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Clinical Benefits After the Implementation of a Protocol of Restricted Perioperative Intravenous Crystalloid Fluids in Major Abdominal Operations

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Abstract

Background Perioperative fluid replacement is a challenging issue in surgical care. The purpose of the present study was to investigate the effect of two different perioperative hydration protocols on the outcome in patients undergoing major abdominal operations.

Methods This was a prospective study involving 61 patients (42 men/19 women; mean age: 52 years; age range: 18–81 years) who underwent major abdominal operations. The study had two distinct phases: before (conventional group; administered 30–50 ml/kg per day of crystalloid fluids; $n = 33$) and after the implementation of a protocol of restricted use of intravenous fluids (restricted group; administered less than 30 ml/kg per day of crystalloid fluids; $n = 28$). The total volume of intravenous crystalloid fluids infused was recorded until postoperative day (POD) 4. Morbidity, mortality, and the length of postoperative hospital stay were the main clinical variables.

Results Mortality was 4.9% ($p > 0.05$ between groups). Intravenous therapy in the restricted group was terminated earlier ($p < 0.001$) and the patients received 2.4 l less crystalloid fluid than did those in the conventional group from POD 1 through POD 4 ($p < 0.001$). The adoption of the restricted protocol shortened the postoperative hospital stay by 2 days ($p = 0.02$) and diminished the morbidity by 25% ($p = 0.04$).

Conclusions Restriction of perioperative intravenous crystalloid fluid is associated with reductions in morbidity and length of postoperative hospital stay after major abdominal operations.

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Introduction

Intravenous fluids are frequently used in surgical practice. Perioperative hydration is commonly provided during the operation, and, in most cases, the therapy continues for many days postoperatively. The rationales for the use of perioperative intravenous fluids in the surgical patient include correction of preoperative fluid deficit, replacement of insensible water loss, preservation of urine output, maintenance of arterial and central venous pressures, as an alternative to enteral feeding due to postoperative ileus, and to avoid the need for blood transfusion [1].

The exact quantity of intravenous fluid required for optimal hydration is not known or is roughly calculated. The correlation between extracellular water volume and fluid administration in surgery is poorly understood, and is a matter for debated. In current practice, the volume of fluids administered in major abdominal procedures can reach 4–6 l during the operation and approximately 10–20 l postoperatively [1, 2]. As a result, an increase in the patient's weight caused by an overload of intravenous fluids is often observed in the postoperative period [3].

During the postoperative period, surgeons routinely prescribe 30–50 ml/kg per day of fluids if the patient cannot tolerate oral/enteral feeding [1]. For example, for a patient weighing 70 kg, the total volume of intravenous fluid for 3 days of therapy ranges from 6.3 to 10.5 l. In this context, the adoption of protocols that restrict intravenous

fluids may reduce the occurrence of postoperative complications and shorten the hospital stay after a major operation [3–5]. An overload of fluids causing weight gain [1, 3–5] is associated with greater morbidity [2–4]. The excess of fluid volume may lead to cardiac dysfunction [2], pulmonary edema [6], gut edema [7], adynamic ileus [2], and episodes of vomiting [1]. Furthermore, larger amounts of intravenous fluids may impair the diffusion of O_2 in many tissues, induce hypoxia, and thus undermine the healing process [8]. Recently, a well-designed randomized trial reported a decrease of both postoperative infectious complications and hospital stay in patients who received a limited amount of intravenous fluid in comparison to a standard regimen [4]. However, the number of clinical trials focusing on the effects of intravenous fluids in surgery is limited, and more trials are necessary. At the Department of Surgery of the Federal University of Mato Grosso (Julio Muller University Hospital), we have recently changed the protocol of perioperative intravenous fluid therapy by adopting a fluid restriction protocol (ACERTO protocol) [9]. To evaluate it effectiveness, we investigated the effect of two different perioperative hydration protocols on the outcome in patients undergoing major abdominal operations.

