The Role of Rapid Urine Myoglobin Test in Early Detection of Renal Involvement in Crushing Injury: Possible Implication in Disaster Medicine

Tzong-Luen Wang, MD, PhD; Aming Chor-Ming Lin, MD, Hon-Ping Ma, MD, Hang Chang, MD, PhD

Abstract

To investigate the role of rapid urine test for myoglobin in early detection of renal involvement in crushing injury, we underwent a prospective investigation to study a urine rapid test specific for myoglobin in the specific population. Fifty-four consecutive patients presenting with crushing injury and a serum creatine kinase (CK) of >5000 IU/L from 1999 to 2001 have been enrolled as study population. Serum CK and its isoenzyme CK-MB, serum and urine myoglobin were also measured. A urine rapid myoglobin test was also performed as comparisons. All of the victims with crushing injury accepted standard medical and surgical treatment as indicated. The rate of renal involvement was about 56% (30 out of 54 patients). Urine myoglobin was present in 29 of these 30 victims (97%) with renal involvement and 2 of 24 patients (8%) without it by the rapid urine myoglobin test. The cut-off value of positive rapid urine myoglobin test was around 50 nmol/L by the ROC analysis with the sensitivity of 98% [95% CI 92-100%] and the specificity 86% [95% CI 80-92%]. In conclusion, the rapid urine myoglobin test can provide a rapid and reliable test for early detection of renal involvement in crushing injury.*(Ann Disaster Med. 2004;2:80-85)*

Key words: Crushing Injury; Renal Injury; Myoglobin; Urine

Introduction

Rhabdomyolysis with renal failure is one of the most serious complications of crushing injury.[1] Rhabdomyolysis was first described in the victims of crush injury in Sicilian earthquake in Messina in 1908 and those in World War I.[1] From then on, the problem of crushing injury with subsequent rhabdomyolysis and acute renal failure became an important issue in any kind of disasters. It therein deserves investigation how to detect early the renal involvement in crushing injury under the circumstances of disasters or mass casualties.

Rhabdomyolysis is defined as the breakdown of muscle fibers with leakage of potentially toxic cellular contents into the systemic circulation. The clinical presentation is often subtle. Preliminary diagnosis of rhabdomyolysis

From Department of Emergency Medicine, Shin-Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan
Address for reprints: Dr. Tzong-Luen Wang, Department of Emergency Medicine, Shin-Kong Wu Ho-Su Memorial Hospital, 95 Wen-Chang Road, Taipei, Taiwan
Received: Nov 3 2003. Revised: Nov 25 2003. Accepted: Dec 25 2003.
TEL: 886-2-28332211 ext 2087 FAX: 886-2-28353547 E-mail: M002183@ms.skh.org.tw

requires a high index of suspicion whereas definitive diagnosis is made by laboratory evaluation. Besides elevation of serum cardiac enzymes such as creatine kinase can provide evidence of rhabdomyolysis, a urine dipstick test for blood has positive results in the presence of hemoglobin or myoglobin. Although the urine dipstick test for blood that has positive findings in the absence of red blood cells suggests myoglobinuria, it provides poor differential power in clinical situations. We therein designed the following prospective investigation to study a urine rapid test specific for myoglobin to determine its role in diagnosis of renal involvement in crushing injury.

Methods

Study population

The consecutive patients presenting with crushing injury and a serum creatine kinase (CK) of >5000 IU/L from 1999 to 2001 have been enrolled as study population. Patients with chronic renal failure, acute myocardial infarction, or any chronic illness with a short life expectancy were excluded from the study. The patients or their relatives gave the informed consent, and the Ethical Committee of our institute approved the study protocol. Twenty healthy controls (12 men and 8 women; mean age 36±8 years) underwent the same protocol as comparisons.

