Cardiocirculatory changes in hemorrhagic shock induced in pigs submitted to three distinct therapeutic methods

Alterações cardiocirculatórias no choque hemorrágico induzido em suínos submetidos a três terapias distantes

Gilberto Fernandes Silva de Abreu, Antônio Roberto Barros Coelho, José Lamartine de Andrade Aguiar, Silvio Amorim Moura Filho

1Preceptor, Department of Surgery, UFPE, Recife-PE, Brazil.
2PhD, Associate Professor, Department of Surgery, UFPE, Recife-PE, Brazil.
3MD Resident, Department of Surgery, Federal University Hospital, Recife, Brazil.

ABSTRACT

Purpose: To evaluate and compare the response of pigs submitted to hemorrhagic shock and treated using three different strategies.

Methods: Thirty-five Dalland pigs were divided into four groups: Control; Bleeding; Saline and Saline + Red Cell Concentrate. Parameters evaluated: heart rate (HR), mean arterial blood pressure (MAP) and central vein pressure (CVP). Hemorrhagic shock was induced by removing (624.25±64.55), (619.30±44.94) and (664.23±39.96) ml of blood respectively, with the following treatment: Bleeding Group – zero volume replacement; Saline Group – replacement with 676 ml of 0.9% saline solution; Saline + Red Cell Concentrate Group – replacement with 440 ml of 0.9% saline solution + 291 ml of red cell concentrate. The treatment was evaluated after 10 (T3), 30 (T4), 45 (T5) and 60 (T6) minutes.

Results: HR: No statistically significant difference was found between the Bleeding and Saline [p=1.000], Bleeding and Saline + Red Cell Concentrate [p=1.000], and Saline and Saline + Red Cell Concentrate [p=0.721] groups. MAP: Significant differences were found between all the groups studied. CVP: No significant difference was found between the groups.

Conclusion: Non-replacement and euvolemic resuscitation maintained a satisfactory hemodynamic pattern in controlled severe hemorrhagic shock in swine. The euvolemic replacement strategies exceeded the limit values of MAP for rebleeding.

Key words: Shock, Hemorrhagic. Trauma. Swine.

RESUMO

Objetivo: Avaliar e comparar as respostas cardiocirculatórias em suínos tratados por três terapias diferentes após choque hemorrágico.

Métodos: Trinta e cinco suínos Dalland foram divididos em quatro grupos: Controle; Sangria; Salina; Salina + Concentrado de hemácias. Parâmetros cardiocirculatórios avaliados: frequência cardíaca (FC), pressão arterial média (PAM) e pressão venosa central (PVC). O choque hemorrágico foi induzido retirando (624,25±64,55) (619,30±44,94) e (664,23±39,96) ml do volume sanguíneo. Terapias: Grupo Sangria - Sem reposição volêmica; Grupo Salina - reposição com 676 ml de solução salina 0,9%; Grupo Salina + Concentrado de hemácias - reposição com 440 ml de solução salina 0,9% + 291 ml de concentrado de hemácias. A avaliação do tratamento foi realizada aos 10 (T3), 30 (T4), 45 (T5) e 60 minutos (T6).

Resultados: FC; Não houve diferença significativa entre os grupos Sangria e Salina [p=1,000]; Sangria e Salina + Concentrado de hemácias [p=1,000]; e Sangina e Salina + Concentrado de hemácias [p=0,721]. PAM; Houve diferença entre todos os grupos. PVC; Não houve diferença entre os grupos estudados. Conclusão: Os procedimentos sem reposição e com reposição euvolêmica mantiveram padrão hemodinâmico satisfatório no choque hemorrágico grave controlado em suínos. As estratégias de reposição euvolêmica ultrapassaram os valores de PAM considerados limites para o resangramento.

Descritores: Choque Hemorrágico. Trauma. Suínos.

Introduction

Hemorrhagic shock with blood loss of at least 40% of the individual’s total blood volume may be secondary to a direct vascular lesion and/or the flow of plasma to damaged tissue. Tissue hypoperfusion leads to the reduction of available oxygen to the cell, hypothermia and metabolic acidosis. The physiopathological response to the state of hemorrhagic shock is characterized by vasoconstriction with a proportional growth in cardiac frequency (HR) and in mean arterial pressure (MAP). The current protocol for treatment advocated by the American College of Surgeons recommends the early use of two to three liters of saline solution as...
a resuscitation liquid for adults and 20 ml/kg for children who have abruptly lost more than 40% of their blood volume³.

This procedure is questionable, as studies demonstrate that conventional resuscitation with the replacement of hydrosaline fluids may cause dilutional coagulopathy and a subsequent increase in blood loss, with better results shown in hypotensive resuscitation in pig hemorrhagic shock models²³.

