TITLE PAGE

Title: Effect of pre-hospital fluid administration on mortality of trauma patients

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Effect of pre-hospital fluid administration on mortality of trauma patients

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ABSTRACT

Background : It has been demonstrated that pre-hospital intravascular (IV) fluid administration worsened trauma patients’ outcome especially when bleeding has not been controlled in penetrating torso injury. However, there are still some controversies in terms of different type of injury and organ involvement.

Objective : To determine the practice of Thai Emergency Medical Service (EMS) Advanced Life Support (ALS) rescue team in the aspect of pre-hospital fluid administration in trauma patients from road traffic accident (RTA) and its influence on patients’ mortality.

Methods : A retrospective cohort study was performed based on the nationally representative EMS registry dataset. We compared the in-hospital mortality between critically injured patients from RTA who received and did not received pre-hospital fluid administration. Additionally, multiple logistic regression analysis was performed in adjustment of age, gender, time to hospital, hemodynamic status, mechanism of injury and organ involvement of the patients.

Results : A total of 51,661 patients with critical injury from RTA were rescued by Thai EMS (ALS) team. 40,039 (77.5%) of them received pre-hospital fluid resuscitation. Patients having pre-hospital IV fluid before admitting to the hospital had higher in-hospital mortality rate than those without IV fluid administration (10.5% versus 4.4%; p<0.001). Multivariable analysis demonstrated the adjusted OR of 1.07 with 95% CI of 0.92, 1.24; p = 0.395 after adjusting for age, gender, time to hospital, hemodynamic status, mechanism of injury and organ involvement of the patients.

Conclusions : We could not demonstrate that pre-hospital IV fluid resuscitation increased in-hospital mortality in severe RTA trauma patients, however, there might be a potentially detrimental effect. Therefore, the routine practice of pre-hospital fluid administration for critically injured patients may not be encouraged. The EMS providers should give priority to hemorrhagic control and transportation to the hospital for definitive intervention.

Keywords : pre-hospital fluid, trauma mortality, road traffic accident, traumatic brain injury

INTRODUCTION

 Trauma is the global leading cause of death and disability, of which Road Traffic Accident (RTA) is the major one. In 2012, a total number of deaths from RTA in Thailand was 7,784 (11.2 deaths/100,000/year)([1](#_ENREF_1)). The establishment of the Emergency Medical Service (EMS) system, specifically Advanced Life Support (ALS) care team has aimed to improve the survival of these patients with pre-hospital management. One of the intervention commenced by ALS providers is the intravenous (IV) fluid resuscitation([2](#_ENREF_2)), which was once believed to help replace blood loss and maintain perfusion to vital organs, although there is not enough evidence to support this practice([3-5](#_ENREF_3)).

On the contrary, some authors even have demonstrated that pre-hospital fluid administration might be harmful to trauma patients([6-8](#_ENREF_6)), especially in uncontrolled hemorrhage from penetrating torso injury.([9](#_ENREF_9)) However, for blunt injury and patients with concomitant traumatic brain injury (TBI), the concept of delayed fluid resuscitation and permissive hypotension is still controversy.([10](#_ENREF_10)) The limitation of studies in blunt trauma patients and the little data on human subject with concurrent TBI leave an uncertainty about the effect of pre-hospital fluid on these groups of patients.([11](#_ENREF_11), [12](#_ENREF_12))

From the above evidence, we performed the first investigation of the nationally representative EMS (ALS) dataset with the hypothesis that patients with critical injury from RTA who received pre-hospital IV fluid had higher mortality than those did not receive fluid.

METHODS

*Study design*

This was the retrospective cohort study using 2 years (2011-2012) record of EMS registry data from all over the country, except Bangkok, under the National Institute for Emergency Medicine (NIEM) organization, Ministry of Public Health. There were totally 4 patient record forms: Dispatch, First Response (FR), Basic Life Support (BLS) and Advanced Life Support (ALS).

The process of EMS operation began when the dispatch center was notified for an event whether via 1669 hotline, radio communications or others. The command center would decide which level of EMS suit to victims. There were 3 levels of pre-hospital medical services: First Response (FR), Basic Life Support (BLS) and Advanced Life Support (ALS). Therefore, every patient was registered with one dispatch form and the other one among FR, BLS and ALS form. Patients were classified into 4 color-code categories depending on their severity, using the triage system: Red for critical patients with life-threatening condition who require an immediate medical intervention to support respiratory, cardiovascular and nervous system; Yellow for patients with urgent conditions requiring medical care; Green for non-urgent patients and White for minor injured patients. The code was recorded as Incident Dispatch Code (IDC) relevant to the severity notified at dispatch center and then was confirmed by EMS providers at scene as the Response Code (RC). We used RC code to classify patients.