Material and methods

The study design was approved by the Ethics Committee of the Julio Muller University Hospital, Cuiaba, Brazil. This was a prospective study involving 61 patients who underwent major abdominal operations in the infirmary of the Department of Surgery of the Julio Muller University Hospital. The study had two distinct phases: before (January 2004 to June 2005; $n = 33$) and after the implementation of the ACERTO protocol restricting the use of intravenous fluids (July 2005 to July 2007; $n = 28$). The operations performed are listed in Table 1. The patients were divided into two groups according to the intravenous fluid protocol they were administered perioperatively: the conventional group (patients who underwent surgery during the earlier phase), who received 30–50 ml/kg per day, and the restricted group (patients who underwent surgery during the later phase), who received no more than 30 ml/kg per day. The intraoperative volume of fluids was under the control of the anesthesiologist and followed the protocol of 10–20 ml/kg per hour [10]. The demographics of the two groups are provided in Table 2. Nutritional status was determined by a subjective global assessment [11]. Patients were classified either as normal or as having malnutrition.

Table 1 Operations performed before and after institution of the restricted intravenous fluids protocol

Operation	Conventional ($n = 33$)	Restricted ($n = 28$)
Duodenopancreatectomy (Whipple)	3	2
Esophagectomy	1	4
Total gastrectomy	5	4
Subtotal gastrectomy	12	8
Colorectal[a]	12	10
Total	33	28

[a] Segmental colectomy, abdominoperineal resection of the rectum, and colorectal pull-through

Unless contraindicated, in both study periods patients received either intravenous kefazolin (1–2 g every 8 h, upper GI surgeries) or cephoxitin (1–2 g every 8 h, colorectal operations) as antibiotic prophylaxis initiated on induction of anesthesia (30–60 min before incision), repeated every 4 h if the operation had not been terminated, and continued for 24 h postoperatively. Re-feeding was programmed to begin on the day after operation, by either the oral or the enteral route, unless contraindicated, and nasogastric tubes were not routinely used. Deep vein thrombosis (DVT) prophylaxis was administered to all moderate-risk and high-risk patients with 20–40 mg of enoxaparin 1–2 h preoperatively and repeated daily during the postoperative period in individual basis. All patients were encouraged to early mobilization during the postoperative period, beginning the day after operation. Combined (thoracic epidural and general) or general anesthesia was employed at the anesthesiologist's discretion.

The total volume of infused crystalloid fluids was recorded until POD 4. The immediate postoperative period was defined as the first 24 h from the end of the procedure; POD 1 comprised the following 24 h, and so on, up to POD 4. Morbidity, mortality, and the length of postoperative hospital stay were the main clinical variables.

The chi-square test or Fisher's exact test was used to compare categorical data. The Mann-Whitney test or Student's *t*-test was used to compare continuous data. A repeated measure analysis of variance (ANOVA) was used to compare the volume of fluids received by the two groups during the 24 h perioperative period. Exact confidence intervals were computed for the overall rate of complications. A 5% ($p \leq 0.05$) level was established for significance.

Results

A total of 61 patients (mean age: 52 years; age range: 18–81 years; 42 men [68.9%] and 19 women [31.1%]) entered the study. The conventional group was comprised of 33 patients (54.1%), and the restricted group had 28 patients (45.9%). The mortality rate was 4.9% (2 deaths in the first

Table 2 Measures of quality of care and demographics of the patients in the two study groups

Variable	Period of the study		
	Early, conventional ($n = 33$)	Late, restricted ($n = 28$)	p Value
Gender (M/F)	23/10	19/9	0.88
Age (years)[a]	53 (18–81)	50 (18–74)	0.67
Operative time (min)[a]	270 (110–510)	230 (105–430)	0.03
Malnutrition (n; %)	14 (42.4)	14 (50)	0.75
Preoperative nutrition (TPN/EN/Oral)	1/8/5	2/6/6	0.70
Postoperative nutrition (TPN/EN/Oral)	7/7/2	3/6/1	0.72
Malignancies (n; %)	21 (63.6)	15 (53.6)	0.43
Blood transfusion (n; %)	13 (39.4)	6 (18.2)	0.13
Volume of blood (ml)	630 (0–2,900)	410 (0–5,000)	0.40
ASA = I/II/III	7/18/8	9/15/4	0.52
Albumin (g/dl)[a]	2.8 (1–4.3)	2.7 (1.2–4.0)	0.76
Use of nasogastric tube (n;%)	2 (6.1)	3 (10.7)	0.84
Re-feeding route (oral/enteral)	23/10	18/10	0.65
Deep vein thrombosis prophylaxis (n; %)	10 (30.3)	12 (42.8)	0.30
Antibiotic prophylaxis[b]	15 (45.4)	17 (60.7)	0.35
Anesthetic procedure (combined/general)	26/7	24/4	0.53