Maintaining a hypotensive state with the careful administration of saline solution may reduce blood loss and may be preferable before definitive surgical repair of the bleeding site⁴. Similar results were obtained by other authors using saline solution up to a MAP of 50 mm of hg, with a lower mortality rate⁵⁶. Furthermore, evidence exists in favor of the use of a 1:1 ratio of red cell concentrate and fresh plasma with an improvement of hemostasis and an increase in the survival rate. The objective of this study is to evaluate the cardiocirculatory responses to hemorrhagic shock therapy in pigs conducted without volemic replacement compared to those treated with isolated saline solution or saline solution combined with red cell concentrate.

**Methods**

Thirty five healthy pigs of the Dalland breed were divided into four Groups: Control (n=5), Bleeding (n=10), Saline Solution (n=10) and Saline Solution + Red Cell Concentrate (n=10), with respective weights of (23.40±1.29), (22.70±2.34), (22.52±1.63) and (24.16±1.45) kilograms.

Anesthesia was accomplished using the pre-anesthetic drug ketamine hydrochloride (20mg/kg) injected in the ear pavilion with 0.9% ClNa solution t (1ml/kg/h); General anesthesia was accomplished with tiopental (5mg/kg), ketamine hydrochloride (10mg/kg) and pancuronium (0.04mg/kg). Respiration under tracheostomy with mechanical ventilation was installed with oxygen with a FiO₂ of 21%. All the animals were submitted to experimental surgical intervention, the Swan model of hemorrhagic shock being induced with initial volemia estimated through the formula IBV (l) = body weight (kg) X 5.5%.

Electrocardiography monitoring was carried out, with catheterization of the left femoral artery for continuous measurement of mean arterial pressure (MAP) and internal jugular veins for measurements of central venous pressure (CVP) and volume replacement when suitable. In all groups except for the control group, serial bleeding was carried out at 10 and 13 minutes, with a total blood volume estimated at 50% of the circulating volume. In the Bleeding Group there was no replacement. In the Saline Group, replacement was carried out with 0.9% ClNa solution with a flow of 6ml/kg/min, whilst in the Saline + Red Cell Concentrate Group, replacement was carried out with 0.9% ClNa solution and with Red Cell Concentrate in the ratio of 1:1.5, with a flow of 6ml/kg/min.

The parameters were evaluated 10 minutes after vascular access and at the following stages: (T₀) – zero minutes; (T₁) – 3.5 minutes – after removal of 1/3 of 50% of the volume; (T₂) - 07 minutes - after removal of 2/3 of 50% of the volume; (T₃) - 10 minutes - after removal of 50% of the volume, 30 minutes (T₄) 45 minutes (T₅) and 60 minutes (T₆). At each stage 15 ml of blood was collected for blood gas analysis. The statistical analysis of T₄, T₅ and T₆ (therapeutic management period) was accomplished through the application of the Bonferroni test on the mean values of parameters verified during the period of application of therapeutic methods, with a confidence level of 95%. This study was approved by the Ethics Committee on Animal Experimentation of the Federal University of Pernambuco – UFPE.

**Results**

When compared variable HR, no significant differences was found between the following group: Bleeding (184.83±13.54) versus Saline Solution (179.30±8.49) [p=1.000]; Bleeding (184.83±13.54) versus Saline Solution + red cell concentrate (192.07±7.93) [p=0.721]. A statistically significant difference was found between the groups Control (153.53±2.27) e Bleeding (184.83±13.54) [p=0.016], Control (153.53±2.27) e Saline Solution (179.30±8.49) [p=0.048], Control (153.53±2.27) and Saline Solution + red cell concentrate (192.07±7.93) [p=0.005], at all studied times after institution of therapeutic methods (Table 1 and Figure 1).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control</th>
<th>Bleeding</th>
<th>Saline</th>
<th>Saline + red cell concentrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR</td>
<td>153.53 ± 2.27</td>
<td>184.83 ±13.54</td>
<td>179.30 ± 8.49</td>
<td>192.07 ± 7.93</td>
</tr>
<tr>
<td>MAP</td>
<td>117.67 ± 1.15</td>
<td>57.83 ± 4.07</td>
<td>85.50 ± 5.41</td>
<td>101.00 ± 0.50</td>
</tr>
<tr>
<td>CVP</td>
<td>-6.13 ± 0.23</td>
<td>-6.90 ± 0.18</td>
<td>-6.60 ± 0.22</td>
<td>-7.27 ± 0.50</td>
</tr>
</tbody>
</table>