The study was conduct in June-July 2013 at Department of Biostatistics and Demography, Faulty of Public Health, Khon Kaen University, Khon Kaen, Thailand.

*Inclusion criteria*

We used the data extracted from Dispatch and ALS activated form, which were filled by members of the team. The ALS form was also completed by a physician or nurse at an emergency department when the team arrived at the hospital. We included patients with critical injury (Red code) from road traffic accidents who received and did not received pre-hospital IV fluid administration documented in ALS form.

*Primary outcome*

The primary outcome variable was in-hospital mortality, which was documented by the end of the month in order to submit to the provincial EMS center within the 5th day of the next month.

*Independent variables*

The primary independent variable was IV fluid administration in the pre-hospital period documented by ALS providers. Other independent variables were age, gender, time from scene to hospital, hemodynamic status, mechanism of injury, torso injury with and without TBI and severity of TBI.

*Statistical analysis*

Owing to using the large national dataset to conduct the study, we did not calculate the sample size. However, the estimate sample size of 51,384 allowed us to estimate the odd ratios of in-hospital death with a precision of about ±5%.

Demographic characteristics of the patients were described with frequency and percentage for categorical data and mean and standard deviation for continuous data. Odd ratios (ORs) and 95% confidence intervals (95% CI) were determined using bivariate analysis for independent variables including pre-hospital IV, age, gender, time from scene to hospital (minute), hemodynamic status (hypotension was defined if systolic blood pressure was less than 90 mmHg), mechanism of injury (penetrating and non-penetrating injury), torso injury with and without concomitant TBI and its severity (defined as mild if Glasgow Coma Score [GCS] ≥13, moderate if GCS 9-12 and severe if GCS ≤8).

Because of several known risk factors for death, we performed multivariable logistic regression analysis adjusting for baseline variables that were considered biologically relevant to in-hospital mortality or that showed a bivariate relationship with the primary outcome. We did not adjust for cardiopulmonary resuscitation and excluded patients who died on arrival.

All analyses were performed using Stata version 12.0 (StataCorp, College Station, TX). A p-value of less than 0.05 was considered statistical significant.

RESULTS

A total of 2,683,821 calls were received by the EMS dispatch center during two year-period between 2011 and 2012. Among these, ALS teams were assigned to fields for 458,273 events notified but only 437,770 events found. RTA was the most common incidence, of which 51,661 of patients were critically injured and were classified as Red code from the triage system. The total number of sample was 51,384 patients after excluding some patients without IV status documented; 77.5% of them received pre-hospital IV fluid (Fig.1).

Dispatch center was notified

n=2,683,821

Activate ALS team

n=458,273

Non road traffic accident (n=320,939)

* Fatigue (n=53,035)
* Respiratory distress (n=51,894)
* Loss of consciousness (n=37,861)
* Seizure (n=27,710)
* Diabetes mellitus (n=25,478)
* Abdominal pain (n=20,100)
* Falling accidents (n=19,901)
* Other (n=84,972)

Event seen

n=437,770

Road traffic accidents

n=92,955

Non critical patients (n=41,341)

* Urgent (Yellow code) (n=38,311)
* Non urgent (Green code) (n=2,914)
* Minor injury (White code) (n=69)

Critical patients (Red code)

n=51,661

Status IV missing (n=277)

Sample participants

n=51,384

Intravenous fluid

n=40,039

No intravenous fluid

n=11,345

Fig. 1 The inclusion flow chart

*Demographic characteristics*

 The predominant patients were adult with mean age about 35 years. Patients in the study were mainly male (75.6%) and most of them were hemodynamic stable and had non-penetrating injury. Most of the patients with concomitant TBI had severe TBI. Patients receiving IV fluid needed more intubation and cardiopulmonary resuscitation (CPR) than those who did not receive IV. They also had higher in-hospital mortality rate compared to those who did not receive IV fluid (10.5% versus 4.4%).

