

## HYPERTONIC/HYPERONCOTIC RESUSCITATION AFTER INTESTINAL SUPERIOR MESENTERIC ARTERY OCCLUSION: EARLY EFFECTS ON CIRCULATION AND INTESTINAL REPERFUSION

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Received 20 Jul 1999; first review completed 9 Sep 1999; accepted in final form 15 Dec 1999

**ABSTRACT**—The objective of the study was to determine the early effects of hypertonic/hyperoncotic starch resuscitation after 2 h occlusion of the superior mesenteric artery (SMA) in comparison to animals reperfused without treatment and isotonic resuscitation. SMA was clamped (18 pigs, 19–23 kg) for 2 h followed by a 2-h reperfusion period, which was initiated with isotonic (ISO) (35 mL/kg 0.9% NaCl and 5 mL/kg 10% hydroxyethyl starch within 30 min) or hypertonic/hyperoncotic resuscitation (HHES) (7.5% NaCl/10% hydroxyethyl starch within 5 min). Cardiac output (CO), mean arterial blood pressure (MAP), serum lactate, antimesenteric serosal Laser-Doppler values (LD), and intramural pHi (tonometry) were measured. Without resuscitation at the onset of reperfusion MAP ( $70 \pm 3$  mmHg) decreased to  $40 \pm 3$  mmHg and CO to 31% of baseline values after 30 min. Serum lactate increased to  $5.1 \pm 1.6$  mmol/L without improvement. The decrease of CO was attenuated only during the initial 30 min of reperfusion in the ISO group, but significantly better counteracted by hypertonic/hyperoncotic resuscitation. Without treatment, LD flow of the ileum (baseline 23–27 LD units) recovered but intramural pH (pHi) remained significantly decreased ( $7.26 \pm 0.05$ ). With isotonic resuscitation LD values ( $21.8 \pm 2.1$  LD units) and intramural pHi ( $7.09 \pm 0.14$ ) decreased even more ( $P < 0.05$ ) whereas the HHES group showed a significant hyperemic reaction and a normalization of the intramural pHi and serum lactate within 30 min. Hypertonic/hyperoncotic resuscitation significantly improves MAP and CO during reperfusion shock and induces an immediate hyperemic reperfusion reaction of the intestinal microcirculation. Adequate isotonic fluid replacement in order to restore the postischemic plasma volume loss may cause a pronounced deterioration of intestinal perfusion.

**KEYWORDS**—Mesenteric vascular occlusion, postischemic intestinal reperfusion, small volume resuscitation, laser doppler flowmetry, tonometry

### INTRODUCTION

Reperfusion of the ischemic intestine is characterized by pronounced shock and additional reperfusion injury of the intestinal wall (1,2). Therefore, the primary therapeutic goal is not only to reestablish an adequate circulation with sufficient arterial blood pressure and cardiac output, but, more specifically, a quick metabolic recovery of reversible intestinal damage (3) avoiding secondary tissue damage. Catecholamines used routinely in clinical shock treatment lead to a further decrease of microcirculatory blood flow and metabolic recovery of the intestine (4). On the other hand, the administration of large fluid volumes for the stabilization of arterial blood pressure includes an increased pulmonary risk. Under these circumstances, “small volume resuscitation” with a severely hypertonic and hyperoncotic solution that is administered over a short period of time might pose an alternative (5). Hypertonic/hyperoncotic treatment combines the beneficial effects of a rapid intravascular fluid redistribution from extravascular sources, swollen endothelia in particular, peripheral arterial vasodilation, increased myocardial contractility, and the improvement of cardiac output and the microcirculation in

vital organs such as brain, liver, and heart, which are described in hemorrhagic and septic shock (6). Comparative studies of early intestinal reperfusion after superior mesentery artery occlusion using hypertonic/hyperoncotic starch solutions are not known.

The aim of the present animal study was to investigate the early effects of a hypertonic/hyperoncotic starch solution (HHES) after intestinal ischemia on hemodynamic parameters, on intestinal microcirculation and intramural pH (pHi) of the ileum in pigs.

