American Journal of Emergency Medicine (2011) **29**, 738–742

The American Journal of Emergency Medicine

www.elsevier.com/locate/ajem

Original Contribution

Prophylactic fluid therapy in crushed victims of Bam earthquake☆

Najafi Iraj[a,b], Safari Saeed[a,b,c,*], Hosseini Mostafa[d], Sanadgol Houshang[e], Sharifi Ali[b], Rashid Farokhi Farin[f], Seirafian Shiva[g], Mooraki Ahmad[h], Hamidreza Samimagham[i], Vahid Pourfarziani[j], Atabak Shahnaz[k], Osareh Shahrzad[l], Boroumand Behrooz[h]

[a]*Urology Research Center, Tehran, Iran*
[b]*Department of Nephrology, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran*
[c]*Department of Emergency medicine, Imam Hossein Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran*
[d]*Department of Epidemiology and Biostatistics, Tehran University of Medical Sciences, Tehran, Iran*
[e]*Department of Nephrology, Zahedan University of Medical Sciences, Zahedan, Iran*
[f]*Department of Nephrology, Kerman University of Medical Sciences, Kerman, Iran*
[g]*Department of Nephrology, Isfahan University of Medical Sciences, Isfahan, Iran*
[h]*Department of Nephrology, Rasool Akram Hospital, Iran University of Medical Sciences, Tehran, Iran*
[i]*Department of Nephrology, Bandarabbas University of Medical Sciences, Bandarabbas, Iran*
[j]*Department of Nephrology, Milad hospital, Tehran, Iran*
[k]*Department of Nephrology, Imam Hossein Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran*
[l]*Department of Nephrology, Hasheminejad Hospital, Iran University of Medical Sciences, Tehran, Iran*

Received 25 October 2009; revised 16 January 2010; accepted 17 February 2010

Abstract

Background: Acute kidney injury (AKI) is a severe and preventable problem of crushed earthquake victims. Early hydration therapy started before fully removing earthquake rubbles has been claimed to play a decisive role in AKI prevention, which saves the necessity of later dialysis. However, the extent, quality, and appropriateness of its know-how are controversial.

Methods: Processing clinical and paraclinical data gathered from Bam earthquake victims older than 15 years, we tried to determine correlations between the time of being under the rubbles (TUR), the level of serum creatine phosphokinase (CPK), the delayed onset of fluid therapy (DFT), and finally the volume of intravenous fluid received per day (VFR) with the formation of AKI and the need for dialysis.

Results: There is a direct and significant relation between the intensity of the trauma (TUR and CPK) and DFT with the occurrence of AKI and need for dialysis ($P < .001$). However, as the VFR increases, the occurrence of AKI and the need for dialysis significantly decrease ($P = .005$). Based on multivariate analysis, the occurrence of AKI and the need for dialysis are primarily affected by CPK, TUR, and VFR; and DFT has been dropped out. The analysis showed the preventive role of VFR more than 6 L in severe rhabdomyolysis patients and of at least 3 L in moderate ones in development of AKI and dialysis.

☆ The research was supported by a grant (3968) from the urology research center of Sina Hospital, Tehran University of Medical Sciences.

* Corresponding author. Resident of Emergency medicine, Department of Emergency medicine, Imam Hossein Hospital, Shahid Beheshti University of Medical Sciences, Tehran 1617763141, Iran. Tel.: +98 2177558081; fax: +98 2177556069.
E-mail address: saeed_safari_2004@yahoo.com (S. Saeed).

doi:10.1016/j.ajem.2010.02.018

Conclusions: In the severely rhabdomyolized patients (CPK ≥15 000), higher volumes of prophylactic fluid (VFR >6 L) are required, whereas in less-traumatized patients, lower volumes (3-6 L) would be effective.