Table 1 Demographic characteristics presented as percentage unless specified otherwise

|  |  |  |  |
| --- | --- | --- | --- |
| Characteristics | Total (n=52,740) | IV fluid (n=41,405) | No IV fluid (n=11,335) |
| Age (years) | 33,934 |  |  |
| <18 year | 5,627 | 16.1 | 18.1 |
| 19-65 year | 26,741 | 79.3 | 77.2 |
| >65 year | 1,566 | 4.6 | 4.7 |
| Mean (sd) |  | 35.1 (16.2) | 34.8 (16.5) |
| Gender  | 29,253 |  |  |
| Male  | 22,116 | 77.4 | 70.5 |
| Female  | 7,137 | 22.6 | 29.5 |
| Time to hospital (min) [mean (sd)] | 45,925 | 8.3 (10.2) | 7.5 (8.3) |
| Hemodynamic status | 51,384 |  |  |
| No hypotension (SBP ≥ 90mmHg) | 48,949 | 5.4 | 2.3 |
| Hypotension (SBP< 90mmHg) | 2,435 | 94.6 | 97.7 |
| Mechanism of injury | 51,384 |  |  |
| Penetrating injury | 121 | 0.3 | 0.1 |
| Non-penetrating injury | 51,263 | 99.7 | 99.9 |
| Organ involvement | 51,348 |  |  |
| Torso injury | 31,011 | 60.1 | 61.2 |
| Torso with TBI | 20,373 | 39.9 | 38.8 |
| Severity of TBI | 16,607 |  |  |
| Mild  | 500 | 2.7 | 5.3 |
| Moderate  | 3,384 | 19.8 | 24.4 |
| Severe  | 12,723 | 77.5 | 70.3 |
| Intubation | 1,951 | 4.8 | 0.4 |
| CPR | 3,570 | 8.1 | 3.1 |
| Death on arrival  | 283 | 0.6 | 0.4 |
| Inhospital death  | 4,712 | 10.5 | 4.4 |

*Factors associated with in-hospital mortality in critically injured patients from RTA*

 On bivariate analysis, the odds ratio of in-hospital death associated with pre-hospital IV fluid administration was 2.56 (95% CI 2.32-2.82; p<0.001) (Table 2). Other factors that were associated with in-hospital death including male gender, hypotension, penetrating injury and concomitant TBI. Additionally, patients who had concurrent severe TBI were significantly at risk of death than the other classes of severity (OR 10.40; 95%CI 6.57-16.49; p<0.001).

Table 2 Odd ratio (OR) representing relationship between each factors on in-hospital mortality: Bivariate analysis using logistic regression

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | number | % | Crude OR | 95%CI | P value |
| Pre-hospital fluid | 4,214 | 89.4 | 2.56 | 2.32-2.82 | <0.001 |
| Age  |  |  | 1.01 | 1.007-1.012 | <0.001 |
| Male gender | 2,415 | 78.3 | 1.19 | 1.08-1.30 | <0.001 |
| Time to hospital |  |  | 0.99 | 0.988-0.996 | 0.001 |
| Hypotension  | 4,574 | 97.1 | 1.69 | 1.53-1.88 | <0.001 |
| Penetrating injury | 26 | 0.6 | 2.72 | 1.76-4.20 | <0.001 |
| With TBI | 3,001 | 63.7 | 2.96 | 2.78-3.15 | <0.001 |
| Severity of TBI |  |  |  |  | <0.001 |
| Mild  | 19 | 0.5 | Reference |  |  |
| Moderate  | 157 | 4.0 | 1.23 | 0.76-2.00 |  |
| Severe  | 3,707 | 95.5 | 10.40 | 6.57-16.49 |  |

 After adjustment using multivariable logistic regression analysis, patients who had pre-hospital IV fluid administration did not have statistically significant higher in-hospital mortality than those without IV fluid (Adjusted OR 1.07; 95 % CI 0.92-1.24; p=0.395) as shown in Table 3.

Table 3 Odd ratio (OR) representing relationship between pre-hospital intravenous fluid administration on in-hospital mortality adjusted for effects of various factors: Multivariable analysis using logistic regression

|  |  |  |  |
| --- | --- | --- | --- |
|  | Adjusted OR | 95%CI | P value |
| Pre-hospital fluid | 1.07 | 0.92-1.24 | 0.395 |
| Age | 1.01 | 1.006-1.011 | <0.001 |
| Male gender | 0.82 | 0.74-0.92 | 0.001 |
| Time to hospital | 1.00 | 0.995-1.007 | 0.547 |
| Hypotension | 2.50 | 1.94-3.23 | <0.001 |
| Penetrating injury | 1.69 | 0.85-3.35 | 0.133 |
| With TBI | 1.03 | 0.94-1.14 | 0.557 |
| Severity of TBI |  |  |  |
| Mild  | Reference |  | <0.001 |
| Moderate  | 1.76 | 0.84-3.66 |  |
| Severe  | 15.67 | 7.74-31.71 |  |

DISCUSSION

The result of the study did not show the significant increased in-hospital mortality in critically injured patients from RTA who received pre-hospital IV fluid. However, with the large sample size of the study, when we considered the magnitude of effect or the 95% CI, pre-hospital fluid administration might be potentially harmful. The patients receiving fluid during pre-hospital period were 24% more at risk of death in hospital than who did not receive fluid.

