Preliminary Communication

Oral alkalinizing solution as a potential prophylaxis against myoglobinuric acute renal failure: preliminary data from healthy volunteers

Ramin Tolouian1, Dorothea Wild1, Mohammad H. Lashkari2 and Iraj Najafi3

1Griffin Hospital, Yale University School of Medicine, Derby, CT, USA and 2Army University of Medical Sciences and 3Tehran University of Medical Sciences, Tehran, Iran

Abstract

Background. Acute renal failure (ARF) secondary to crush injury is one of the leading causes of hospitalization and death in survivors of massive disasters. The standard therapy for crush injury, intravenous (i.v.) hydration and alkalinization of urine, is often not feasible after a mass disaster; therefore, oral rehydration and urinary alkalinization may be a useful substitute.

Methods. We developed and evaluated an oral alkalinizing solution (OAS) to induce alkaline diuresis. We enrolled 12 volunteer Iranian Army recruits (mean age 19.4±0.8 years) who drank an average of 650 ml of OAS for 12 h. We checked the volume and pH of their urine every hour, and measured venous blood gas and electrolytes at 6, 12 and 15 h.

Results. All subjects tolerated the OAS without adverse events, and had active diuresis (>200 ml/h) after an average of 3.0±0.7 h. Their urine became alkaline (pH > 7.0) within an average of 3.25±0.8 h. There were no significant electrolyte abnormalities.

Conclusions. OAS seems to be a safe and promising means of inducing alkaline diuresis. It may be a feasible alternative to i.v. hydration to prevent ARF secondary to crush injuries in the context of mass disasters where i.v. hydration is not possible. A dose of 10 ml/kg/h may be the correct amount to induce alkaline diuresis within the first 12 h after crush injuries. The use of OAS for this purpose should be evaluated further.

Keywords: crush injury; oral solution; earthquake rhabdomyolysis

Introduction

Mass disasters have gained media attention, one of the most recent being a strong earthquake in the city of Bam, Iran, which culminated in >41 000 deaths [1], and this was followed even more recently by the tsunami in December 2004. Acute renal failure (ARF) secondary to muscular crush injuries is one of the leading causes of hospitalization and death among survivors of massive disasters [2]. Many victims of earthquakes develop kidney problems a few days after the event, because of rhabdomyolysis leading to crush syndrome [3]. The percentage of patients who were registered as having renal failure after the earthquake in Marmara, and who required at least one form of renal replacement therapy, has been reported to have been ~75% [4], and mortality among patients who required dialysis has been reported at between 14 and 17.2% [2,5].

A study in 1984 showed that early volume replenishment prevented ARF in disaster casualties with crush syndrome [6]. Another study suggests that early transportation to medical centres and intensive therapy improves survival [7]. Several studies have shown that crush injury outcomes are improved with early treatment and that prompt and adequate fluid replenishment is the key to preventing renal failure after such injuries.

Although prompt intravenous (i.v.) hydration and urinary alkalinization is the standard therapy for crush injury, it is often not feasible to administer these in situations of mass disaster. The number of victims may overwhelm the resources of the health care system, and it is impossible for casualties to always receive standard treatment [8]. Recent experiences from the Bam earthquake show that emergency rescue squads may not arrive from neighbouring cities before 12–15 h after the event, and the incoming squads may not themselves have all the needed (type and quantity) resources. If local
medical facilities are still intact, they too may lack sufficient human resources and supplies to provide i.v. access and fluids to all the victims. Even if i.v. materials are available to treat patients, many survivors may not agree to come to the hospital, being themselves involved in operations to rescue family members or neighbours.

Therefore, in the absence of i.v. hydration, oral rehydration and urinary alkalinization may be a useful substitute. Oral rehydration solutions (ORSs) have been used successfully to treat diarrhoeal dehydration [9,10]. The addition of alkali to the regimen not only ameliorates the acidosis associated with shock and the hyperkalaemia, it can also protect the kidneys against the nephrotoxicity of myoglobin and urate by alkalinizing urine [11]. The use of an oral alkalinizing solution (OAS) for the prevention of the sequelae of rhabdomyolysis is attractive on several counts. The first is the argument that using OAS is similar to using ORS, as it provides interim care until patients get better service in well equipped facilities. Secondly, survivors could drink OAS while participating in rescue efforts. Thirdly, OAS does not depend on technical instruments, such as i.v. needles, refrigerators, expert personnel or the availability of diluents. For all these reasons, administering OAS early may decrease the morbidity (including ARF) in survivors of mass disasters.

We therefore developed and evaluated an oral solution to induce diuresis and to alkalinize urine.

