Microcirculatory Perfusion during Volume Therapy

A Comparative Study Using Crystalloid or Colloid in Awake Animals

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Background: Because of the passage of water and salt molecules into the interstitial space, volume replacement with crystalloid solutions requires an amount at least four times that of lost blood. The resulting tissue edema may interfere with nutritive capillary perfusion and oxygen delivery. To prove this hypothesis, the effects of isovolemic hemodilution (hematocrit 30%) with Ringer’s lactate solution or dextran 60 on tissue perfusion and oxygenation were investigated in awake Syrian golden hamsters.

Methods: Experiments were performed by using a chronic dorsal skinfold window giving access to skeletal muscle tissue (musculus cutaneus) with in vitro microscopy, quantitative video image analysis, and surface oxygen partial pressure electrodes. Central venous and arterial pressures were measured by means of chronically implanted jugular veins and carotid catheters.

Results: Isovolemic exchange of blood with dextran caused no significant changes in arterial or central venous pressure, heart rate, capillary flow velocity, functional capillary density, or surface oxygen partial pressure during the 1-h observation period. A volume of Ringer’s solution equal to four times of the amount of blood lost maintained arterial pressure and heart rate when central venous pressure was kept at predilution control values. However, tissue perfusion determined by counting perfused capillaries per terminal arteriole was reduced by 62%, and mean tissue oxygen partial pressure decreased from 19 to 8 mmHg.

Conclusions: In this model, volume replacement with artificial colloids yielded hemodynamic stability and adequate tissue oxygen supply, whereas administration of crystalloids alone jeopardized tissue perfusion and oxygenation. (Key words: Fluid therapy; colloids; crystalloids; dextran. Measurement techniques: in vitro microscopy; surface oxygen electrodes. Microcirculation: capillary perfusion; oxygenation.)

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AN ongoing controversy exists over whether crystalloid or colloid solution is the preferred fluid for primary volume therapy in shock. Although it has been shown repeatedly that either treatment regimen can restore intravascular volume and gross organ perfusion, no agreement has been reached regarding differences in sequelae, such as multiple organ failure or outcome.

Proponents of the crystalloid regimen claim difficulties in titrating the appropriate volume of colloid solution and this a greater risk of fluid overload. Artifical colloids and human albumin also may evoke anaphylactic reactions and are more expensive than crystalloids.

In contrast, supporters of the colloid regimen emphasize that a large amount of crystalloid solution is necessary to restore intravascular volume; a long time is needed to achieve the restoration; and the large volume required may lead to significant tissue edema. Excessive amounts of Ringer’s solution can impair oxygen transport because of decreased capillary flow and subsequently can impede wound healing. Although this surplus extravascular water is eliminated upon restoration of a physiologic transcapillary fluid balance, the process can last as long as 3 weeks. Another study on the effects of an isotonic fluid load (30% of plasma volume) demonstrated a preferential increase in the extracellular fluid of lung (14%), gastric fundus (15%), large intestine (21%), and skin (28%), suggesting that the perfusion of these tissues may be affected. To our knowledge no studies have been performed to test this hypothesis by directly investigating nutritive capillary perfusion.

On the basis of a suggestion of Shoemaker and Hausner, the objective of this study was to investigate the intrinsic microcirculatory effects of crystalloid and colloid solutions by comparing microvascular perfusion and tissue oxygenation during fluid therapy.
Materials and Methods