[a] Median and range

[b] Eighteen (54.6%) patients in the conventional group and 11 (39.3%) in the restricted group received antibiotics for more than 24 h (mean: 10 days; range: 5–25 days)

study period and 1 death in the second period; $p = 1.00$). The various measures of quality of care and other demographic data were similar in the two groups (Table 2).

Intravenous fluids

Data regarding the volume of crystalloid intravenous fluids during perioperative evolution are shown in Table 3 and Fig. 1. Only 9% (3/33) of patients treated by the conventional protocol were not receiving intravenous fluids by POD 4, whereas 39.2% (11/28) of patients under the restricted protocol no longer needed intravenous fluid administration by POD 4 ($p < 0.001$). In addition, patients in the conventional group received larger volumes of intravenous fluids than those in the restricted group ($p < 0.001$). The volume of crystalloid fluids was similar in the two groups at both the intraoperative (restricted: 17 ± 5 ml/kg per hour; conventional: 20 ± 9 ml/kg per hour; $p = 0.44$) and immediate postoperative period (restricted: 30 ± 12 ml/kg per hour; conventional: 37 ± 20 ml/kg per hour; $p = 0.49$). However, from POD 1 through POD 4, the fluid volume was significantly greater in the conventional group ($p < 0.01$). Patients in the restricted group received a mean volume of 2.4 l less than the conventional group in the postoperative period (conventional: 11,668 ± 3,034 ml; restricted: 9,263 ± 3,061 ml; $p < 0.001$). The mean volume of fluids

Table 3 Volume of crystalloid fluids infused in the two groups (mean ± SD)

Group	Intraoperative	IPO	POD 1	POD 2	POD 3	POD 4
Total volume of intravenous crystalloid (liters)						
Conventional**	5.4 ± 1.9	2.4 ± 1.3	2.7 ± 0.8*	2.5 ± 0.8*	2.3 ± 0.7*	1.9 ± 0.7*
Restricted	4.4 ± 1.6	2.2 ± 0.8	1.9 ± 1.2	1.8 ± 1.1	1.4 ± 1.0	1.2 ± 0.8
Intravenous crystalloid fluids per kg of body weight (ml/kg)						
Conventional**	20 ± 9[a]	37 ± 20	41 ± 12*	38 ± 12*	35 ± 10*	30 ± 11*
Restricted	17 ± 5[a]	30 ± 12	29 ± 18	28 ± 17	22 ± 15	19 ± 13

IPO immediate postoperative period-the first 24 h from the end of the operation; *POD* postoperative day-beginning with the first day following the IPO

* $p < 0.05$ (Student's t-test or Mann-Whitney test)

