

The Use of Hypertonic Saline in Management of Hemorrhagic Shock

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ABSTRACT

Background: The most appropriate solution for volume replacement in hemorrhagic shock is controversial, however, hypertonic saline (HTS) solutions have recently gained widespread acceptance.

Aim of the work: to study the use of hypertonic saline with the resuscitation fluids in patients with hemorrhagic shock to evaluate the impact of this solution on the extent of early bacterial translocation and blood pressure.

Material and method: Forty patients were involved in this prospective study with class II & III hemorrhagic shock. They were randomized into 2 groups, each of 20 patients. Initial resuscitation in group I was done by using Lactated Ringer's (LR) solution with or without blood according to the patient requirements and in the second group of patients (group II), HTS 7.5% with dose of 4 ml /kg body weight was added to the resuscitation fluids. Regular monitoring of vital signs was done and blood samples were withdrawn 1, 30, and 90 minutes after commencement of the resuscitation and sent for blood culture for both aerobic and anaerobic growths.

Results: The mean arterial blood pressure in the group I before resuscitation was found to be about 65mm Hg and the mean was raised to 105 mm Hg after 2 hours of resuscitation with LR \pm blood. The mean amount of LR used in this group to resuscitate the patients was found to be 40 ml/kg body weight. In group II, the mean arterial blood pressure was found to be 62 mm Hg and it was efficiently controlled by HTS, LR \pm blood and the mean arterial blood pressure 2 hours after commencement of resuscitation was elevated to 124 mm Hg. The mean amount of LR used in this group to resuscitate the patients was found to be 18 ml/kg body weight. The blood cultures were positive in 5% of the patients of group II and in 40% of patients of group I. *Escherichia coli* were the most commonly isolated organism.

Conclusion: hypertonic saline was found to be effective for decreasing the rate of early bacterial translocation to blood and also for more efficient restoring of the mean arterial pressure in patients with hemorrhagic shock.

Key Words: Hypertonic saline, bacterial translocation, hemorrhagic shock.

INTROIUCTION

The gastrointestinal tract has been considered to be a potential source of sepsis from the bacterial translocation that may occur after shock, burns, and other major injuries (Frank et al, 2011). Bacterial translocation (BT) occurs when the bacteria and/or their cell wall components pass across the intestinal wall to the mesenteric lymph nodes and in turn to peripheral blood (Gustavo et al, 2008). Factors which have been shown to predispose to BT include reduced splanchnic blood flow, intestinal mucosal damage, immune deficiency, parenteral nutrition, antibiotic therapy, and bacterial overgrowth (Yada et al, 2000). The route of entry of these bacterial products and other non bacterial soluble factors into the systemic circulation is the mesenteric lymphatics and not the portal vein (Gustavo et al, 2008). Three basic mechanisms have been proposed to promote BT, which, include; intestinal mucosal injury by hypo-perfusion, decreased intracellular killing of bacteria and decrease of intracellular generation of nitric oxide and super oxide with intestinal arteriolar vasoconstriction (Wade, 2002). Volume replacement alone seems to be not the only factor to prevent this process (Frank et al, 2011). However, the most appropriate solution for volume replacement remains controversial; the Vietnam War established the current standard use of isotonic crystalloid fluids (normal saline (NS) and Ringer's lactate

RL) for the resuscitation of hemorrhagic shock (Alam, 2011). Reports have shown that crystalloids represent an effective and inexpensive means to restore intravascular volume and offer a survival advantage over colloids in the resuscitation of traumatic hemorrhagic shock (Alam, 2011). More recently, small volume resuscitation with 4 mL of 7.5% NaCl per kilogram of body weight of hypertonic saline (HTS) has been proposed to be very effective in the treatment of hemorrhagic shock (Alejandra et al, 2006). The aim of this work is to study the use of hypertonic saline with the resuscitation fluids in patients with hemorrhagic shock to evaluate the impact of this solution on the extent of early bacterial translocation and blood pressure.

Material and Methods:

This prospective study was performed in King Abdul-Aziz Hospital, Taif, Saudi Arabia from December 2010 to April 2012. The study was approved by the local committee of human research, and all patients gave written informed consent to participation. Forty patients were involved in the study with class II & III hemorrhagic shock. They were randomized into 2 groups, each of 20 patients. Initial resuscitation in group I was done by using Lactated Ringer's (LR) solution with or without blood according to the patient requirements and in the second group of patients (group II), HTS, 7.5% with dose of 4 ml /kg body weight

was added to the resuscitation fluids. Regular monitoring of vital signs was done and blood samples were withdrawn 1, 30, and 90 minutes after commencement of the resuscitation and sent for blood culture for both aerobic and anaerobic growths. The blood samples were then incubated for 48 hours in blood sheep agar, and Mc Conkey's agar, and in liquid thiogluconate for anaerobic culture. Colonizing samples were incubated with vitamin K hemin blood agar for another 48 hours at 37°C. The sample was considered to be positive for bacterial translocation if the bacterial count was higher than 100 colony forming units (CFU)/gram. Positive blood cultures were passed into blood agar for determining the morphology.