### MATERIALS AND METHODS

#### Animals and preparation

Experiments were performed in accordance with the German legislation on protection of animals and the “Guide for the Care and Use of Laboratory Animals” [DHEW Publication No. (NIH) 85–23] and approved by the review board of the university. Eighteen pigs (19–23 kg body weight, 9 weeks old) were anesthetized with thiopental–sodium (250–350 mg/h) and piritramid (7.5 mg/h) and were ventilated mechanically after tracheotomy (Bennett MA-1B, inhalation volume 350–450 mL, respiration rate 16 breaths/min,  $\text{FiO}_2 = 0.3$ ). The animal was placed on a homeothermic blanket to maintain a constant body temperature of 38–38.5°C: Catheters were inserted into the abdominal aorta (blood pressure), the superior vena cava, and the superior mesenteric vein (blood samples). A thermodilution catheter (7.5F Swan Ganz balloon catheter) was placed into the pulmonary artery. Systemic arterial, central venous and pulmonary arterial pressures were registered continuously (Siemens Sirecust 404.1).

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After a median laparotomy, the aortic origin of the superior mesenteric artery (SMA) was prepared for later clamping. A catheter for the tonometric measurement of intestinal pHi (Tonometrics Inc. USA) was inserted into a proximal loop of the ileum. The middle part of the ileum was prepared for later laser Doppler (LD) scanning of the microcirculation (Vasamedics Inc., USA) and mobilized outside the abdomen and, shortly before the beginning of the control phase of the experiment, was fixed in a special mounting device for repeated scanning (cf. experimental design below).

### Experimental design

Three groups with six pigs each were randomized after finishing the preparation of the superior mesenteric artery. All groups received 20 mL/kg/h electrolyte solution beginning with laparotomy to replace the normal fluid loss (ventilation, open abdomen, preparation). In preliminary experiments in sham-operated animals, this amount of fluid substitution was found necessary to maintain a stable hematocrit.

After preparation, the experiments started with a control phase of 30 min. Baseline measurements of cardiac output, blood pressure, blood gas analysis, and intestinal LD flowmetry were taken. The SMA was clamped for 2 h to induce mesenteric ischemia. Hemodynamic measurements (blood pressure, cardiac parameters) and blood samples were taken 30, 60, and 120 min after onset of ischemia. Reperfusion after reopening of the clamped SMA lasted 2 h with hemodynamic measurements (cardiac output, blood samples) after 15, 30, 60, 90, and 120 min.

The following experimental groups were formed:

*Group 1* (n = 6; CONTROL) had no additional fluid replacement during the posts ischemic reperfusion phase.

*Group 2* (n = 6; ISO) received isotonic fluid replacement (40 mL/kg BW containing 35 mL of 0.9% sodium–chloride and 5 mL of 10% hydroxyethyl starch 200000/0.5) during the first 30 min of the reperfusion phase. Two-thirds of the total reperfusion volume were given within the first 15 min after removing the clamp from the superior mesenteric artery.

*Group 3* (n = 6; HHES) received 5 mL/kg BW 7.5% sodium–chloride/10% hydroxyethyl starch 200000/0.5 within 5 min starting simultaneously with reopening of the superior mesenteric artery.

### Tonometry

Tonometric estimation of the intramural pHi (sigmoid catheter of Tonometrics Inc. USA) was performed during the control phase, after 30, 60, and 120 min of ischemia and reperfusion as inaugurated by Fiddian–Green (7) and validated by Antonsson et al. (8) using a constant equilibration time (30 min, correction factor 1.47) and a Ciba Corning 288 blood gas system. The correction factor for the tonometric pCO<sub>2</sub> measurements depends on the equilibration time and, therefore, was determined *in vitro*. To do so, the tonometric catheter was placed into a air-tight glass bottle filled with bicarbonate-buffered (20 mEq/l) saline at 37°C and bubbled with different air/CO<sub>2</sub> mixtures. pCO<sub>2</sub> in the fluid was controlled by repeated measurements using a Radiometer ABL blood gas analysis system. The tonometric catheter was filled with 2.5 mL 0.9% NaCl. pH and pCO<sub>2</sub> of the catheter were measured after equilibration times between 10 and 60 min. During the *in vivo* experiments an equilibration time of 30 min (correction factor 1.47) was used to estimate intramural pHi during control phase and after 30, 60, and 120 min of ischemia and reperfusion. Data were multiplied by the correction factor to obtain the steady state pCO<sub>2</sub> (pCO<sub>2ss</sub>) of the intestinal wall. pHi was calculated from pCO<sub>2ss</sub> and from the arterial bicarbonate concentration using the Henderson–Hasselbalch equation.