** $p < 0.001$ (repeated measures ANOVA)

[a] Data are ml/kg per hour of operative time

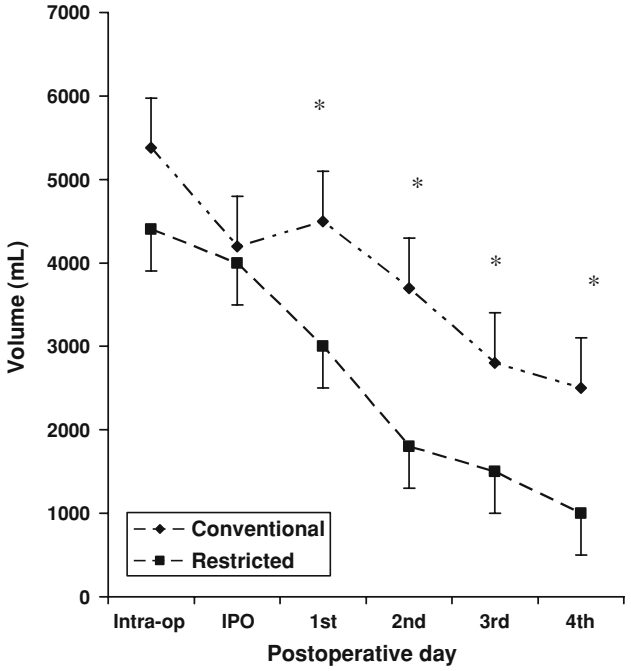

Fig. 1 Evolution of intravenous fluids received by the patients in the two groups. Data are mean and SEM. *Intra-op* intraoperative period; *IPO* immediate postoperative period. *$p < 0.01$ versus restricted group

received per day in the restricted group (1,852 ± 612 ml) was significantly lower in comparison to the conventional group (2,333 ± 606 ml; $p < 0.01$). The total volume received during the immediate postoperative period plus POD 1 was greater in the conventional group than in the restricted regimen (conventional, 5,098 ± 1,645 ml; restricted, 4,157 ± 1,509 ml; $p = 0.04$).

Perioperative nutritional management

All malnourished patients received either parenteral (1 patient in the conventional group and 2 patients in the restricted group) or oral/enteral therapy (all other malnourished patients in the 2 groups) for 7–10 days preoperatively. The patients undergoing restricted volume therapy re-initiated oral feeding one day earlier than the patients in the conventional fluid replacement group (conventional group: POD 2; range: POD 1 through POD 7; restricted: POD 1; range: POD 1 through POD 6; $p = 0.001$). Sixteen (48.5%) patients from the earlier phase of the study and 10 (35.7%) patients from the later phase received specialized nutritional therapy during the postoperative period for various reasons such as anastomotic dehiscence, hyporexia, and failure to attain the expected nutritional goals ($p = 0.31$).

Length of hospital stay

The total length of hospital stay was longer in patients who received conventional hydration (mean: 17 days; range: 7–103 days) than in patients from the restricted group (mean: 11 days; range: 4–41 days; $p = 0.03$). The postoperative stay was reduced by 2 days (conventional: mean: 12 days; range: 5–93 days; restricted: mean: 10 days; range: 2–24 days; $p = 0.02$) after the implementation of the restricted protocol.

Morbidity

The distribution of morbidities is shown in Table 4. The postoperative morbidity was reduced by 25% after the change in protocol (conventional group, 14/33, [42.4%]; restricted group, 9/28 [32.1%]; $p = 0.046$; OR, 2.86; 95% CI, 1.01–8.19). The incidence of anastomotic breakdown was similar in the two groups (conventional group, 6/33 [18.2%]; restricted group, 2/28 [7.1%]; $p = 0.27$; OR, 2.89; 95% CI, 0.53–15.6). In the patients with complications, the number of complications was similar between the two groups ($p = 0.14$). Pulmonary complications were more frequent in the conventional group than in the restricted group ($p = 0.05$). In the conventional group, only one case of DVT followed by pulmonary embolism occurred. No case of DVT occurred in the restricted group. All other patients with pulmonary complications had either pneumonia or atelectasis.

Table 4 Distribution of morbidities in the two groups

Complications	Conventional group ($n = 33$)	Restricted group ($n = 28$)	p Value
Surgical site infection	6	4	0.74
Anastomotic dehiscence	6	2	0.27
Pulmonary	9	2	0.05
Sepsis	2	2	1.00
Shock	2	1	1.00
Total number of complications[a]	25	11	< 0.01
No. of patients with complications	14	9	0.04
No. of complications per patient with complication	1.7	1.2	0.14

[a] Some patients had more than one complication

Discussion

The results obtained after the change in protocols showed that the restriction of postoperative intravenous fluids was possible and safe. Moreover, the postoperative routine of infusion of 30 ml/kg per day or less of crystalloid fluids was followed by earlier hospital discharge after major abdominal operations. In addition, postoperative morbidity was reduced with the restricted protocol. The overall findings suggest that the restriction of intravenous fluids not only is safe but also can reduce the length of hospitalization and diminish the incidence of postoperative infection.

