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Fluid Retention is Alleviated by Crystalloid but Not by Colloid Fluid after Induction of General Anesthesia: An Open-Labeled Clinical Trial

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Abstract

Background: Renal fluid conservation, which is possible to quantify by urine analysis, is often caused by dehydration. The present study aimed to determine whether such fluid retention could be reversed by crystalloid and/or colloid fluid during surgery.

Methods: Urine colour, specific weight, osmolality and creatinine concentration were used to calculate a "fluid retention index" (FRI) in 108 patients undergoing major abdominal surgery. Urine was collected at baseline and after flow-guided fluid volume optimisation with hydroxyethyl starch 130/0.4 (n=86) or Ringer's lactate (n=22). The third sample was taken after one hour of surgery.

Results: The mean preoperative FRI was 3.4 (SD 1.1) and did not change during the volume optimization. The FRI was unchanged from starch during the first hour of surgery, whereas it decreased from 3.6 to 2.9 in response to Ringer´s lactate ($P<0.01$). The urine became more concentrated when the urinary excretion was below 100 ml/hour. Preoperative fluid retention (FRI ≥ 4.0), which is cut-off for renal fluid conservation consistent with a body fluid deficit amounting to 3% of the body weight, was present in 32% of the patients. Such retention increased the risk of a minor postoperative increase in serum creatinine (n=15, odds ratio 6.4) despite a higher creatinine clearance during the surgery (155 versus 80 ml/min; $P<0.02$).

Conclusions: Ringer´s lactate, but not hydroxyethyl starch, decreased the urinary markers of fluid retention in the perioperative setting. Fluid retention increased the risk of a postoperative increase in serum creatinine.

Keywords: Dehydration; Fluid therapy; Serum creatinine

Introduction

The assessment of dehydration in the preoperative setting is of potential clinical value [1]. Although technical methods exist, they are rarely applied. Therefore, such assessments are usually based on anamnesis and body inspection.

An often overlooked but simple method for examining the degree of dehydration is urine analysis of the renal conservation of fluid. The principle is that, if the kidneys conserve fluid, metabolic waste products excreted at a relatively constant rate appears in higher urinary concentrations. Urine analysis of dehydration has been used mainly in sports medicine [2-4] but more rarely in the hospital care setting. However, accumulating evidence suggests that concentrated urine is of importance to health in hospital patients. Concentrated urine strongly affects how patients humans handle intravenous fluid [5,6] and is associated with a higher incidence of postoperative complications after hip fracture surgery [1] and higher mortality in acute geriatric care [7].

The present study explores the effects of four fluid programs on renal conservation of fluid before and during surgery. The hypothesis is that the liberal administration of crystalloid and/or colloid fluid during the induction of anesthesia and surgery alleviates or eliminates signs of preoperative dehydration in urinary samples. We also examined for a correlation between concentrated urine and a postoperative rise in serum creatinine.

Methods

Patients

The study comprised 111 patients (American Society of Anaesthesiologists [ASA] class I or II) who underwent laparoscopic (n=73) or open gastrointestinal (n=38) surgery under intravenous general anaesthesia for treatment of known or suspected gastric, colonic or rectal cancer. The exclusion criteria were liver or renal dysfunction, coagulation disturbances, obstructive pulmonary disease, atrial fibrillation and mental disorders.

The protocol was approved by the Ethics Committee of the First Affiliated Hospital, College of Medicine, Zhejiang University (Hangzhou, PR of China; No. 2011150, Official in charge: Zhangfei Shou). The study was registered at the Chinese Clinical Trial Registry (http://www.chictr.org/en; No ChiCTR-TNRC-14004479). Written informed consent was obtained from each subject.

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Procedure

The patients fasted overnight, and no premedication was given. The patients were anaesthetized at 8:00 am by using total intravenous anesthesia (continuous infusion of propofol and remifentanil), which was supplemented by sevoflurane, to reach a BIS value of 40–60. Tracheal intubation was facilitated with cisatracurium. The patients were mechanically ventilated using a tidal volume of 8 ml/kg at a positive end-expiratory pressure of 3 cm H_2O. The body temperature was maintained at 35.5°C or higher.

Fluid therapy was initiated after the anesthesia was induced. It consisted of volume optimization with 9 ml/kg in the form of three bolus infusions followed by a continuous infusion of 12 ml/kg during the first hour of the surgery.