### Laser Doppler measurements

In the present study, a “scan” of LD measurements (LDF monitor, Vasamedics, USA, 0.8 mm probe diameter) of the intestinal microcirculation at 50 randomly determined sites was taken during the control phase, after 110 min of ischemia and after 10, 60, and 120 min of reperfusion at the antimesenteric side of the ileum to determine the quality of microcirculation and percentage of low flow values (9). The median of these 50 flow values was used for further calculations and represents regional serosal flow. Values below 15 LD units were defined as “low flow areas” as a further parameter of microcirculatory quality.

### Plasma volume

Plasma volume (PV) changes were calculated by hematocrit measurements using the following formula (10):

$$dpV\% = \frac{100}{100 - (\text{Hct}_{\text{pre}})} \times \frac{100 \times (\text{Hct}_{\text{post}})}{\text{Hct}_{\text{post}}}$$

[dpV% = percentage of plasma volume change;  
Hct = hematocrit; pre = preischemic; post = posts ischemic]

### Plasma chemistry

Central venous and femoral artery blood samples were collected at the end of the control phase, after 30, 60, and 120 min of superior mesenteric artery occlusion, and after 30, 60, and 120 min of reperfusion. Blood gas analysis was performed from arterial and venous samples using a Ciba Corning 288 blood gas system. Plasma Na<sup>+</sup> was determined by a Boehringer Mannheim/ Hitachi 717 Automatic Analyzer. Plasma lactate was measured with a Model 23 Lactate Analyzer (Yellow Springs Instr., OH).

### Statistics

Data were analyzed within each group between baseline and subsequent phases of intestinal ischemia and reperfusion. Within-group differences were determined by the Friedman repeated measures test on ranks followed by pairwise multiple comparisons using the Student–Newman–Keuls method on ranks. Statistical tests for differences between the groups were performed with the Kruskal–Wallis one-way ANOVA-procedure using Dunn’s test for pairwise multiple comparisons. Differences were considered significant at  $P < 0.05$  (all statistics and graphics with Sigma-Stat and Sigma-Plot software, Jandel Scientific Erkrath, Germany). Values are presented graphically as means ± standard error of the mean (SEM). Statistically significant differences of parameters within one group during the course of the experiment are not shown in tables or figures but are only stated in the text.

## RESULTS

All three experimental groups were well comparable in baseline parameters; there were no statistically significant differences of haemodynamic data or of blood gases. Occlusion of the SMA went along with an increase of mean arterial pressure (MAP) of up to 20 mmHg (Fig. 1). During the 2 h of ischemia, MAP remained stable in all three groups without significant differences between the groups. With the onset of reperfusion, MAP dropped to 52 ± 6 mmHg after 30 min in the untreated control group (CONTROL) with a slow further decrease to 40 ± 3 mmHg at the end of the study. The treatment with isotonic reperfusion (ISO) led to an initial improvement of MAP during early reperfusion, which was 50 ± 3 mmHg at the end of the experiment. The HHES group had the best arterial pressure during the reperfusion phase, without any observation of arterial hypotension upon bolus injection of the hypertonic/ hyper-

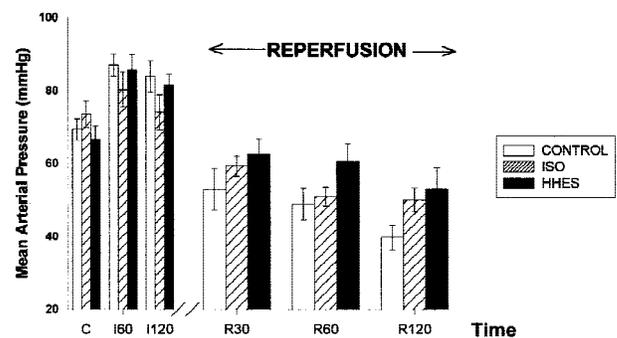


FIG. 1. Mean arterial pressure before (B), during (I60, I120) and after (R30, R60, R120) 2 h of superior mesenteric artery occlusion. Means ± SEM; Open bars: untreated controls; hatched bars: ISO; filled bars: HHES.

oncotic fluid. MAP was  $53 \pm 6$  mmHg at the end of the study. However, there were no statistically significant pressure differences between the three groups.