Statistical analysis was determined by the Fisher's exact and Mann-Whitney tests. A value of $P < 0.05$ was considered to be statistically significant.

RESULTS:

The mean arterial blood pressure in the group I before resuscitation was found to be about 65mm Hg and the mean was raised to 105 mm Hg after 2 hours of resuscitation with LR \pm blood. The mean amount of LR used in this group to resuscitate the patients was found to be 40 ml/kg body weight.

In group II, the mean arterial blood pressure was found to be 62 mm Hg and it was efficiently controlled by HTS, LR \pm blood and the mean arterial blood pressure 2 hours after commencement of resuscitation was elevated to 124 mm Hg.

The differences among these groups did not reach statistical significance ($P > 0.05$). The mean amount of LR used in this group to resuscitate the patients was found to be 18 ml/kg body weight and the difference between both groups was significant ($P < 0.05$) and the amount of LR used in group II was significantly lower than group I.

The blood cultures were positive only in the samples taken 90 minutes after commencement of resuscitation and the mean time from onset of trauma to detect the BT in peripheral blood was 3 hours. It was positive in 1/20 patients (5%) of group II and in 8/20 patients (40%) of group I. The differences among the groups were significant ($P < 0.05$) and bacterial translocation was significantly higher in group I. Table 1 shows summary of these results.

Escherichia coli was the most commonly isolated organism followed by *Enterobacter*, *Bacteriodes*, *Pseudomonas aerogonasa*, *Staphylococcus aereus*, and the least was *Proteus*.

Table 1: Summary of the results.

Finding	Group I	Group II
Number of patients	20	20
Mean ABP (before resuscitation)	65	62
Mean ABP (after resuscitation)	105 mm Hg	124 mm Hg
BT	40%	5%
Mean amount of LR used	40 ml/kg	18 ml/kg

ABP; Arterial Blood Pressure, BT;
Bacterial translocation, LR; Lactated
Ringer's

DISCUSSION:

The popularity of HTS has been increased in the last two decades showing a trend to increased post-traumatic survival both in the early phase and in the late phase (Alejandra et al, 2006). In the early phase (<12 hours after trauma), the effect of HTS is believed to be due to a functional increase in cardiac preload, primarily by inducing intravascular shift of the osmotic fluid from the cells and interstitium leading to increase in systemic blood pressure and cardiac output as well as decrease in small vessel capacitance (Gustavo et al, 2008). The barrier function of the intestinal mucosa is deranged in animals subjected to severe injury leading to bacterial translocation which has been proved to play the major role in the late (days to weeks after trauma) post-traumatic morbidity and mortality (Deitch

et al, 2003).The late morbidity and mortality of traumatic hemorrhage have been attributed to the “second hit”; that is, a relatively less important inflammatory event as pneumonia, aspiration or minor surgery that occurs days to weeks after the injury and in presence of the translocated bacteria and abnormal neutrophil function it initiates progression to the systemic inflammatory response syndrome (SIRS), organ failure, and eventual death (Frank et al, 2011). The mechanisms to be proposed involve intestinal mucosal injury by hypoperfusion, decrease in intracellular killing of bacteria and arteriolar vasoconstriction, the effects which had been proved to be reversed if hypertonic saline is used in resuscitation and it has been proved also that HTS has immune modulation of leukocytes, in particular neutrophils (Murao et al,2003 and Frank et al, 2011). Alejandro et al (2006) suggested that resuscitation with hypertonic saline solutions present significant potential as an immunomodulator agent for hemorrhagic shock and trauma victims.

Yada et al, (2000) found that translocation occurs in hemorrhagic shock and develops acutely within 1-4 hours, extending over the next several days. In this study, bacterial translocation to the peripheral blood was seen about 3 hours (mean) after hemorrhagic shock and bacteria were grown in 40% of blood derived from the patients who did not receive HTS as part of their resuscitation

fluid and only in 5% of patient who received HTS.