Study protocol

All of the subjects underwent routine blood examinations such as complete blood cell count, prothrombin time, activated partial thromboplastin time, and biochemistry tests (including renal function test, liver function tests and electrolytes). In addition, serum CK and its isoenzyme CK-MB, serum and urine myoglobin were also measured. A urine rapid myoglobin test was also performed as comparisons. All of the victims with crushing injury accepted standard medical and surgical treatment as indicated. They also underwent forced alkaline diuresis to maintain urine output to 150 mL/hr and a urinary pH of >7.0. Intravenous furosemide was given as indicated. None of the patients received mannitol and none were dialyzed. Significant muscle compartment syndrome was detected in five patients, but the situation resolved without surgical intervention.

A Foley catheter was inserted for urine collection, and an intra-arterial cannula was inserted for hemodynamic monitoring and blood sampling. The urine was collected in fractions of 6 hrs, the volumes were measured, and aliquots were taken for analyses. Blood samples were taken at the study baseline and at 6-hr intervals. All the analyses from the sera were made from unfrozen samples. Urinary samples were alkalinized *in vitro* to pH 8.5-9.0 to improve the stability of myoglobin and stored at -70∞C until thawed and analyzed on a single occasion.

Serum myoglobin concentration was determined with an immunoturbidimetric assay on a Hitachi 917 automatic analyzer (Hitachi Medical, Tokyo, Japan) immediately. Myoglobin has been shown to be stable in serum for at least 1 month when stored at 2-8∞C. The reference range for serum myoglobin in our laboratory is <3.8 nmol/L for men and <3.2 nmol/L for women. For urinary myoglobin, the reference value is <1.0 nmol/L for both sexes.

Creatinine clearance was calculated by using the following equation: creatinine clearance = $\text{creatinine}_{\text{urine}}$ x urine flow (mL/min)/

$creatinine_{serum}$. The reference values for creatinine clearance are age dependent. In our patient population, the lowest limit of reference ranges varies from 55 mL/min to 90 mL/min. The myoglobin clearance was calculated similarly, using myoglobin concentrations in serum and urine. The clearance values were calculated for every 6-hr interval, using the measured volume of urine during this time period. The mean value of serum concentrations at the starting and end point of the interval was used in calculations.

Rapid urine myoglobin test was performed by a commercially available one-step immunochromatography kit (The Myoglobin Insta Test, Cortez Diagnostics Inc., CA, USA). The presence of myoglobin at level 100 ng/ml or higher can be detected in 5 minutes.

Results

Fifty-four consecutive patients were enrolled in the study. The mean age was 37±10 years.

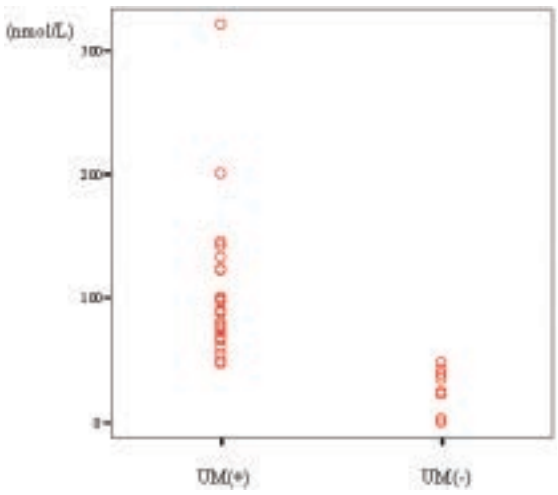

Figure. Plotting scheme showing the distribution of urine myoglobin concentrations between those with positive urine myoglobin test and those with negative results. (UM means urine myoglobin)

Thirty-eight (69%) of them were men and 16 (31%) women. The involved areas were upper extremities (n=32, 60%), lower extremity (n=18, n=33%) and abdomen (n=4, 7%). Among them, 4 had symptoms and signs of shock and all of them were abdominal crushing injury.

We firstly compared the evolution of creatinine clearance and the presence of urine myoglobin by rapid urine myoglobin test. If the renal involvement was defined as the creatinine clearance decline more than 10% of the baseline values and/or the creatine clearance being lower than 50 mL/min, the rate of renal involvement was about 56% (30 out of 54 patients). Urine myoglobin was present in 29 of these 30 victims (97%) with renal involvement and 2 of 24 patients (8%) without it by the rapid urine myoglobin test. The sensitivity and specificity of rapid urine myoglobin test were thus 94% and 86%, respectively.