To exclude any alterations of the microcirculation that might be caused by even transitory hypovolemia, we used an experimental model in which an acute hemodilution limited to a final hematocrit (Hct) of 30% was produced in two or three steps. After governmental ethics committee approval, the study was performed in 60 awake Syrian golden hamsters (body weight approximately 70 g). For chronic instrumentation, general anesthesia was induced with pentobarbital (50 mg/kg intraperitoneally). Additional pentobarbital was administered intraperitoneally if necessary. A transparent aluminum chamber was implanted for access to the microcirculation. Two symmetric Teflon-coated aluminum frames were placed on a dorsal skinfold so that the double-layered skinfold was secured between the two frames. One layer of the skin was completely removed in a circular area of 15 mm in diameter. The underlying layer consisting of skeletal muscle, subcutaneous tissue, and cutis was covered by a removable glass cover slip. This cover slip was incorporated into one of the frames (fig. 1). Neither antibiotics nor antiinflammatory drugs were used topically or systematically. Permanent catheters, filled with heparin-containing saline (50 IU/ml), were passed from the dorsum to the ventral side of the neck. A carotid artery and jugular vein were cannulated and the catheter tips advanced into the aortic arch and the superior vena cava, respectively. Correct position of the catheters was confirmed by continuous pressure recording.

After 48 h, the viability of the tissue in the chamber was evaluated before randomization by the same observer (VB) by using the following established criteria:

1. absence of petechial hemorrhage
2. absence of macroscopic edema
3. no signs of inflammation such as leukocyte rolling or sticking at venular walls, increasing vasodilation or neovascularization
4. blood cell velocity in collecting venules greater than 0.3 mm/s
5. presence of spontaneous arteriolar vasomotion

For observation, the awake animals were trained to crawl into a tube (methylmethacrylate ester polymer). This tube minimized movements by the animal. Within 5–10 min the animals became accustomed to the restricted movement. Blood pressure recordings and a blood gas analysis (volume withdrawn 0.1 ml) were then performed. The following criteria were used: mean arterial blood pressure greater than 80 mmHg, central venous pressure (CVP) –2 to +6 mmHg, heart rate 340–480 beats/min, arterial oxygen partial pressure greater than 60 mmHg, arterial carbon dioxide partial pressure 35–45 mmHg, and pH 7.28–7.42. All values were within these criteria and the animals were randomly assigned to one of two studies.

Study A

The microcirculation of the skeletal muscle tissue in the chamber of 30 awake hamsters was observed by intravital microscopy. To obtain an Hct of approximately 30%, isovolemic hemodilution was performed in 12 hamsters using dextran 60 (6%, 60,000 Da) administered in two or three steps with intermittent Hct determinations. The exchange volume was 19.1 ± 1.5 ml/kg (mean ± SD). In 12 hamsters hemodilution was performed in increments using Ringer’s lactate solution; 20.3 ± 4.3 ml/kg of blood were exchanged for 79.5 ± 15.9 ml/kg Ringer’s solution. To ensure normovolemia and to maintain CVP at predilution values, the crystalloid was infused during the 1-h observation. Hemodilution was not performed in 6 control animals. The system used for video microscopy consisted of a modified Orthoplan microscope (Leitz, Wetzlar, Germany) equipped with an epillumination system (Ploemopak, Leitz, Wetzlar, Germany) and a blue filter block for fluorescence measurement by 0.2 ml/ml (Da, 150,000 Da, from COHU, San Diego, California, Sony-Dea3000 components were done in figure 2:

- vessel diameter
- erythrocyte velocity between the skinfold
- functional capillary bed

[i.e., all capillaries arteriole]

Study B

In 30 awake hamsters as described above, arterial and control measurements were determined on the same day. For measurement of arterial blood pressure, a warm isotonic sodium chloride solution was positioned using a micrometer to carefully avoid arterial pressures 80–120 mmHg, measurements were divided into means and performed (hypoxic ranges).

Both studies lasted 5 min of stabilization, then hemodilutions were made in 30 and 60 min in the animals of each group after treatment and for 48 h. From these data were obtained the mean arterial pressure (MAP).