1. Introduction

Acute kidney injury (AKI) is an important and also preventable problem in earthquake crushed victims [1,2]. The pathology may be summarized as constriction of renal arteries due to dehydration and precipitation of nephrotoxic substances resulting from cell destructions in renal tubules [1,3]. The AKI risk factors may be grouped into 3 major categories: severity of muscle trauma, time to treatment, and the quantity/quality of prophylactic fluid therapy. Early hydration therapy started before fully removing earthquake rubbles has been claimed to play a decisive role in AKI prevention, which saves the necessity of later dialysis [3,4,5]. However, the quantity, quality, and appropriateness of its know-how are controversial. Different studies have suggested, for instance, a range of 3 to 12 L in 24 hours [1-7]. Our previous study [6,8] and also that of Ensari et al [9] suggest that even delayed hydration therapy may prevent AKI and need for dialysis. Existing hydration protocols have proven ineffective in coping with the crisis and the large number of victims under the catastrophic conditions [10,11]. In our preceding articles, we referred to factors affecting the formation of AKI and presented the rule of thumb and AKI score for early detection of patients at high risk for AKI during disasters [12]. This article is mainly concerned with the role of effective factors, especially in-hospital hydration therapy, in both occurrence of AKI and the need for dialysis.

2. Subjects and methods

On the first day of the Bam earthquake, the Iranian Society of Nephrology, in collaboration with the International Society of Nephrology, developed a questionnaire and sent it to all hospitals expected to treat crush patients (15 centers in 7 cities: Kerman, Tehran, Esfahan, Zahedan, Bandarabbas, Bushehr, and Shiraz). The questionnaires were designed to register the basic demographic data and the key clinical and biological parameters of all rescued victims arriving in those hospitals. In each hospital, a local key person was identified to ensure the completeness and accuracy of the responses to the questionnaires; and the first author had regular contact by e-mail and telephone with all these key persons to cross-check accuracy of the data.

In this study, *AKI* was defined as at least 2 reported serum creatinine values of at least 1.6 mg/dL (≥141 μmol/L), *moderate rhabdomyolysis* as patients with 1000 ≤ creatine phosphokinase (CPK) < 15 000 IU/L (mean, 7000), and *severe ones* as CPK of at least 15 000. All rhabdomyolized patients (aged ≥15 years) who were hospitalized and had a documented renal status (AKI and dialysis) and CPK level greater than 1000 IU/L were included in the analyses. In addition, patients with a history of chronic renal failure and AKI due to other causes except crush were excluded. The registered factors were serum creatinine, blood urea nitrogen, CPK, time of being under the rubble (TUR), delayed onset of the fluid therapy (DFT), and the volume of intravenous fluid received per day (VFR). Because parameters were collected according to local practices, not all parameters were available in all patients.

We tried to determine correlations between (1) TUR (as a clinical intensity index of the trauma); (2) CPK (as a paraclinical intensity index of the trauma); (3) DFT; and finally, (4) VFR with the occurrence of AKI and the need for dialysis. The oral intake was not considered in this study because of lack of precise data.

2.1. Statistical analysis

After preliminary description of the data, Student *t* test was used to compare means of the parameters between the AKI and other rhabdomyolysis patients. χ^2 test was used to investigate the relationship between 4 parameters (CPK, TUR, VFR, and DFT) and the occurrence of the AKI and the need for dialysis. To study the effect of multiple risk factors, multivariate logistic regression analysis was carried out; and the adjusted odds ratios (ORs) and the corresponding 95% confidence intervals (CIs) were estimated. P value < .05 was taken as statistically significant. All analyses were performed using STATA (8.0; StataCorp LP, College Station, TX).

3. Results

Out of an admission of 2962 victims with minimum relevant data, 638 (21.5%) patients fulfilled the inclusion criteria, 41.9% of whom were female. There were 134 (21%) of 638 people with AKI, 82.1% (110/134) of whom needed dialysis.