Figure illustrates the correlation of urine myoglobin levels in the presence or absence of positive rapid urine myoglobin test. The cut-off value of positive rapid urine myoglobin test was around 50 nmol/L by the ROC analysis with the sensitivity of 98% [95% CI 92-100%] and the specificity 86% [95% CI 80-92%].

Discussion

This study revealed that a rapid urine test specific for myoglobin can provide a rapid and reliable examination for early diagnosis of acute renal failure in those with crushing injury.

As disaster medicine progressed, it has become an important issue to prevent the victims of devastating disaster from rhabdomyolysis and acute renal failure. The number of ARF patients is influenced largely by local

circumstances, such as the severity of the shock, the size of the disaster area, the quality of the buildings, the time needed for extrication, the triage and identification procedures, and the availability of local rescue teams and medical facilities. However, the lack of immediate reliable diagnostic tools in the disaster circumstances may also be one of the contributing factors. Acute renal failure develops in 30-40% of patients with rhabdomyolysis. Possible mechanisms include precipitation of myoglobin and uric acid crystals within renal tubules, decreased glomerular perfusion, and the nephrotoxic effect of ferrihemate.[1-4] Some investigations suggested that predictors for the development of renal failure include peak CK more than 6000 IU/L, dehydration (hematocrit >50, serum sodium >150 mEq/L, orthostasis, pulmonary wedge pressure <5 mm Hg, urinary fractional excretion of sodium <1%), sepsis, hyperkalemia or hyperphosphatemia, and hypoalbuminemia.[5-17] Most of the conditions can be met in the victims of disasters. Our study provided a simple test for detection of urine myoglobin that has been proven to be highly associated with the occurrence of acute renal failure.

Increased likelihood of mass casualty incidents and high public expectations for an appropriate and timely response mandate careful and complete planning. Mass casualty planning requires thorough knowledge of adjacent service capacities and response times.[18,19] Planning must account for the fact that traditional transport and communications system will break down. Field personnel must be specifically trained in mass casualty triage and stabilization because austere field conditions change management strategies. However, in the viewpoints of DMAT, rapid and reliable diagnostic tools or kits may provide invaluable benefit in subsequent management for some specific situations. Rapid diagnostic kits such as bioterrorism kits or chemical kits may be examples. Early detection and prevention of acute renal failure for those with crushing injury and high risk of renal involvement is another important issue. Mobility, easy performance, and power-independence are important considerations in laboratory setting in the mass casualty scenes. The rapid urine test can fulfill these criteria.

The major limitation in this study is the limited cases. A large-scale prospective study may be needed to confirm the result. Another limitation is that most of our participants were checked urine via a Foley catheter collection which may prevent from contamination with blood or other tissue fluid. In a real disaster field, most of the victims can not be treated like this. The possible contamination may be another interfering factor for correct diagnosis.

In conclusion, our data provide preliminary experience about the application of a rapid urine myoglobin test in early detection of myoglobinuria. We expect the utilization of such a tool can provide help in the real disaster fields.

References

1. Better OS. The crush syndrome revisited (1940-1990). Nephron 1990;5:97-103
2. Better OS, Stein JH: Early management of shock and prophylaxis of acute renal failure in traumatic rhabdomyolysis. N Engl J Med 1990 22;322:25-9
3. Gabow PA, Kaehny WD, Kelleher SP. The spectrum of rhabdomyolysis. Medicine 1982;61:141-52