Cardiac output (CO) of the three groups was 4.3–5.0 L/min during the control period (Fig. 2) and decreased about 20–25% during intestinal ischemia without significant differences between the groups. At the beginning of reperfusion, CO of the untreated control group was 44% of baseline values seen after 30 min of reperfusion, with a gradual decline to  $1.5 \pm 0.14$  L/min at the end of the experiment. The ISO group showed significantly better CO values after 30 min of reperfusion ( $3.3 \pm 0.13$  L/min) as compared to the control group with a marked CO reduction during the remaining reperfusion time (final CO:  $1.9 \pm 0.29$  L/min). The HHES treatment with hypertonic/hyperoncotic fluid prevented the initial CO reduction during reperfusion, and cardiac output remained significantly better ( $P < 0.05$ ) than in the CONTROL group during the complete reperfusion phase. CO with  $3.2 \pm 0.27$  L/min was significantly better than that of the ISO group after 60 min of reperfusion.

Calculation of SVR and PVR are seen in Table 1 showing an increase of vascular resistance during intestinal ischemia in all groups. The values remained elevated during the complete reperfusion phase especially in the control group as compared to the other groups. PV changes calculated from the hematocrit data in all groups showed a loss of approximately 3–10% during mesenteric ischemia. In the control group the PV loss with 32.4% became more pronounced during the first 30 min of reperfusion. In the ISO group, a positive fluid balance was achieved after 30 min of reperfusion by the isotonic volume replacement ( $P < 0.05$  vs. control and HHES). At the end of the experiment, PV with  $-7\%$  was slightly reduced as compared to basal values. With HHES, however, the secondary reduction of PV during reperfusion was largely prevented without reaching control values.

Central venous plasma lactate levels in all groups increased significantly during ischemia. During reperfusion there was a further increase of plasma lactate in the untreated control and the ISO group (Table 1). The control group showed no improvement at all of the plasma lactate level during reperfusion. Opposed to this, the ISO group displayed a near complete return of plasma lactate to basal values at the end of reper-

fusion, whereas in the HHES group, normal plasma lactate levels were already seen after 30 min reperfusion ( $P < 0.05$  vs. CONTROL and ISO within the first 60 min of reperfusion).

Intestinal blood flow as determined by laser Doppler scanning was comparable in all three groups during baseline conditions (Fig. 3). Tissue sections with readings  $<15$  LD units had been defined as “low flow areas” and were found at less than 15% of the measuring sites during baseline conditions (Table 2). Biological zero determined post mortem was between 3 and 5 LD units. During ischemia, the median flow dropped to 33% of baseline values in all groups, with more than 70% of readings indicating “low flow areas” ( $<15$  LD units). After onset of reperfusion, the control group median flow remained decreased below the preischemic baseline with 22.5% “low flow areas,” a percentage which nearly normalized towards the end of the experiment. The median LD flow of the ISO group was even more depressed during reperfusion ( $P < 0.05$  vs. CONTROL). The HHES group showed a pronounced hyperemic reaction of the intestinal wall ( $P < 0.05$ ) after onset of reperfusion (10 min). Median flow remained above basal levels during the 2-h reperfusion phase. The percentage of “low flow areas” was significantly lower ( $P < 0.001$ ) during the first 60 min of reperfusion as compared to the untreated control group and even lower than the initial baseline values.

Intramural acidosis of the ileum developed during ischemia with a decrease of intramural pH<sub>i</sub> (Fig. 4) below 7.0 in all groups, without significant differences between the groups. The pH<sub>i</sub> of the CONTROL group slowly increased during reperfusion of the superior mesenteric artery, without ever again achieving baseline values, however. The isotonicly reperfused ISO group showed an even more depressed recovery of pH<sub>i</sub> during reperfusion ( $P < 0.05$  vs. control group). After “small volume resuscitation” (HHES) at the beginning of reperfusion, within 30 min pH<sub>i</sub> of the ileum had normalized to physiological values. The differences in pH<sub>i</sub> are highly significant ( $P < 0.001$  vs. CONTROL and ISO).

