | SBP (mmHg) | RR (breaths/min) | HR (beats/min) |
|------------------------|------------|------------------|----------------|
| Femoral fracture       |            |                  |                |
| At arrival             | 120 ± 20   | 19.5 ± 5.9       | 107 ± 21       |
| At 2 h                 | 101 ± 49   | 15.4 ± 7.3       | 97 ± 34        |
| $p$ value within group | 0.003      | <0.001           | 0.008          |
| Non-femoral fracture   |            |                  |                |
| At arrival             | 124 ± 20   | 19 ± 3.6         | 98 ± 20        |
| At 2 h                 | 125 ± 19   | 18.1 ± 4.5       | 93 ± 18        |
| $p$ value within group | 0.828      | 0.015            | <0.001         |
| $p$ value between groups | <0.001   | 0.001            | 0.001          |

SBP: systolic blood pressure; RR: respiratory rate; HR: heart rate.
Hemoglobin and coagulation profile

The mean of hemoglobin decreased in both groups after hydration; the decline was more evident in the femoral fracture group \( (p < 0.001) \). The range in the femoral fracture group was 12.4–10.5 g/L, and in the non-femoral fracture group was 13.8–12.2 g/L. Hydration also worsened the factors in the coagulation profile, with significant changes only in the PT and INR values before and after hydration. It should be noted, however, that the fracture group had higher PT, PTT, and INR levels. A significant reduction was seen in the mean value of fibrinogen after hydration in both groups, particularly in the non-femoral fracture group. Table 4 shows the values for hemoglobin and coagulation profiles.

Discussion

Fluid therapy is an important component of the management of trauma patients. Fluid therapy to patients was based on ATLS guideline (10th edition).10 The present study aimed to investigate the effects of fluid therapy on the vital signs, blood gas analyses, and coagulation profiles of patients with or without femoral bone fractures.

The results showed that patients with bone fracture experienced a decrease in heart and respiratory rates after crystalloid infusion. Moreover, these patients had more acidosis and greater disruption of their coagulation profiles. According to other studies, patients with long bone fractures secrete higher levels of mediators of patients with or without femoral bone fractures. The results of this study also support international and national guideline, which recommend the use of blood products in these patients. Although the complications of blood transfusion in conditions other than trauma are considered to be between 7 and 9,11,12 these values are acceptable in the acute phase of trauma.10,16 Under such circumstances, the use of heart rate, blood pressure (also shock index), and base deficit in making decisions about blood transfusions seems more rational.13 Therefore, in the acute phase of trauma, a number of 7–9 is not very suitable. If there is a clinical presentation of shock in the patient based on the heart rate, blood pressure, and base deficit values after one to two liters of crystalloids, blood and blood products should be given, as more crystalloid infusion reduces oxygen carrying capacity and increases coagulopathy.3

Using colloid resuscitation in femoral fracture group and severe trauma patients has a worsening prognosis. A study15 investigated the safety and efficacy of synthetic colloid resuscitation among severely trauma patients. This study suggests that synthetic colloid resuscitation provide no beneficial effects and will be harmful in patients who are severe trauma. The results of this study also support international and national guideline, which recommend using crystalloid in trauma patients.

Another study determined the effect of resuscitation deaths on colloid fluids compared with crystalloid resuscitation. Revitalization with colloids was associated with an increased risk of 4% mortality. This systematic review did not support using colloids to replace volume in critically ill patients.20

Based on the results of the present study, it is recommended that the treatment of multiple-trauma patients with femoral bone fractures be more concerned with the need for the infusion of vasopressors such as norepinephrine; if there is evidence of clinical shock, excessive crystalloid infusion (limited to 1 L) should be avoided, and the infusion of blood and blood products should be initiated as soon as possible. The amount of crystalloid between the two groups did not differ statistically. Giving 1 L of crystalloid is the minimum amount based on ATLS protocol. Some patients will receive 2 L because we do not have blood refrigerator room and and diuretic therapy, and some agree with liberal fluid therapy.2

Based on the results of the current study, unlike in patients without femoral fractures, patients with bone fractures experienced a drop in blood pressure, despite fluid therapy. Thus, the question of whether action other than fluid therapy is necessary in these patients is raised.