The theoretical principle explaining the harm of pre-hospital fluid resuscitation in trauma patients is not only increase scene time and delay of transport to hospital, but also that fluid given increases blood pressure, dislodges clots already formed, reverses vasoconstriction and causes dilutional coagulopathy. As a result, it promotes rebleeding and causes further cellular hypoperfusion. A computer model of patients with major hemorrhage showed that pre-hospital fluids would only be beneficial if a rate of bleeding was between 25 and 100 ml/min, a fluid infusion rate at least equal to the bleeding rate and a pre-hospital time exceeded 30 minutes.([3](#_ENREF_3)) Therefore, the limited volume infused during transportation, particularly in urban environment with pre-hospital time certainly less than 30 minutes would not be advantageous.

According to The National Institute for Health and Clinical Excellence (NICE), pre-hospital initiation of fluid replacement therapy in adult and older children trauma patients is recommended only when absence of a radial pulse and IV fluid should be titrated in boluses of no more than 250 ml crystalloid solutions until a radial pulse is palpable. The IV fluid should be given en route to avoid unnecessary delays in the transport to definitive care and only two attempts should be made by ALS trained healthcare professionals.([13](#_ENREF_13), [14](#_ENREF_14))

The cannulation procedure is time-consuming and requires skillful personnel, particularly during shock, this intervention is much more difficult. Moreover, to provide excellent medical treatment at a road crash needs specific training and experience.([15](#_ENREF_15)) Normally, an ALS unit is a hospital-based ambulance with western standard features and the team consists of either a physician or a registered nurse, who are special trained in emergency rescue and trauma care, and two other personnel. However, in the shortage of trained ALS providers, especially among community hospitals in Thailand, which sometimes have only one physician and a small number of nurses on duty, the rapid transport of patients to the hospital may be the higher priority.([4](#_ENREF_4))

The concept of “delayed resuscitation” (withholding fluid therapy until operative intervention achieves definitive hemostasis) and “hypotensive resuscitation or permissive hypotension” (some amount of fluid given to the lower than normotensive endpoint)([16](#_ENREF_16)) has been accepted for practice in trauma patients particularly in penetrating injury and intraoperative hemorrhagic resuscitation.([9](#_ENREF_9)) However, because of the heterogeneity of trauma patients, it is still questionable about the applicability and safety of this approach in blunt trauma and patients with concurrent TBI.([10-12](#_ENREF_10), [16](#_ENREF_16), [17](#_ENREF_17)) The primary concern in pre-hospital care is to maintain cerebral perfusion by preventing episodes of hypotension and hypoxia.([18](#_ENREF_18)) The initial fluid resuscitation might play role for correcting hypovolemia and hypotension. In our study, there were many patients suffering with severe TBI, which may be the consequence from motorcycle accidents without helmet wearing in rural region of the country. This factor showed strong association with mortality of RTA trauma patients.

*Limitations*

The retrospective study has some limitations regarding the dataset used. Some information was not shown in the record, for example, the amount of fluid infused and unclear mechanism of injury. The mechanism of injury defined in the study was based on whether patients had penetrating injury or not because blunt injury was not clearly documented in data record form.

The documentation regarding results of treatment while patients were in the hospital had to be completed by the end of the month and then submitted to the provincial EMS center within the 5th day of the next month. Therefore, there might be some patients died beyond this time frame but were recorded as alive. Furthermore, the in-hospital mortality depends on several factors while patients admitting in the hospital and the lack of detailed information about this may confound our results.

CONCLUSIONS

From the national EMS dataset, we could not demonstrate that pre-hospital IV fluid resuscitation increased in-hospital mortality in severe RTA trauma patients. However, it signaled us that the routine practice of ALS rescue team concerning pre-hospital fluid administration for critically injured patients may not be beneficial, on the other hand, it might be potential to have detrimental effect. Therefore, this routine practice may not be encouraged and the EMS providers should give priority to hemorrhagic control and transportation to the hospital for definitive intervention.

RECOMMENDATIONS

The future studies evaluating the effect of pre-hospital IV fluid therapy should be undertaken with the consideration of specific patient groups, such as in young children and infants, and patients with blunt injuries. Moreover, we hope this study encourage the NIEM to revise the national data record process in order to have more informative data available for future analysis.

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