**Methods**

We developed an iso-osmolar OAS with a tolerable taste using a high sodium concentration to help maintain intravascular volume and bicarbonate to make the urine alkaline. Potassium was not added to the solution, because hyperkalaemia is common in rhabdomyolysis. We prepared the solutes for OAS by mixing glucose 120 mmol/l, bicarbonate 25 mmol/l, chloride 55 mmol/l and sodium 80 mmol/l. The powdered formulation was packaged as 28.4 g sachets, each to be dissolved in 1 l of water. It was tested in the Air Force Hospital in Tehran, Iran. The volunteer subjects were recruited among soldiers on an Air Force military base who had passed a military medical check-up. We enrolled 12 volunteer men (mean age 19.4±0.8 years). After obtaining informed consent, their basal body weights, venous blood gases (VBG) and electrolytes were determined.

The subjects were asked to drink as much OAS as they could for 12 h and were allowed to eat food ad libitum during the study. They were monitored for adverse reactions for 24 h. Subjects were weighed at the beginning and end of the study. We checked their urine volumes and pH every hour; VBG and electrolytes were checked at 6, 12 and 15 h. We measured time to active diuresis, defined as urine output >200 ml/h and time to the voiding of alkaline urine, pH >7.0, as measured by dipsticks and a pH meter. The laboratory results were double-checked in two different laboratories. The local Institutional Review Board approved all protocols and procedures.

**Statistical analysis**

Data were analysed with a standard statistical package (SAS v8, the SAS Institute, NC). We performed repeated-measures ANOVA for venous pH, bicarbonate, electrolytes, glucose and body weight. For dosing purposes, we constructed a 2 × 2 table. We divided the subjects into those who imbibed 10 ± 1 ml/kg/h of OAS and those who did not, as well as those in whom diuresis and the voiding of alkaline urine occurred simultaneously (or nearly so) and those in whom they did not.

We compared the statistical significance of the differences between them with Fisher’s exact test.

**Results**

All the subjects were healthy young men between 18 and 20 years old (average 19.4±0.8 years). Their characteristics at baseline are listed in Table 1. All subjects reported tolerating the OAS without any adverse reactions such as nausea, vomiting or diarrhoea. They drank an average of 650 ml/h of OAS over 12 h and on average produced 445 ml/h of urine and gained 2.7 ± 0.4 kg in body weight.

The changes in their weights and laboratory results and the times to alkaline diuresis are shown in Tables 2 and 3. Their serum bicarbonate and pH changed significantly, but still remained within the normal range. No major electrolyte abnormalities were noted. Glucose also increased significantly, but again not above the upper limit of normal. The subjects’ urine became alkaline (pH > 7.0) within an average of 3.25 ± 0.8 h. All subjects had active diuresis after an average of 3.0 ± 0.7 h, and the specific gravity of their urine was minimum after an average 5.6 ± 2.1 h of using OAS. All subjects regained their basal body weight within 12 h after stopping drinking the OAS. No significant changes were observed in blood pressure during the study (Tables 2 and 3).

**Discussion**

Ideally, patients with crush injuries should receive i.v. fluid, to induce diuresis, and possibly also bicarbonate, to maintain their urine pH in the alkaline range. Since this is frequently not feasible in the context of mass disaster, we designed this pilot study to evaluate the safety and effectiveness of OAS as a stop-gap measure to induce alkaline diuresis and prevent acute renal failure. OAS may also be

**Table 1. Patient characteristics at baseline**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>19.4 ± 0.8</td>
</tr>
<tr>
<td>Men</td>
<td>12</td>
</tr>
<tr>
<td>Smokers</td>
<td>3</td>
</tr>
<tr>
<td>Average blood pressure (mmHg)</td>
<td>110/75 ± 10/5</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>175 ± 12.9</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>64.8 ± 7.6</td>
</tr>
</tbody>
</table>
The OAS is a promising tool, and it may be a safe alternative to i.v. hydration. We speculate that with this technique, the morbidity and mortality associated with crush injury might be reduced. The physiological tolerability and safety of OAS should be evaluated in populations that are more representative of the diversity of crush victims of disaster. If proven safe, OAS could be used in the aftermath of future mass disasters in areas that cannot provide hospitalization or i.v. facilities for patients; and injured persons could use it until they are able to get to a hospital. Therefore, an OAS is an attractive, easily administrable supplement that should be evaluated further in the next mass disaster.

**Acknowledgements.** The authors thank the Besat Air Force Hospital employees and laboratory personnel. We are especially indebted to Dr Jafari for his assistance in the laboratory evaluations, Dr Moghaisi, PharmD, for the preparation of the OAS, Col. Asghar Tolouian for his technical assistance, and Dr Asghar Rastegar and Audrey Cooper Nolan, RN, for final editing and revision.

**References**


*Received for publication: 8.10.04*
*Accepted in revised form: 9.2.05*