## DISCUSSION

Reperfusion after small bowel ischemia from temporary SMA occlusion results in a reperfusion injury syndrome, which combines local alterations such as tissue acidosis (11) and an enhanced occurrence of “low-flow” areas with systemic changes such as cardiac dysfunction (9,12), increases of the systemic and pulmonary vascular resistance, and plasma volume loss. The systemic changes are in part due to a translocation and resorption of endotoxins from the gut which in turn generate or release cardiodepressant and vasoactive factors, which may be removed partially by hemofiltration (1,13). Local alterations of the intestinal wall induced by reperfusion are characterized by an increased local adherence and infiltration of neutrophils and the release of numerous vasoactive and inflammatory agents, such as oxygen-derived radicals, arachidonic acid products and cytokines, which may also affect organs not directly involved by intestinal ischemia such as lung and liver (14,15).

Microvascular consequence of reperfusion injury is endothelial swelling, which develops during ischemia and may con-

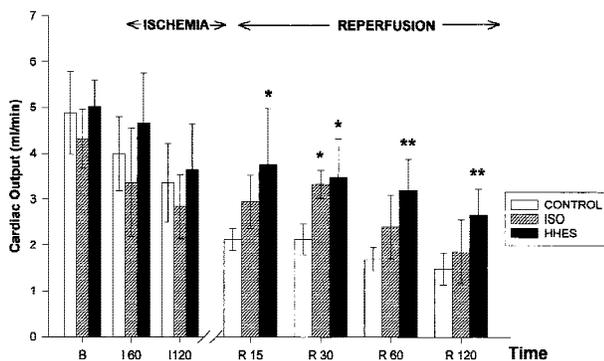


FIG. 2. Cardiac output before (B), during (I60, I120), and after (R15, R30, R60, R120) 2 h of superior mesenteric artery occlusion. Means  $\pm$  SEM; \* $P < 0.05$ ; \*\* $P < 0.05$  vs. control and ISO; Open bars: untreated controls; hatched bars: ISO; filled bars: HHES.

TABLE 1. Changes of systemic vascular resistance (SVR), pulmonary resistance (PVR), plasma volume (PV), and central venous plasma lactate levels (Lac) during mesenteric ischemia and 2 h of perfusion

Group	Baseline	Ischemia 120 min	Reperfusion 30 min	Reperfusion 60 min	Reperfusion 120 min
SVR (dyn s cm <sup>-5</sup> )					
Control	1150 ± 324	2163 ± 993	1918 ± 265**	2264 ± 666**	2290 ± 935
ISO	1223 ± 265	1614 ± 360	1143 ± 245	1447 ± 293	1747 ± 407
HHES	1049 ± 238	1883 ± 556	1451 ± 146	1527 ± 192	1638 ± 421
PVR (dyn s cm <sup>-5</sup> )					
Control	132 ± 39	178 ± 68	338 ± 82	548 ± 137**	545 ± 111
ISO	157 ± 49	209 ± 71	248 ± 162	286 ± 102	459 ± 226
HHES	131 ± 36	233 ± 68	249 ± 68	313 ± 156	404 ± 150
PV (%)					
Control	0	-10.4 ± 15.1	-32.4 ± 11.7	-33.3 ± 15.9	-21.9 ± 21.8
ISO	0	-3.7 ± 7.9	+14.4 ± 10**	-4.1 ± 7.4	-7.0 ± 8.1
HHES	0	-12.1 ± 15.3	-15.3 ± 13.9	-19.6 ± 12.0	-16.4 ± 14.7
Lac (mmol/L)					
Control	3.0 ± 1.1	5.1 ± 1.6	6.0 ± 1.6	5.4 ± 1.5	5.2 ± 1.4
ISO	2.1 ± 1.1	3.8 ± 0.9	5.5 ± 0.6	3.2 ± 0.5*	2.7 ± 0.7*
HHES	2.8 ± 1.1	3.5 ± 0.6	3.0 ± 0.4**	2.4 ± 0.7**	2.9 ± 1.3*

Means ± SEM, \**P* < 0.05 vs. control; \*\**P* < 0.05 vs. both other groups.

continue in the postischemic phase. The resulting vascular narrowing of the capillary bed has been shown to impede recirculation and metabolic recovery (10,16,17). As a consequence no-reflow or slow-reflow with secondary ischemia and an increased tissue damage by a prolonged duration of ischemia may develop. In our study the results of the untreated CONTROL group with a delayed recovery of intestinal pH<sub>i</sub>, permanently increased plasma lactate levels, and a depression of microcirculatory perfusion with an increased percentage of "low flow areas" in the LD measurements indeed indicate a prolongation of intestinal ischemia which together with reduced cardiac output and arterial pressure may further augment intestinal tissue damage (18).