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Significant difference was found in mean values of MAP between the following groups: Control (117.67±1.15) versus Bleeding (57.83±4.07) \( [p=0.000] \); Control (117.67±1.15) versus Saline Solution (85.50±5.41) \( [p=0.000] \); Control (117.67±1.15) versus Saline Solution + red cell concentrate (110.00±0.50) \( [p=0.002] \); Bleeding (57.83±4.07) versus Saline Solution (85.50±5.41) \( [p=0.000] \), Bleeding (57.83±4.07) versus Saline Solution + red cell concentrate (110.00±0.50) \( [p=0.000] \), Saline Solution (85.50±5.41) e Saline Solution + red cell concentrate (110.00±0.50)\( [p=0.003] \), at all studied times after institution of therapeutic methods (Table 1 and Figure 2).
No statistically significant difference was found in mean values of CVP between the following groups; Control (-6.13±0.23) versus Bleeding (-6.90±0.18) \( [p=0.420] \); Control (-6.13±0.23) versus Saline Solution (-6.60±0.22) \( [p=0.620] \); Control (-6.13±0.23) versus Saline Solution + red cell concentrate (-7.27±0.50) \( [p=0.269] \); Bleeding (-6.90±0.18) versus Saline Solution (-6.60±0.22) \( [p=1.000] \); and Saline Solution (-6.60±0.22) versus Saline Solution + red cell concentrate (-7.27±0.50) \( [p=1.000] \) at all studied times after institution of therapeutic methods (Table 1 and Figure 3).

Discussion

Previous studies conducted on animals to evaluate hemodynamic response in hemorrhagic shock treatment have shown that the replacement of 1 to 1.5 times the lost volume with lactated ringer brought about effective resuscitation with superior survival rates compared to vigorous replacement and no treatment\(^9\). Experiments on rabbits showed that the hypovolemic resuscitation strategy reduced the seric concentration of tumor necrosis factor (TNF alpha) and interleucine 6 when compared to vigorous blood replacement\(^10\).

Wistar-Kyoto rats, when treated with the HDACI (histone deacetylase inhibitors) enzyme and without blood replacement after deep hemorrhagic shock, showed a greater rate of survival in the first 3 hours when compared to unresuscitated animals\(^11\). In this study, there was no difference in the therapeutic options employed concerning HR and CVP. The HR parameter showed a statistical difference between the Control group and the groups that underwent hemorrhagic shock. MAP showed a gradual recuperation of levels compatible with life, with steady growth in the Bleeding group, reaching mean values of 57 mmHg, considered to be the limit for rebleeding that was exceeded in Saline and Saline + Red Cell Concentrate Groups. The evolution of MAP revealed a two-phase pattern above the minimum level for rebleeding\(^2\) in the Saline Solution Group, showing that replacement of blood volume with saline solution may produce a transitory response translated as improvement in pressure levels, evidence of endothelial dysfunction and the lowest remnant of the solution in the intravascular space\(^12\)\(^-\)\(^15\). The Saline Solution + Red Cell Concentrate group showed a stable response in MAP recuperation levels, maintaining these levels during the studied period of 50 minutes after the start of therapy. Zakaria et al.\(^12\) suggest that resuscitation strategies that contain blood are associated with a better preservation of hemodynamics, with a lower degree of microvascular dysfunction. Sondeen et al.\(^5\) show that a secondary hemorrhage event after fluid therapy can be predicted through MAP monitoring, establishing a safety margin for resuscitation while there is no control of the primary source of bleeding\(^16\). There is no difference in the CVP responses. The loss of 50% of the total blood volume of the animals studied produced transitory hemodynamic alterations without compromising the compensation mechanisms for the reduction of the intravascular content.

Considering the wide variety of resuscitation liquids currently available and the diverse ways in which organic injuries can cause deep hemorrhagic shock, it is recommended that the therapeutic approach be determined by an individual evaluation of each victim, contrary to the standardized and protocol approach recognized by some authors, services and entities. The ideal moment and quantity of liquid to be administered to hemorrhagic shock patients still remains undefined, a fact that determines the need for more controlled and randomized study, in order to establish a more effective strategy for blood replacement\(^17\)\(^-\)\(^20\).
Conclusion

Non-replacement and euvolemic replacement procedures maintained a satisfactory hemodynamic pattern in this experimental model of controlled severe hemorrhagic shock in swine. When the source of bleeding was controlled, strategies of euvolemic replacement exceeded the limit values of MAP for rebleeding.

References


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Correspondence:
Gilberto Fernandes Silva de Abreu
Avenida 17 de Agosto, 2483/2201
52061-540 Recife – PE Brazil
Phone: (55 81)3442-8692/3445-6627
gabreu01@uol.com.br

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