4. Visweswaran P, Guntupalli J. Rhabdomyolysis. Crit Care Clin 1999; 15: 15-28, ix-x
5. Beese MS, Winkler G, Maas R, Bucheler E. [MRI of musculature in myalgiaóindications and image findings]. Aktuelle Radiol 1996;6:119-29
6. Berger RP, Wadowksy RM. Rhabdomyolysis associated with infection by Mycoplasma pneumoniae: a case report. Pediatrics 2000;105: 33-6
7. Boucree MC. Legionnaireís disease and acute renal failure: a case report and literature review. J Natl Med Assoc 1988;80:1065-71
8. Brumback RA, Feeback DL, Leech RW. Rhabdomyolysis in childhood. A primer on normal muscle function and selected metabolic myopathies characterized by disordered energy production. Pediatr Clin North Am 1992;39:821-58
9. Chariot P, Ruet E, Authier FJ, et al. Acute rhabdomyolysis in patients infected by human immunodeficiency virus. Neurology 1994;44:1692-6
10. Jolly BT, Talbot-Stern J. Rhabdomyolysis secondary to keyboard overuse: occupational hazard of the computer age. Am J Emerg Med 1995; 13: 644-6
11. Putterman C, Levy L, Rubinger D. Transient exercise-induced water intoxication and rhabdomyolysis. Am J Kidney Dis 1993;21:206-9
12. Sinert R, Kohl L, Rainone T, Scalea T. Exercise-induced rhabdomyolysis. Ann Emerg Med 1994;23:1301-6
13. Singh U, Scheld M. Infectious etiologies of rhabdomyolysis: three case reports and review. Clinical Infectious Diseases 1996;22:642-9
14. Will MJ, Hecker RB, Wathen PI. Primary varicella-zoster-inducedrhabdomyolysis. South Med J 1996;89:915-20
15. Wrenn KD, Oschner I. Rhabdomyolysis induced by a caffeine overdose. Ann Emerg Med 1989;18:94-7
16. Ward MM. Factors predictive of acute renal failure in rhabdomyolysis. Arch Intern Med 1988;148:1553-7
17. Zager RA. Rhabdomyolysis and myohemoglobinuric acute renal failure. Kidney Int 1996;49:314-26
18. Koenig KL, Schultz CH. Disaster medicine: advances in local catastrophic disaster-response. Acad Emerg Med 1994;1:133-6
19. Waeckerle JF. Disaster planning and response. N Engl J Med 1991;324:815-21

尿液快速肌紅蛋白檢驗對於偵測壓碎傷中的腎臟傷害所扮演的角色：對於災難醫學可能的影響

王宗倫　連楚明　馬漢平　張珩

摘要

為研究尿液快速肌紅蛋白檢驗對於偵測壓碎傷中的腎臟傷害所扮演的角色，我們進行了以特定族群為對象的前瞻性研究。從 1999 到 2001 年，共有 54 名病患受到壓碎傷並且 creatine kinase(CK) > 5000 IU/L 參與的這項研究。同時也檢驗了血清中的 CK，CKMB，及肌紅蛋白與尿液中的基紅蛋白。尿液快速肌紅蛋白的偵測也一同比較。所有的患者都接受了標準的內科或外科療法。涉及腎臟的傷害佔了 56% (54 名病患中有 30 名)。尿液快速肌紅蛋白檢驗在這 30 名病患中有 29 名的尿液呈陽性反應(97%)，而沒有腎臟傷害的 24 名病患中有 2 人呈陽性反應(8%)。經由 ROC 分析將尿液快速肌紅蛋白檢驗的分界點定於 50 nmol/L 可以有 98% 的敏感度 (95% CI 92-100%)與 86%的特異性(95%CI 80-92%)。尿液快速肌紅蛋白檢驗對於可以提供偵測壓碎傷中的腎臟傷害一快速可靠的結果。*(Ann Disaster Med. 2004;2:80-85)*

關鍵字：壓碎傷；腎臟傷害；肌紅蛋白；尿液

財團法人新光吳火獅紀念醫院急診科[1]
抽印本索取：王宗倫　台北市士林區文昌路 95 號　財團法人新光吳火獅紀念醫院急診科
收件：92 年 11 月 3 日　　修正：92 年 11 月 25 日　　接受刊載：92 年 12 月 25 日
電話：(02)28332211 分機 2087　傳真：(02)28353547　E-mail：M002183@ms.skh.org.tw