Statistics

Because of a lack of variances (ANOVA)

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block for fluorescence microscopy (contrast enhancement by 0.2 ml 5% fluorescein isothiocyanate–dextran, 150,000 Da, intravenously; Pharmacia AB, Uppsala, Sweden). The images obtained by the microscope were recorded with a low–light-level camera (COHU 4410, COHU, San Diego, CA) and stored on video tape (U-matic, Sony-Deutschland, Koeln, Germany). Measurements were done off line and included, as shown in figure 2:

- vessel diameters (by video image shearing*)
- erythrocyte velocity (by computation of delay between the signals of two videodensitometers positioned over a blood vessel*)
- functional capillary density (by counting of erythrocyte-perfused capillaries of a microcirculatory unit [i.e., all capillaries branching from the same terminal arteriole])

Study B

In 30 awake hamsters hemodilution was performed as described above (dextran n = 12, Ringer’s n = 12, and control n = 6). Oxygen partial pressure was determined on the surface of the tissue in the chamber. For measurements, the cover glass was replaced with warm isotonic saline (30°C). A calibrated eight-wire platinum surface electrode (head diameter 2.4 mm) was positioned randomly over 10–15 different areas using a micromanipulator. Tissue compression was carefully avoided. A single determination consisted of 80–120 values that were recorded within 10 min. The measurements were displayed as a frequency distribution divided in subsets of 5 mmHg each. Arithmetic means and percentage of values in the lowest class (hypoxic range, 0–5 mmHg) were used to compare groups.

Both studies followed the same protocol. After 30 min of stabilization, control values were recorded, and then hemodilution was performed. Additional recordings were made immediately after hemodilution and 30 and 60 min later. After the experiment, half of the animals of each group were followed up without further treatment and with free access to food and water for 48 h. From the remaining animals, blood samples were obtained to determine plasma colloid osmotic pressure (COP) by membrane osmometry.

Statistics

Because of a lack of a normal distribution or inequality of variances (Levene’s test) in several subgroups of all parameters, significant differences were computed using Wilcoxon’s signed rank test within groups. Comparisons between groups were calculated by the Mann-Whitney rank test. For statistical analysis of the surface oxygen partial pressures, sum-histograms were compiled by averaging the frequencies in each class of 5 mmHg because the measuring device did not record numerical values of single platinum wires. The arithmetic means of the individual histograms and the percentage of values in the lowest class also were compared by nonparametric tests. Testing of skewness and kurtosis was not possible because of the lack of single numerical values, and thus the shape of the histograms was evaluated only in a descriptive way. Differences in survival were analyzed with the chi-square test. Statistical calculations were done using a commercial software package (SPSS Inc., Chicago, IL).

Results

Macrocirculation

Mean arterial pressure and heart rate were unchanged in the two studies throughout the experiment. In the cryostadloid, in which 20.3 ± 4.3 ml/kg blood had been replaced by 79.7 ± 15.9 ml/kg cryostadloid, an additional 60.9 ± 31.9 ml/kg Ringer’s had to be infused during the observation period to maintain COP at predilution values. In this group, COP decreased

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significantly compared with that in the undiluted control animals (26.4 ± 4.4 vs. 13.4 ± 2.5 cmH₂O, \( P < 0.001 \)), and body weight increased by 13%. These parameters did not change in dextran-treated animals. During hemodilution, there were no significant changes in arterial oxygen partial pressure or arterial carbon dioxide partial pressure.

**Microcirculation**

In all three experimental groups no statistically significant change in the diameters of the terminal arterioles, capillaries, and collecting venules was observed. In control and colloid-treated animals, capillary erythrocyte velocity (table 1) remained at predilution values. In contrast, a statistically significant decrease in mean capillary erythrocyte velocity was observed in the crystalloid group. Figure 3 shows the velocity distribution profile in the dextran group mean capillary erythrocyte velocity was unchanged until 60 min after dilution. The profile for the Ringer’s group was bi-modal: in 70 of the 109 vessels flow had ceased, whereas the erythrocyte velocity in the perfused capillaries remained in the predilution range. The reduced functional capillary density \( (P < 0.01, \text{table } 1) \) also indicated heterogeneity of perfusion during crystalloid dilution. Erythrocyte velocity and functional capillary density did not change in control or colloid-treated animals.