Based on these considerations a primary goal of a rational reperfusion therapy is a fast and efficient improvement of the parenchymal microcirculation. "Small volume resuscitation" with eight times hypertonic saline plus a hyperoncotic admixture mobilizes interstitial water especially from the endothelium and from red blood cells. The resulting lowered hydraulic resistance (10,16,19) facilitates the washout of toxic metabo-

lites that have accumulated during ischemia. The dramatic increase of laser Doppler flow in the early reperfusion phase (Fig. 2 and Table 3) with a significant reduction of "low-flow areas" illustrate this effect. As a consequence, plasma lactate and intramural pH<sub>i</sub> had already normalized after 30 min reperfusion in this group. The data underline the synergistic effect exerted by "small volume resuscitation" on macro- and micro-hemodynamics, which is not achieved by pure volume replacement as done in the ISO group. Although the normalization of plasma volume in the ISO group went along with a rapid but temporary recovery of arterial pressure and cardiac output, there was even a deterioration of the intestinal microcirculation and pH<sub>i</sub> in comparison to the untreated CONTROL group.

The term "small volume resuscitation" has been introduced originally by Nakayama (20). But there are no data of hypertonic/hyperoncotic resuscitation for reperfusion shock after mesenteric vascular occlusion. Intestinal ischemia seems to be particularly accessible to hypertonic/hyperoncotic treatment due to the severe reduction of plasma volume during ischemia and early reperfusion. In the current experiments reperfusion of the ischemic intestine after 2 h of SMA occlusion without treatment led to shock and a marked decrease of CO to 40% of baseline values. This decrease is largely explained by the loss of plasma volume (33%), which represents about 22% of the estimated intravascular volume. Together with the reduced CO, systemic and pulmonary vascular resistance were increased. These changes were attenuated by hypertonic/hyperoncotic treatment. PV changes showed a less pronounced plasma loss during reperfusion explainable by the direct osmotic effects of

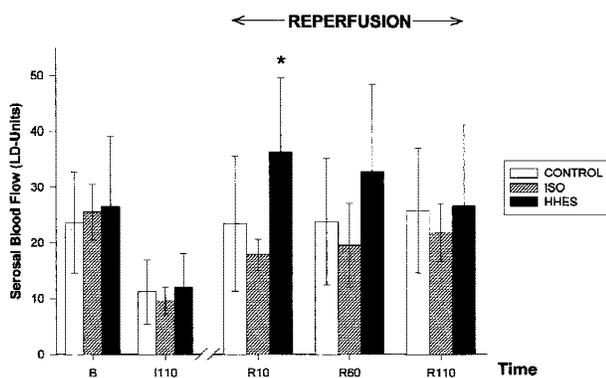


FIG. 3. Median of serosal ileal blood flow determined by Laser doppler flowmetry before (C), during (I110) superior mesenteric artery occlusion, and 2 h of reperfusion (R10, R60, R110). Means ± SEM, \**P* < 0.05 vs. control, Open bars: untreated controls; hatched bars: ISO; filled bars: HHES.

TABLE 2. Percentages of laser doppler low flow values (<15 LD units) during mesenteric ischemia (I) and 2 h of reperfusion

Group	Baseline	I110	R10	R60	R120
Control	12.6%	77.3%	22.5%	16.0%	15.0%
ISO	10.7%	79.4%	36.1%	31.9%	17.1%
HHES	13.6%	72.8%	12.2%*	6.7%*	12.3%

\**P* < 0.05 vs. CONTROL and ISO.

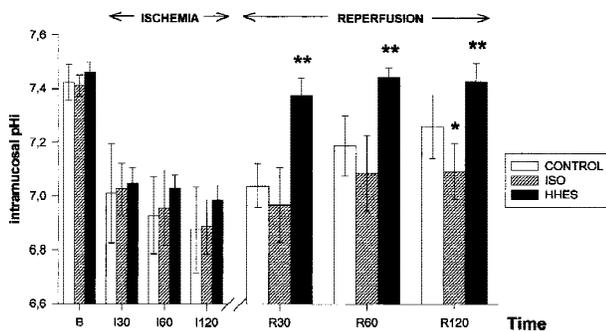


FIG. 4. Tonometrically determined pHi of the intestine before (B), during (I30, I60, I120) superior mesenteric artery occlusion, and 2 h of reperfusion (R30, R60, R120). Means  $\pm$  SEM, \* $P < 0.05$  vs. control, \*\* $P < 0.05$  vs. control and ISO; Open bars: untreated controls; hatched bars: ISO; filled bars: HHES.