The European Guideline for Bleeding and Coagulopathy Management12 recommends the use of a vasopressor, such as norepinephrine, in conjunction with fluid therapy to maintain arterial pressure and tissue perfusion. It is also believed that norepinephrine causes visceral blood flow to vital organs.13 Despite the controversy over vasopressor injection in trauma patients,14 some studies have confirmed its use13,14 and have shown that it can improve cardiac output and increase inferior vena cava (IVC) flow.15

Another action may be the reduction of crystalloid infusion and the early use of blood products in these patients. Although the complications of blood transfusion in conditions other than trauma are considered to be between 7 and 9,11,12 these values are acceptable in the acute phase of trauma.10,16 Under such circumstances, the use of heart rate, blood pressure (also shock index), and base deficit in making decisions about blood transfusions seems more rational.13 Therefore, in the acute phase of trauma, a number of 7–9 is not very suitable. If there is a clinical presentation of shock in the patient based on the heart rate, blood pressure, and base deficit values after one to two liters of crystalloids, blood and blood products should be given, as more crystalloid infusion reduces oxygen carrying capacity and increases coagulopathy.3

Using colloid resuscitation in femoral fracture group and severe trauma patients has a worsening prognosis. A study15 investigated the safety and efficacy of synthetic colloid resuscitation among severely trauma patients. This study suggests that synthetic colloid resuscitation provide no beneficial effects and will be harmful in patients who are severe trauma. The results of this study also support international and national guideline, which recommend using crystalloid in trauma patients.

Another study determined the effect of resuscitation deaths on colloid fluids compared with crystalloid resuscitation. Revitalization with colloids was associated with an increased risk of 4% mortality. This systematic review did not support using colloids to replace volume in critically ill patients.20

Based on the results of the present study, it is recommended that the treatment of multiple-trauma patients with femoral bone fractures be more concerned with the need for the infusion of vasopressors such as norepinephrine; if there is evidence of clinical shock, excessive crystalloid infusion (limited to 1 L) should be avoided, and the infusion of blood and blood products should be initiated as soon as possible. The amount of crystalloid between the two groups did not differ statistically. Giving 1 L of crystalloid is the minimum amount based on ATLS protocol. Some patients will receive 2 L because we do not have blood refrigerator room and

| Table 4 | Coagulation and hemoglobin level before and after fluid resuscitation in two groups. |
|---------|----------------------------------|-------|-------|--------|--------|
|          | Group                             | Hb (g/L) | PTT (s) | PT (s) | INR    | Fibrinogen (g/L) |
| Femoral fracture | Before resuscitation | 12.4 ± 2.2 | 33.3 ± 8.9 | 13.8 ± 2.8 | 1.3 ± 0.5 | 229.3 ± 117.1 |
|          | After resuscitation              | 10.5 ± 2.5 | 36.7 ± 11.6 | 14.5 ± 3.4 | 1.9 ± 0.4 | 82.3 ± 133.2 |
|          | p value                          | <0.001   | 0.038   | 0.210  | 0.247  | <0.001           |
| Non-femoral fracture | Before resuscitation | 13.9 ± 3.6 | 33.2 ± 6  | 13.2 ± 1.8 | 1.1 ± 0.3 | 233.3 ± 93.6 |
|          | After resuscitation              | 12.2 ± 2.1 | 35.4 ± 9.3 | 13.2 ± 2.2 | 1.2 ± 0.2 | 59.5 ± 11.3 |
|          | p value                          | <0.001   | <0.001  | 0.864  | 0.436  | <0.001           |

Hb: hemoglobin, PTT: partial thromboplastin time, PT: prothrombin time, INR: international normalized ratio.
sometimes it is necessary to give another 1 L of crystalloid to receive blood from the blood bank.

**Funding**

There has been no significant financial support for this work that could have influenced its outcome.

**Ethical statement**

This study was approved by the Ethics Committee of the Shiraz University of Medical Sciences.

**Declaration of competing interest**

We wish to confirm that there are no known conflicts of interest associated with this publication.