**Surface Oxygen Partial Pressures**

In all three groups tissue surface oxygen partial pressures were distributed in a bell-shaped, physiologic histogram during the predilution phase (fig. 4). The apparent distribution of oxygen partial pressure remained unchanged in control and colloid-treated animals, indicating homogeneous tissue oxygenation during colloid dilution. The mean values did not change significantly (table 1). In contrast, the histogram of the crystalloid-treated animals appeared shifted to the left 60 min after dilution. Mean surface oxygen partial pressure was markedly reduced at this time, and 36% of the values were in the hypoxic range of 0–5 mmHg \( (P < 0.01; \text{table } 1) \).

**Table 1. Hematocrit (Hct), RBC Velocity (vRBC), Functional Capillary Density (FCD), Mean Surface \( P_o \), and Percentage of \( P_o \) Values in the Lowest Class (Hypoxic Range) during Control Experiments (Ctrl) and before, Immediately, and 60 Minutes after Hemodilution (HD) with Dextran 60 (Dx) or Ringer’s Lactate Solution (RL).**

<table>
<thead>
<tr>
<th></th>
<th>Before HD</th>
<th>End of HD</th>
<th>60 min Later</th>
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<tbody>
<tr>
<td>Hct (%)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Ctrl (n = 12)</td>
<td>49 ± 2</td>
<td>49 ± 2</td>
<td>48 ± 2</td>
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<tr>
<td>Dx (n = 22)</td>
<td>46 ± 3</td>
<td>29 ± 6</td>
<td>30 ± 1</td>
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<tr>
<td>RL (n = 22)</td>
<td>46 ± 3</td>
<td>30 ± 1</td>
<td>30 ± 1</td>
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<tr>
<td>vRBC (mm/s)</td>
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<tr>
<td>Ctrl (74 caps)</td>
<td>0.34 ± 0.1</td>
<td>0.37 ± 0.1</td>
<td>0.34 ± 0.2</td>
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<tr>
<td>Dx (96 caps)</td>
<td>0.34 ± 0.1</td>
<td>0.35 ± 0.1</td>
<td>0.30 ± 0.2</td>
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<tr>
<td>RL (105 caps)</td>
<td>0.35 ± 0.1</td>
<td>0.30 ± 0.2</td>
<td>0.10 ± 0.2† §</td>
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<tr>
<td>FCD (n/unit)</td>
<td></td>
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<tr>
<td>Ctrl (n = 6)</td>
<td>8 ± 2</td>
<td>8 ± 2</td>
<td>8 ± 2</td>
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<tr>
<td>Dx (n = 10)</td>
<td>9 ± 3</td>
<td>9 ± 3</td>
<td>7 ± 4</td>
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<tr>
<td>RL (n = 10)</td>
<td>11 ± 6</td>
<td>9 ± 5</td>
<td>3 ± 3† §</td>
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<td>( P_o ) (mmHg)</td>
<td></td>
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<tr>
<td>Ctrl (n = 6)</td>
<td>19 ± 3</td>
<td>19 ± 4</td>
<td>19 ± 4</td>
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<tr>
<td>Dx (n = 12)</td>
<td>19 ± 4</td>
<td>19 ± 4</td>
<td>18 ± 4</td>
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<tr>
<td>RL (n = 12)</td>
<td>20 ± 5</td>
<td>15 ± 3† §</td>
<td>8 ± 3† §</td>
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<tr>
<td>Hypoxic range (%)</td>
<td></td>
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<tr>
<td>Ctrl (n = 6)</td>
<td>0 ± 1</td>
<td>0 ± 1</td>
<td>0 ± 1</td>
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<tr>
<td>Dx (n = 12)</td>
<td>0 ± 1</td>
<td>1 ± 1</td>
<td>3 ± 2</td>
</tr>
<tr>
<td>RL (n = 12)</td>
<td>1 ± 1</td>
<td>2 ± 3</td>
<td>35 ± 20† §</td>
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Values are mean ± SD.  
CAPS = total number of registered capillaries in each group.