Those with AKI had on average DFT of 2.8 ± 2.6 day, with significant difference with other rhabdomyolysis (1.2 ± 1.3, P < .001). The average TUR was 6.3 ± 3.1 hours as compared with 2.4 ± 1.6 for others (P < .001). The muscle enzyme levels of CPK, lactate dehydrogenase, and serum glutamic-oxaloacetic transaminase in those with AKI were 26706 ± 29146, 5050 ± 3658, and 584 ± 427 IU/L, respectively, compared with 4084 ± 6004, 941 ± 838, and 134 ± 230 in other rhabdomyolized patients (P < .001 for 3

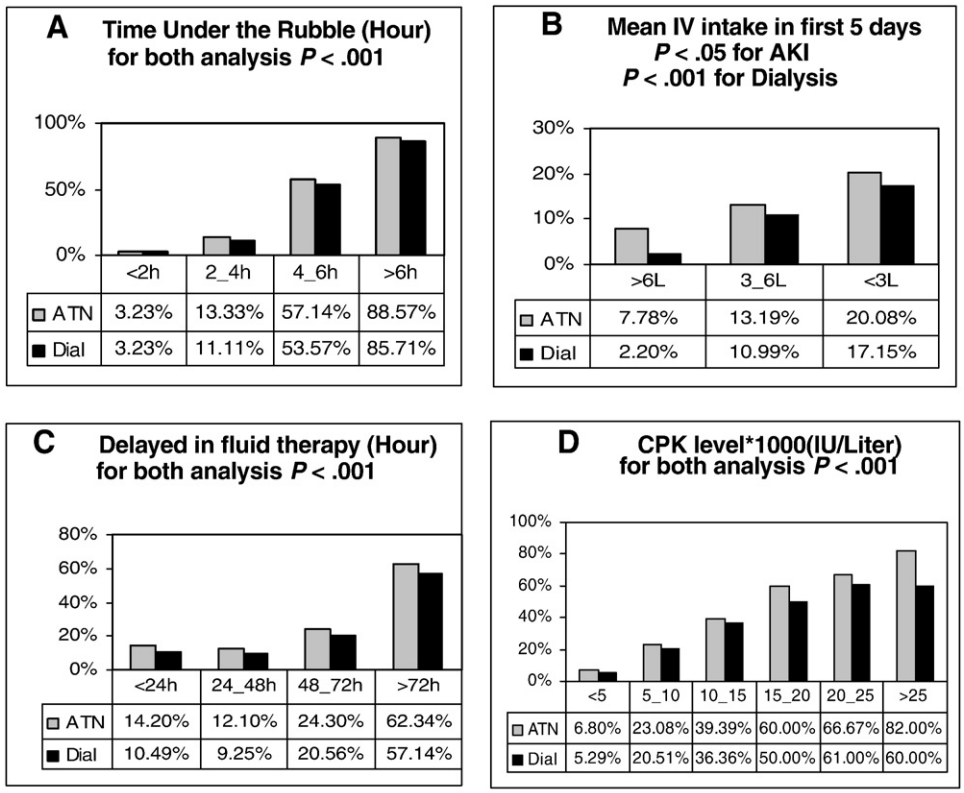

Fig. 1 Relations between the time under the rubbles, delayed fluid therapy, CPK level, and the amount of intravenously received liquid with the percentage of the admission with AKI and the need for dialysis (univariate analysis).

comparisons). The AKI patients received on average 2.8 ± 2.5 L during the first 5 days of admission, which was 1.2 (95% CI, 0.6-1.9) less than other rhabdomyolysis ($P < .001$).

3.1. Univariate analysis

The relationship between the TUR, DFT, CPK, and VFR with the occurrence of AKI and the need for dialysis are presented in different parts of Fig. 1. As Fig. 1A, C, and D show, there are positive and significant associations between the intensity of the trauma (TUR and CPK) and DFT with the occurrence of AKI and need for dialysis ($P < .001$ for all analyses). In contrast, as the mean of VFR in the first 5 days increases from less than 3 L to more than 6 L, the need for dialysis and the occurrence of AKI significantly decrease ($P < .001$ and $P < .05$, Fig. 1B). The mean CPK levels of patients in these 3 groups were not significantly different ($P = .80$). The mean and maximum levels of CPK for VFR less than 3 L were 7637.9 and 37 650 IU/L; for 3 < VFR < 6, these were 8647.0 and 75 000 IU/L; and for VFR >6, these were 7735.6 and 140 000 IU/L, respectively.