“small volume resuscitation.” The stabilization of the circulating intravascular volume goes along with a significantly better CO as compared to the untreated CONTROL group and to the ISO group. Similar effects with an improved cardiac function have also been described after the treatment of experimental shock from endotoxemia or hypovolemia (5,21,22). A positive inotropic effect on the myocardium as an additional mechanism has not been proven (23).

The immediate improvement of organ perfusion on the microcirculatory level by hypertonic/hyperoncotic recirculation apart from the mechanisms discussed so far affects outcome by interrupting the vicious cycle of an initial slow/low/no-reflow followed by secondary ischemia with further disturbances of the microcirculation. The occurrence of this phenomenon is indirectly evidenced as an incomplete recovery of intramural pHi even after 2 h of reperfusion. A reduced pHi is indicative of anaerobic metabolism after inadequate tissue oxygenation of the intestinal wall (8,24). Moreover, tonometric measurements of pHi under zero flow conditions lead to an underestimation of mucosal acidosis (8). Small volume resuscitation appears to interrupt the vicious cycle at its very beginning by flushing the capillary bed and thereby removing toxic metabolites or adhering cells as well as supplying oxygen and nutrients. Similar effects are described for myocardial, pancreatic and liver perfusion (25,26).

To evaluate the effect of hypertonic/hyperoncotic treatment a group with isotonic reperfusion (40 mL/kg BW) as opposed to the 5 mL/kg BW hypertonic/hyperoncotic solution was introduced in the present investigation. Containing the same amount of electrolytes and 10% hydroxyethyl starch isotonic reperfusion volume was 8 times that of the “small volume resuscitation” group. Both groups only differed in the infused volume and the time course of its administration. The use of ISO goes along with a minor improvement of the MAP (without significance) and a somewhat better CO after 30 min of reperfusion despite a sufficient replacement of the plasma volume loss. Compared to the CONTROL group, SVR and PVR were improved, however, with a marked secondary increase during the second hour of reperfusion. Plasma lactate levels showed a delayed normalization starting also after 60 min of reperfusion. Most important are the results of the tonometric

determination of intestinal pHi and of LD flowmetry. They indicate a worsening of the microcirculatory perfusion even in comparison to the untreated CONTROL group with significantly reduced laser doppler values and a delay of intramural pHi recovery till the end of the reperfusion phase. A persistently depressed microvascular blood flow despite adequate isotonic resuscitation has also been observed in reperfusion studies after hemorrhagic shock using LD flowmetry or microspheres for investigations of the intestinal microcirculation (14,27,28). In the case of mesenteric vascular occlusion, the quality and quickness of an adequate intestinal reperfusion is not a matter of improving a low-normal perfusion but may be the difference between survival and demise of the ischemic intestine. To transfer these promising data to the clinical situation, further experimental follow-up studies are necessary.

Small-volume resuscitation has been studied most thoroughly in hypovolemic shock (5,27,29), where the use of hypertonic/hyperoncotic solutions seems to be superior to standard fluid treatment or simple hypertonic resuscitation (29). Another application of small-volume resuscitation is septic shock (21) and increased intracranial pressure (30,31). The use of hypertonic saline is limited by the resulting hypernatremia (32). In a recent clinical study, small-volume resuscitation during aortic aneurysm resection seemed to improve the hemodynamic parameters, the overall fluid balance, and the microcirculatory perfusion (33). The use of small-volume resuscitation for reperfusion of the ischemic intestine (e.g., embolic occlusion of the superior mesenteric artery) is not described but appears a logical consequence of the current study.

## CONCLUSIONS

In the present study, hypertonic/hyperoncotic resuscitation during reperfusion shock goes along with a significant improvement of the systemic hemodynamics and a rapid normalization of the intestinal intramural pHi caused by a hyperemic local blood flow, which is not sufficiently explained by the volume substitution alone as compared to isotonic infusion.

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