\[ * P < 0.05, \text{within group.} \]
\[ † P < 0.05, \text{within group.} \]
\[ $ P < 0.05, \text{Dx versus RL.} \]
\[ † P < 0.05, \text{Dx versus RL.} \]

**Discussion**

Despite much discussion, there is no agreement as to which is best performed using colloid solutions such as saline and crystalloids and colloids or dextran. As far as the investigators most investigated the colloids and advantages. In fact, large amounts of fluid is administered because of their colloid osmotic gradient.
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**Fig. 4.** Distribution profiles of surface oxygen pressures before, immediately after, and 60 minutes after hemodilution with dextran or Ringer's solution. For each study, the histograms combine n single determinations performed in 6 control animals and 12 animals in each experimental group; *x* is the arithmetic mean value.

**Survival**

All of the control (*n* = 6) and colloid-treated (*n* = 12) animals survived the 48-h observation period. In contrast, only 7 of the 12 hamsters treated with Ringer's solution were alive 24 h (*P < 0.05*) after dilution. After 48 h, only 2 animals in this group were alive (*P < 0.01*). No signs of pulmonary edema could be found on macroscopic section. In 1 animal (Ringer's group, death on the 2nd day), the venous catheter had perforated the vena cava. All other catheters were positioned satisfactorily.

**Discussion**

Despite much discussion over the past two decades, there is no agreement on whether volume resuscitation is best performed with exclusively crystalloid solutions, such as saline and Ringer's, or a combination of crystalloids and colloids, such as hydroxyethylstarch or dextran. As far as pulmonary function is concerned, most investigators agree that neither the crystalloid nor the colloid regimen has specific advantages or disadvantages. In fact, the lungs remain unaffected by large amounts of fluid and a wide variation in COP, perhaps because of their capacity to increase lymphatic drainage by up to 400%. The adjustment of transcapillary osmotic gradients by redistribution of interstitial alumin may be an additional mechanism of pulmonary adaptation to large volume or COP shifts. However, function of tissues other than the lungs, where these mechanisms are less effective, might be compromised by large volume or COP shifts.

Most previous investigations that studied organ perfusion during fluid resuscitation used models of severe circulatory shock. In these models, the capillary endothelium may have been altered before the onset of volume therapy by persistent ischemia and hypoxia or circulating toxins. However, clinical practice is different: hypovolemia can be caused by an increase in vascular volume in the capacitance system (vasodilating anesthetics, or ventilation using positive end-expiratory pressure), fluid redistribution into a “third space,” blood loss during surgery, or trauma. These are situations where early fluid substitution is intended to maintain normovolemia in patients with an intact vascular system. Moreover, previous studies comparing the crystalloid and colloid treatment regimens did not investigate the effect of fluid composition on nutritive capillary perfusion, which is crucial for organ function and tissue viability.

The most direct method to investigate the microcirculation is by in vitro microscopy. With our technique, the microvessels in the hamster skinfold chamber could be studied in the awake animal without acute surgical trauma. This technique also avoids the side effects of anesthesia, controlled ventilation, and trauma-induced acute inflammation that are inevitable accompaniments of other microcirculation models. Electron-microscopic studies demonstrated the structural integrity of this chronic preparation. The observations in the current study were confined to the microcirculation of a bundle of skeletal muscle from the dorsal midline of the skin to the anterolateral thorax (musculus cutaneus), but the results may be representative for skeletal muscle tissue.

A protocol using incremental isovolemic hemodilution was chosen to minimize endothelial trauma, activation of mediator cascades, and baroreceptor reflexes that may occur even during transitory hypovolemia. The exchange volume of approximately 19.5 ml/kg is comparable to an acute blood loss of 1,300 ml in an adult human. In accordance with previous studies, a four times larger volume of crystalloids was infused to maintain the intravascular fluid volume as estimated by measuring CVP despite the rapid transcapillary equilibration of these solutions. In a shock model used by Wang and coworkers, a rapid infusion of four times
of the volume lost increased CVP to nearly 200% of preshock level, but microcirculatory blood flow as measured by laser Doppler flowmetry could not be restored. In the animals of the colloid group no further fluid therapy was necessary to maintain CVP at predilution values.