Intravenous fluid replacement during operation and in the early postoperative period after an abdominal operation is not only useful but is vital to keeping the patient in stable condition [1]. Hypovolemia may lead to poor perfusion and oxygenation of tissues, impairment of various organ functions, and may lead to death. However, the overload of intravenous fluids is also deleterious and may cause more harm than benefit. The evidence is increasing, as reflected in recent publications, that there is danger associated with the excess administration of intravenous fluids perioperatively [1–4, 9, 12]. Too much water and sodium may lead to a prolonged period of ileus and increase the rate of postoperative complications [2–4, 12].

The mechanism(s) by which the overload of intravenous fluids causes these negative effects is poorly understood. However, there is some evidence that excessive intravenous hydration diminishes tissue oxygenation and leads to edema [1, 8, 9]. This effect may also be implicated in deficient anastomotic healing. Fluid accumulation in the lungs may cause deterioration of respiratory function, and thus may induce pulmonary complications [13]. In accordance with our review, an overload of intravenous fluids increased pulmonary morbidity in one study [4]. Conversely, multimodal protocols that include a restricted regimen of intravenous fluids are associated with fewer postoperative complications and a reduction in the length of hospital stay [9, 14].

It could be argued that patients who have a complicated postoperative course have a prolonged hospital stay and may therefore require larger amounts of intravenous fluids. Thus, the excess of fluids would be more an effect than a cause of both postoperative complications and prolongation of hospitalization. A recent randomized trial has addressed this question. The authors compared two distinct intraoperative fluid regimens in abdominal operations and reported significantly increased morbidity and prolonged hospitalization in patients receiving conventional intraoperative replacement of fluids [4]. In agreement, our findings showed that the total of the fluid volume received by patients in the perioperative 24 h plus the POD 1 (when all patients were receiving intravenous therapy) was greater in the conventional group, which was the group associated with a longer hospital stay. This early difference in the volume of fluids received favors a causative role rather than an effect of longer hospitalization.

The two groups in our series were similar with regard to many measures of quality of care and clinical characteristics, such as the incidence of malnutrition, nutritional therapy dispensed, malignancies, American Society of Anesthesiologists (ASA) score, serum albumin level, and volume of blood transfused. However, the duration of the operative procedure in the conventional group was significantly greater: the exact median difference between the two groups was 40 min. However, the two groups had similar operations and we do not believe that the difference in operative time was sufficient to jeopardize the findings. In addition, the mean amount of intravenous fluids administered during surgery was similar, taking into account the volume of fluids infused over time.

The present study, however, does have some limitations. The two groups were not randomized and our conclusions were based on comparisons between two periods of time. Thus, the improved results could reflect the evolution of perioperative care. However, the data were prospectively collected over a 3.5-year period and the operative procedures in the two groups were performed only 1.5 years apart. Routines of perioperative care in our institution, such as the use of prophylactic antibiotics, deep vein thrombosis prophylaxis, nutritional support dispensed, and early postoperative mobilization, did not change over the period of the study. Moreover, the routine use of nasogastric tubes had been abandoned before the study commenced, and early postoperative feeding has been routinely implemented in our hospital since 2002 [15].

The implementation of the restricted protocol was associated with early feeding, postoperatively. This was most relevant and suggests a reduced duration of adynamic ileus. Some studies in either minor or ambulatory surgeries suggest that high-dose fluid replacement may ameliorate discomfort, nausea, and vomiting after operation [16, 17]. However, these studies can not be extrapolated to the conditions accompanying a major abdominal procedure, in which third space fluid accumulation and altered capillary permeability may occur [2]. The increase in body weight associated with the excessive administration of intravenous fluids reported in other studies supports this argument [3, 4]. Furthermore, positive fluid balance may contribute to gut edema, which may lead to gut motility dysfunction. In agreement, elimination of flatus and feces seems to be delayed with the conventional regimen in comparison to the restricted regimens [2].

In summary, our data support previous reports demonstrating that conventional fluid replacement therapy after

abdominal operations should be discouraged in favor of a restricted protocol. Thus, we conclude that the restriction of perioperative intravenous crystalloid fluids is associated with reduced morbidity and length of hospital stay after major abdominal operations.

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