In addition, further analyses for different VFR cutoffs and its association with AKI and dialysis were carried out; and the results are shown in Fig. 2. As shown in this figure, 39.2% of rhabdomyolized patients with VFR less than or equal to 1 L developed AKI. This percentage declines to 18.2% for those with VFR less than or equal to 5 L and does not diminish appreciably even for VFR less than or equal to 9 L, with the most striking decrement seen in VFR of 1 to 3 L. In the other words, the increase of VFR from less than 1 L to less than or equal to 3 L causes 19.2% absolute and 48.9% (ie, [39.2% − 20%]/39.2%) relative reduction of AKI occurrence. Similar pattern was observed for those who needed dialysis. The mean CPK levels for the corresponding VFR cutoffs were not significantly different ($P = .90$).

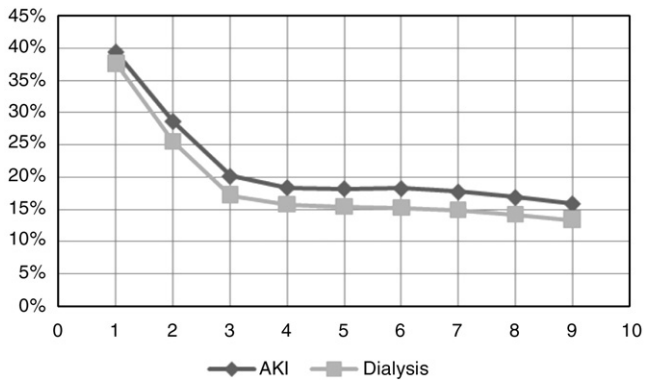

Fig. 2 Occurrence of AKI and dialysis in patients with different mean intravenous intake per 24 hours at first 5 days in patients with CPK greater than 1000 IU/L.

Table 1 Multivariate logistic regression analysis of TUR, CPK, VFR, and DFT [a] with AKI and dialysis

Variable		AKI		Dialysis	
		OR (95% CI)	*P* value	OR (95% CI)	*P* value
CPK (IU/L)	≥ 15 000 [b]	23.7 (3.6-156.6)	.001	18.0 (1.9-171.2)	.012
TUR (h)	>5 [c]	15.5 (3.0-80.6)	.001	14.1 (2.5-78.6)	.003
VFR (L)	>6 [d]	0.076 (0.01-0.50)	.007	0.04 (0.004-0.36)	.004

[a] DFT lost its significance in the multivariate analysis for both AKI and dialysis.
[b] Reference group = CPK less than 15 000 IU/L.
[c] Reference group = TUR less than or equal to 5 hours.
[d] Reference group = Mean intake less than 3 L.

3.2. Multivariate analysis

The results of multivariate analysis are summarized in Table 1. For both AKI and dialysis, important risk factors at a *P* value ≤ .05 were considered in a multivariate logistic regression analysis, separately. For AKI, analysis showed that CPK of at least 15 000 (OR, 23.7; 95% CI, 3.6-156.6), TUR longer than 5 hours (OR, 15.5; 95% CI, 3.0-80.6), and VFR of at least 6 L (OR, 0.076; 95% CI, 0.01-.0.50) remained as significant independent risk factors.

For dialysis, after adjustment for the other exposure variables, CPK of at least 15 000 (OR, 18.0; 95% CI, 1.9-171.2), TUR longer than 5 hours (OR, 14.1; 95% CI, 2.5-78.6), and VFR of at least 6 L (OR, 0.04; 95% CI, 0.004-0.36) were the significant independent risk factors.

Delayed onset of the fluid therapy was dropped out of the multivariate analysis for both AKI and dialysis.