During hemodilution systemic oxygen delivery is maintained by increasing cardiac output to compensate for the decreased Hct. The increased flow results in a greater organ perfusion as measured by the radioactive microsphere technique or by electromagnetic flowmeters (for review, see Messmer23). This increase in perfusion is usually attributed to capillary recruitment23 (an increase in perfused capillaries per tissue volume). However, in our study functional capillary density remained constant. Another possible consequence of increased organ perfusion could be an increase in capillary erythrocyte velocity, which also remained unchanged in our study. Similar observations were reported in other models of isovolemic hemodilution in which erythrocyte velocity and erythrocyte flux (the number of erythrocytes passing a capillary per unit time) remained unchanged.24,25 These observations suggest a regulation of erythrocyte flux, which is constitutive for local oxygen delivery.26 During normal conditions, the volume fraction (tube Hct) of erythrocytes in microvessels (diameter <500 mm) is as much as 50% less than systemic Hct, mainly because of a fluid dynamic phenomenon, the Fahraeus effect27: blood cells in the center of the flow profile travel up to two times faster than the marginal plasma layer. Thus, the constancy of capillary erythrocyte flux and velocity (local oxygen transport capacity) during hemodilution with dextran despite an increased organ blood flow may be the result of an increase in capillary plasma velocity. This would be equivalent to a reduction of the Fahraeus effect. Unfortunately, capillary plasma velocity cannot be quantified with current techniques. However, this hypothesis is confirmed by experiments showing that erythrocyte flow fraction (discharge Hct) of biologic capillaries approximates systemic Hct at various degrees of hemodilution.28 In addition, an increased ratio of tube to systemic Hct during progressive hemodilution has been shown.29 Both observations agree with an increase in capillary plasma velocity while erythrocyte velocity remains unchanged.

The mechanism of the presumed increase in capillary plasma velocity remains difficult to understand because dextran does not increase plasma fluidity. (Hemodilution increases whole-blood fluidity by diluting the blood cells, which generate most of blood's viscosity.) However, dextran has recently been shown to form a 50–100-nm-thick layer on the luminal surface of capillary endothelium thereby reducing negatively and positively charged domains.29 It may be that plasma flow is facilitated by reduced interaction of endothelial receptors with specific plasma proteins (e.g., procoagulatory factors or albumin).

The decreases in capillary perfusion and tissue oxygenation in the animals hemodiluted with Ringer's occurred progressively. This finding suggests that a slow process initiated by Ringer's lactate infusion rather than the rheologic properties of that solution caused the changes in our study. The progressive formation of tissue edema may be the underlying mechanism of these changes. In the Ringer's group, gradual worsening of the quality of the microscopic pictures (blurring of cellular and vascular boundaries) was observed 30–60 min after dilution and may have been caused by the increasing tissue edema. Because of the nearly unrestricted passage of Ringer's into the interstitial space, the Starling forces establish a new pressure balance across the capillary wall: interstitial hydrostatic pressure increases by fluid accumulation, and the increasing dilution lowers interstitial oncotic pressure to a greater extent than intravascular oncotic pressure. The resulting inward forces increase intraluminal hydrostatic pressures in capillaries and collecting venules and reduce the arteriolar-to-venular pressure difference. The compensation for increased filtration by lymphatic drainage as in the pulmonary system is insufficient in soft tissues.30 At the same time, endothelial and erythrocyte edema also occur.31 Both factors increase hindrance to capillary perfusion. This is reflected in our data by the decrease in capillary erythrocyte velocity and functional capillary density. The resulting tissue hypoxia may cause or perpetuate metabolic acidosis as demonstrated during crystalloid resuscitation by Brueckner et al.44

Our findings agree with theoretical calculations by Mirashemi et al.23 Their computer model of total body circulation consists of both series and parallel coupled vascular compartments and a constant pressure and flow source. In their model the lower whole-blood viscosity increases arteriolar pressure and thus the arteriolar-to-venular pressure difference. However, this benefit of hemodilution is only preserved when solutions used that are isoncotic to plasma.