In this study, it was clearly evident that HTS decreases bacterial translocation in hemorrhagic shock. Volume replacement itself is probably not very effective, considering that, patients of group I, were given LR \pm blood had a high rate of translocation. Alejandra et al, (2006) demonstrated that Small volume of hypertonic saline would be beneficial as the initial fluid replacement in hypodynamic sepsis and he found that the use of HTS minimized the need for other resuscitation fluids. In this study it was found that the requirement of LR to restore the arterial blood pressure in shocked patient had been reduced from 40 ml/kg to 18 ml/kg when HTS was added. Similar results are also seen by Wade (2002), Oliveira et al (2002) and Hotchkiss and Karl (2003).

in a large controlled USA multicenter study, Alam, (2011) reported that hypertonic saline as initial treatment of hemorrhagic shock had a significant improvement of arterial pressure with significant decrease in long term mortality rate in patients with an entry mean arterial pressure below 70 mmHg. In this study the mean arterial blood pressure in the group I before resuscitation was found to be about 65mm Hg and the mean was raised to 105 mm Hg after 2 hours of resuscitation with LR \pm blood. In group II, the mean arterial blood pressure was found to be 62 mm Hg and it was efficiently controlled by HTS,

LR \pm blood and the mean arterial blood pressure 2 hours after commencement of resuscitation was elevated to 124 mm Hg. Assalia et al, (2001) concluded that HTS and LR showed significant reduction in bacterial translocation with efficient control of blood pressure. In other studies, hypertonic saline was shown to induce hemodynamic improvement in hemorrhagic shock (Alam, 2011). In this series hemodynamic control was achieved by LR \pm blood, however better control with less amount of RL was achieved when HTS was used. Whereas isotonic fluid administration requires large volumes, hypertonic resuscitation offers the advantages of ease of transport, speed of administration, and almost instantaneous hemodynamic effect, moreover, its value in reversal of intestinal arteriolar vasoconstriction and reduction of the extent of bacterial translocation (Frank et al, 2011). All these evidences require additional research and careful evaluation in more clinical trials.

Conclusion: hypertonic saline was found to be effective for decreasing the rate of early bacterial translocation to blood and also for more efficient restoring of the mean arterial pressure in patients with hemorrhagic shock.

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ملخص عربي

استخدام المحلول الملحي مفرط التركيز في علاج الصدمة النزفية

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خلفية: إن المحلول الأنسب لعلاج الصدمة النزفية مثير للجدل ومع ذلك، فإن استخدام المحلول الملحي مفرط التركيز قد اكتسب في الآونة الأخيرة قبولاً واسع النطاق.

الهدف من هذا العمل: دراسة لاستخدام المحلول الملحي مفرط التركيز مع سوائل الإنعاش في المرضى الذين يعانون من صدمة نزفية لتقييم أثر هذا الحل على مدى الإزفاء البكتيري المبكر وضغط الدم.

المرضى وطريقة العمل: وشارك أربعون مريضاً يعانون من صدمة نزفية من الدرجة الثانية والثالثة في هذه الدراسة وتم تقسيمهم إلى مجموعتين كل واحدة تضم 20 مريضاً.

وعولج مرضى المجموعة الأولى باستخدام لبنات الرينجرز مع إعطاء الدم حسب احتياجات المريض وفي المجموعة الثانية من المرضى اضيف للعلاج السابق محلول ملحي مفرط التركيز (7.5%). (بجرعة 4 مل لكل كجم من وزن الجسم مع. وقد تم متابعة المؤشرات الحيوية، وجرى سحب عينات الدم 1، 30، و 90 دقيقة بعد بدء الإنعاش وإرسالها لعمل مزرعة دم لاكتشاف أي نمو بكتيري هوائي أو لا هوائي .

النتائج: متوسط ضغط الدم الشرياني في المجموعة الأولى قبل بداية الإنعاش كان 65 مم زئبق ورفع المتوسط إلى 105 مم زئبق بعد ساعتان من الإنعاش مع دم \pm لبنات الرينجرز. وكانت الكمية المطلوبة من لبنات الرينجرز في هذه المجموعة لإنعاش المرضى 40 مل / كجم من وزن الجسم في المتوسط. في المجموعة الثانية، وجد أن متوسط ضغط الدم الشرياني قبل الإنعاش 62 مم زئبق، وتم العلاج بشكل فعال عند إعطاء المحلول الملحي مفرط التركيز مع الدم ولبنات الرينجرز وارتفع متوسط ضغط الدم الشرياني بعد ساعتان من بدء الإنعاش إلى 124 مم زئبق.

ولوحظ أن الكمية المطلوبة من لبنات الرينجرز المستخدمة في هذه المجموعة لإنعاش المرضى قد انخفضت لتكون 18 مل / كجم من وزن الجسم. كانت مزرعة الدم ايجابية في 5% من المرضى من المجموعة الثانية، وفي 40% من المرضى من المجموعة الأولى وكان أكثر أنواع البكتيرية شيوعاً هي البكتيرية القولونية.

والخلاصة: إن استخدام المحلول الملحي مفرط التركيز في علاج الصدمة النزفية كان فعالاً في منع الإزفاء البكتيري المبكر وكذلك لاستعادة أكثر كفاءة للضغط الشرياني المتوسط في هؤلاء المرضى.