**References**

1. Cottingham CA. Resuscitation of traumatic shock: a hemodynamic review. AACN Adv Crit Care. 2006;17:317–326. https://doi.org/10.1097/01256961-200607000-00011.
2. Anderson MW, Watson GA. Traumatic shock: the fifth shock. J Trauma Nurs. 2013;20:37–43. https://doi.org/10.1097/JTN.0b013e318286620a.
3. Sisak K, Dewar D, Butcher N, et al. The treatment of traumatic shock: recent advances and unresolved questions. Eur J Trauma Emerg Surg. 2011;37:567–575. https://doi.org/10.1007/s00068-011-0150-1.
4. Han J, Ren HQ, Zhao QB, et al. Comparison of 3% and 7.5% hypertonic saline in the treatment of traumatic shock. Shock. 2015;43:244–249. https://doi.org/10.1097/SHK.0000000000000203.
5. Kobbe P, Vodovotz Y, Kaczorowski DJ, et al. Patterns of cytokine release and evolution of remote organ dysfunction after bilateral femur fracture. Shock. 2008;30:43–47. https://doi.org/10.1097/SHK.0b013e31815d190b.
6. Probst C, Mirceyan MJ, Mommsen P, et al. Systemic inflammatory effects of traumatic brain injury, femur fracture, and shock: an experimental murine polytrauma model. Mediators Inflamm. 2012;2012. https://doi.org/10.1155/2012/136020.
7. Levy RM, Prince JM, Yang R, et al. Systemic inflammation and remote organ damage following bilateral femur fracture requires Toll-like receptor 4. Am J Physiol Regul Integr Comp Physiol. 2006;291:R970–R976. https://doi.org/10.1152/ajpregu.00793.2005.
8. Kobbe P, Vodovotz Y, Kaczorowski DJ, et al. The role of fracture-associated soft tissue injury in the induction of systemic inflammation and remote organ dysfunction after bilateral femur fracture. J Orthop Trauma. 2008;22:385–390. https://doi.org/10.1097/BOT.0b013e318175d886.
9. Martini WZ, Dubick MA, Blackbourne LH. Comparisons of lactated Ringer’s and Hextend resuscitation on hemodynamics and coagulation following femur injury and severe hemorrhage in pigs. J Trauma Acute Care Surg. 2013;74:732–739. https://doi.org/10.1097/TA.0b013e31827f156d.
10. 10th Edition of the Advanced Trauma Life Support® (ATLS®) Student Course Manual. Chicago (IL): American College of Surgeons; 2018.
11. Rossaint R, Bouillon B, Cerny V, et al. The European guideline on management of major bleeding and coagulopathy following trauma. Crit Care. 2016;20:100. https://doi.org/10.1186/s13054-016-1265-x. fourth ed.
12. Rochwerger B, Hyland’s M, Moller M, et al. CCCS-SSA Registry clinical practice guideline: vasopressors in early traumatic shock. Can J Anaesth. 2017;64:766–768. https://doi.org/10.1007/s12630-017-8379-2.
13. Giraud R, Siegemihler N, Arroyo D, et al. Impact of epinephrine and norepinephrine on two dynamic indices in a porcine hemorrhagic shock model. J Trauma Acute Care Surg. 2014;77:564–569. https://doi.org/10.1097/TA.0000000000000409.
14. Fangio P, Asehnoune K, Edouard A, et al. Early embolization and vasopressor administration for management of life-threatening hemorrhage from pelvic fracture. J Trauma. 2005;58:978–984. https://doi.org/10.1097/01.TA.0000163475.39881.26.
15. Polytrauma Guideline Update Group. Level 3 guideline on the treatment of patients with severe/multiple injuries: AWMF Register-Nr. 012/019. Eur J Trauma Emerg Surg. 2018;44:3–271. https://doi.org/10.1007/s00068-018-0922-y.
16. Figueiredo S, Taconet C, Harrois A, et al. How useful are hemoglobin concentration and its variations to predict significant hemorrhage in the early phase of trauma? A multicentric cohort study. Ann Intensive Care. 2018;8:76. https://doi.org/10.1186/s13613-018-0420-8.
17. Shahi V, Shahi V, Mower WR. Using serial hemoglobin levels to detect occult blood loss in the early evaluation of blunt trauma patients. J Emerg Med. 2018;55:307–312. https://doi.org/10.1016/j.jemermed.2018.06.017.
18. El-Menayar A, Goyal P, Tilley E, et al. The clinical utility of shock index to predict the need for blood transfusion and outcomes in trauma. J Surg Res. 2018;227:52–59. https://doi.org/10.1016/j.jss.2018.02.013.
19. Hilbert-Carius P, Schwarzkopf D, Reinhardt K, et al. Synthetic colloid resuscitation in severely injured patients: analysis of a nationwide trauma registry (Trauma Register DGU). Sci Rep. 2018;8:11567. https://doi.org/10.1038/s41598-018-30053-0.
20. Lu YQ, Cai XJ, Gu LH, et al. Experimental study of controlled fluid resuscitation in the treatment of severe and uncontrolled hemorrhagic shock. J Trauma Acute Care Surg. 2007;63:798–804. https://doi.org/10.1097/TA.0b013e31815202c9.