4. Discussion

During the Marmara earthquake in 1999, great Hanshin in 1995, and Armenia in 1988, more than 1000 cases of crush-related AKIs were reported [13,14,15]. The statistics concerning crush syndromes as a consequence of such catastrophes as earthquakes, floods, storms, and even wars demonstrate the dire need for crisis management and special protocols [16].

Unfortunately, most of the existing protocols regarding fluid therapy do not meet the demands of the real situation of a disaster's aftermath. In fact, the present protocols of crush syndrome are more appropriate to the limited number of victims after the destruction of a building block or complex rather than the extensive threats of the deadliest earthquakes. Our previous study showed the important role of biochemical factors in predicting AKI threats [12]. In this article, the role of effective factors, especially in-hospital hydration therapy, in the occurrence of AKI and the need for dialysis is presented.

The TUR is an important factor for both medical and logistical concerns [15,17,18]. The results of univariate analysis showed direct and additive effect of TUR on the occurrence of AKI and need for dialysis, which is quite the opposite of the finding in the Marmara earthquake; this is explained by differences in building architecture [13]. Our findings also demonstrated a direct relationship between the CPK and DFT with an increase in the occurrence of AKI and dialysis. However, regarding VFR, this relationship is indirect. The literature emphasizes the early fluid therapy even before the complete extrication of the victims, but there are controversies regarding the volume and quality of such therapies. In case of satisfactory urine output, Oda et al [7,14] recommend 6 L per day, whereas Better and Stein [3] advocate 12 to 14 L per day. In the Hanshin earthquake, some received up to 24 L per day [5]. Vanholder et al [19] suggest that when the physician cannot supervise fluid therapy; it would be safer to limit the fluid volume to less than 6 L per day to avoid the risk of volume overload.

Fig. 2 shows a declining pattern of AKI and dialysis occurrence with increasing VFR of less than or equal to 1 L to less than or equal to 9 L. The most striking decrement is seen in VFR of 1 to 3 L. In the other words, the increase of VFR from less than 1 L to less than or equal to 3 L results in 19.2% absolute and 48.9% (ie, [39.2% − 20%]/39.2%) relative reduction of AKI occurrence. Our finding regarding VFR is consistent with the recommendation of Vanholder et al of prophylactic hydration therapy. However, despite a 19.2% decline in the incidence of AKI due to escalating the fluid volume up to 3 L per day, volumes greater than 3 L have trivial encouraging effect. Whereas almost 60% of victims with CPK greater than 10 00 IU/L and VFR less than or equal to 1 L have not been affected with AKI and dialysis, at least 10% of patients with VFR even up to 9 L experienced these complications. It emphasizes the role of other factors apart from VFR in developing of this scenario.

Based on multivariate analysis (Table 1), the occurrence of AKI and the need for dialysis are primarily affected by CPK, TUR, and VFR; and DFT has lost its significance. Comparing different cut points, patients with CPK of at least 15 000 IU/L and TUR longer than 5 hours had the highest risk for developing aforementioned complications; and also, the VFR of more than 6 L showed its preventive role in these high risk patients. The VFR of less than 3 L has no significant effect here in lowering AKI and dialysis and lost its significance. As it

has been shown, the recommended VFR by univariate compared with multivariate analysis is different, which is explained by the different severity of patients included in each analysis. The most severe cases with mean CPK level of 15 000 were in the multivariate, whereas all victims with different spectrum of muscle trauma and CPK levels were in the univariate analysis. This emphasizes the need for justification of fluid therapy in earthquake-crushed victims based on trauma severity.

4.1. Limitations

The chaotic situation in the aftermath of an earthquake, missing data, multicenter management with different hydration protocols, lack of evidence regarding the type of different solutions that were used, different laboratory kits, and weakness of TUR as a prognostic factor that is influenced by the type and structures of buildings are among the most important limitations that have affected our study.

5. Conclusions

Regarding prophylactic hydration therapy for earthquake victims, in the severely rhabdomyolized patients (CPK $\geq$15 000), higher volumes of prophylactic fluid (VFR >6 L) are required, whereas in less-traumatized patients, even lower volumes (3-6 L) would be effective.