The severity of the complications after crystalloid therapy is highlighted by the low survival rates among the hamsters treated.

Within hours after surgery the loss of appetite and as signs of circulatory and oxygen-carrying capacity is usually considered the dextran group. The consequence of qualitative and vascular collapse.

The reduction of oxygen delivery in the hamster model was maintained by cell compensation for hypovolemic hypovolemia. The increased oxygen delivery in the hamster model was maintained by cell compensation for hypovolemic hypovolemia. It has been demonstrated that the oxygen supply to the adult respiratory distress syndrome is sufficient to the evidence that the artificial respiration effects of an artificial respiration effect on microcirculation.

The authors thank A. Greiner for an extensive review of the literature.

References


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the hamsters treated with Ringer’s solution in our study. Within hours after the experiment, the animals showed loss of appetite and droveness, which we interpreted as signs of circulatory failure. Because the change of oxygen-carrying capacity was kept within the range usually considered to be tolerable and was identical in the dextran group, the high mortality is likely to be a consequence of a primary lesion of the terminal vascular bed.

The reduction in oxygen transport capacity in our hamster model is comparable to an acute blood loss of 19.5 ml/kg. When normovolemic conditions are maintained by cell-free substitutes, this reduction is compensated for by an increase in cardiac output. With colloid-containing solutions this compensation is achieved without compromising peripheral oxygen delivery. In contrast, the large volume of crystals needed to maintain normovolemia caused severe edema in skeletal muscle and presumably in other soft tissues. It has been demonstrated in humans in comparable conditions that the resulting malperfusion and hypoxia jeopardize the outcome by increasing the incidence of adult respiratory distress syndrome. Our results add to the evidence that volume therapy should include artificial colloids with their long-lasting, beneficial effect on microvascular perfusion and tissue oxygenation.

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References


\[ pH = \text{function of glucose, oxygen, and carbon dioxide levels} \]

\[ \text{Metabolism = function of pH and oxygenation} \]

A Study of pH-Stat and Metabolic Hypothesis

**Background:** The major goal of this study was to determine if the increase in the brain blood flow (BBF) of the brain during hemorrhagic shock can be improved by profound hypocapnia and normothermia during the early phases of the shock. The rationale for this study was based on the hypothesis that a decrease in the BBF would be associated with a decrease in the oxygen consumption of the brain. The study was also designed to evaluate the effects of a constant rate of oxygen delivery on the oxygen consumption of the brain in relation to the BBF.

**Methods:** New Zealand White rabbits were anesthetized with halothane and placed on a mechanical ventilator. The arterial blood was monitored to ensure a constant level of oxygen saturation and a constant rate of oxygen delivery. The BBF was measured continuously with a laser Doppler flowmeter. The BBF was expressed as a percentage of the pre-shock value. The effects of a constant rate of oxygen delivery on the BBF were evaluated by observing the changes in the BBF over time. The effects of a constant rate of oxygen delivery on the oxygen consumption of the brain were evaluated by observing the changes in the oxygen consumption of the brain over time.

**Results:** The results of the study showed that the oxygen consumption of the brain was negatively correlated with the BBF. The BBF was found to increase with a decrease in the arterial oxygen saturation and a decrease in the arterial carbon dioxide tension. The BBF was also found to decrease with a decrease in the arterial oxygen saturation and an increase in the arterial carbon dioxide tension.

**Conclusions:** The results of the study suggest that the BBF of the brain during hemorrhagic shock can be improved by a constant rate of oxygen delivery. The results also suggest that the oxygen consumption of the brain is negatively correlated with the BBF.