Acknowledgments

The contributions of Amini M, Hosseini F, Mehrani M, Babaee Rasool, Ghafoorian M, Maleki Z, and Dr Saboori Kashani at varying phases of the project are acknowledged and greatly appreciated.

References

[1] Ukai T. The great Hanshin-Awaji earthquake and the problems with emergency medical care. Ren Fail 1997;19(5):633-45.

[2] Vanholder R, Sever MS, Erek E, et al. Acute renal failure related to crush syndrome: towards an era of seismo-nephrology? Nephrol Dial Transplant 2000;15:517-21.

[3] Better OS, Stein JH. Early management of shock and prophylaxis of acute renal failure in traumatic rhabdomyolysis. N Engl J Med 1990; 322(12):825-9.

[4] Gunal AI, Celiker H, Dogukan A. Early and vigorous fluid resuscitation prevents acute renal failure in the crush victims of catastrophic earthquakes. J Am Soc Nephrol 2004;15(7):1862-7.

[5] Shimazu T, Yoshioka T, Nakata Y, et al. Fluid resuscitation and systemic complications in crush syndrome: 14 Hanshin-Awaji earthquake patients. J Trauma 1997;42(4):641-6.

[6] Atef MR, Nadjafi I, Rastegar A, et al. Acute renal failure in earthquake victims in Iran: epidemiology and management. Q J Med 1994;87(1): 35-40.

[7] Oda J, Tanaka H, Yoshioka T, et al. Analysis of 372 patients with crush syndrome caused by the Hanshin-Awaji earthquake. J Trauma 1997;42:470-6.

[8] Najafi I, Atef MR, Broumand B, Rastegar A. Suggested guidelines for treatment of acute renal failure in earthquake victims. Renal Failure 1997;19(5):655-64.

[9] Ensari C, Tüfekçioglu O, Ayli D, et al. Response to delayed fluid therapy in crush syndrome. Nephron 2002;92(4):941-3.

[10] Better OS. The crush syndrome revisited (1940-1990). Nephron 1990; 55:97-103.

[11] Tolouian R, Wild D, Lashkari MH, Najafi I. Oral alkalinizing solution as a potential prophylaxis against myoglobinuric acute renal failure: preliminary data from healthy volunteers. Nephrol Dial Transplant 2005;20:1228-31.

[12] Najafi I, van Biesen W, Sharifi A, et al. Early detection of patients at high risk for acute kidney injury during disasters: developing of a scoring system based on the Bam earthquake experience. J Nephrol 21: 776–782.

[13] Sever MS, Erek E, Vanholder R, Akoglu E, Yavuz M, Ergin H, et al. Marmara Earthquake Study Group. The Marmara earthquake: epidemiological analysis of the victims with nephrological problems. Kidney Int 2001;60(3):1114-23.

[14] Oda Y, Shindoh M, Yukioka H, Nishi S, Fujimori M, Asada A. Crush syndrome sustained in the 1995 Kobe, Japan, earthquake; treatment and outcome. Ann Emerg Med 1997;30(4):507-12.

[15] Noji EK, Armenian HK, Oganessian A. Issues of rescue and medical care following the 1988 Armenian earthquake. Int J Epidemiol 1993; 22(6):1070-6.

[16] Sever MS, Vanholder R, Lameire N. Management of crush-related injuries after disasters. N Engl J Med 2006;345:1052-63.

[17] Noji EK. Prophylaxis of acute renal failure in traumatic rhabdomyolysis. N Engl J Med 1990;323(8):550-1.

[18] Schultz CH, Koenig KL, Noji EK. A medical disaster response to reduce immediate mortality after an earthquake. N Engl J Med 1996; 334(7):438-44.

[19] Vanholder R, Sever MS, Erek E, Lameire N. Rhabdomyolysis. J Am Soc Nephrol 2000;11:1553-61.