The fluid used for the bolus infusions was HES (6% hydroxyethyl starch 130/0.4; Voluven®; Fresenius Kabi, Bad Homburg, Germany. This conventional fluid was previously used for volume optimization [8]. At the end of the study, a test group of patients received volume optimization with Ringer's lactate (RL).

To prevent preoperative dehydration, at 3 h before the surgery, 30 patients were given preloading with 500 mL of RL in a slow drip over 2 h.

The patients who had received RL for preloading or volume optimization were also given RL for the continuous infusion. Those who had received only HES for volume optimization received either HES or RL during the first hour of surgery. The patients were not allocated individually to the fluid programs but in groups of 25–30 subjects. These programs were chosen to provide several combinations of first-line and second-line fluid choices. The groups were as follows: (A) bolus and continuous with HES; (B) preloading with RL, bolus with HES, continuous with RL; (C) bolus with HES, continuous with RL; and (D) bolus and continuous with RL.

Figure 1 is a show-chart showing the different fluid groups and the number of patients in each group.

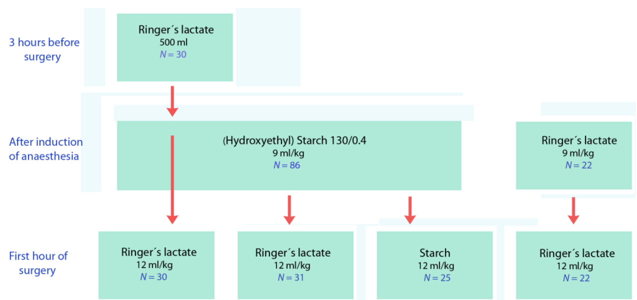

Figure 1: Flow-chart showing the different fluid groups and the number of patients in each group.

After the first hour of surgery, the fluid therapy was managed according to the discretion of the attending anesthetist.

Measurements

The anesthesia was titrated to maintain a bispectral index (BIS) value between 40 and 60. Central hemodynamics was followed using the FloTrac™/Vigileo system and recorded every 10 min up to the first hour of surgery. Pulse oximetry, electrocardiography and heart rate were also monitored. Urine was collected on three occasions via an indwelling bladder catheter, which was inserted routinely after tracheal intubation was performed.

The first urine sample was collected immediately before flow-guided volume optimization was initiated; the second sample was collected after the bolus infusions were completed (35-45 min later); and the third sample was taken after the completion of the one-hour continuous infusion.

The urine color was assessed immediately in a well-lit room where a 10-ml tube of urine was compared with a color scale [9]. The colors ranged from very pale to brownish green. Urine colors 1–3 were “pale”, 4–5 were “intermediate” and 6–8 were “dark”. The samples were then sent to a certified clinical chemistry laboratory (Shaoxing People's Hospital Laboratory) for the analysis of osmolality (freezing point depression), creatinine concentration (enzymatic method) and specific gravity (refractometry).

Calculation of Fluid Retention Index (FRI)

The measurements performed on the urine were used as markers of renal conservation of fluid. These markers were specific gravity and osmolality, which are measures of the weight and number of solutes in the urine. Urine colour is caused by end products from the breakdown of erythrocytes. Creatinine is a remnant from the metabolism of muscle. Confounders caused by diet, disease and medication are expected to affect only one of these four markers, which makes the final, calculated fluid retention index (FRI) a robust measure of water conservation. Hence, FRI shows how the kidneys are set to excrete or retain fluid, which is most commonly a sign of a body fluid deficit.

In previous studies of the urine concentrating process, specific gravity was found to be the most stable urinary marker of dehydration [4]. Using urine-specific gravity as the reference method, each of the four results is given a previously published score based on the correlation between them (Table 1).

Fluid retention score	1	2	3	4	5	6
Specific gravity	≤ 1.005	1.01	1.015	1.02	1.025	1.03
Osmolality (mosmol/kg)	< 250	250–450	450–600	600–800	800–1000	> 1000
Creatinine (mmol/L)	< 4	4–7	7–12	12–17	17–25	> 25
Colour (shade)	1	2	3	4	5	6

Table 1: Scheme for calculating the fluid retention index (FRI), which is the mean of the dehydration scores for 4 urinary markers of fluid retention.

The fluid retention index (FRI) is based on the mean of the four scores. The composition of the index is then checked for outliers, which are determined by calculating the standard deviation (SD) for the mean of the four scores. An outlier typically raises the SD to > 1.0. The individual scores are then reviewed, and any single outlier omitted, followed by the recalculation of the index. The new value is accepted if the SD is ≤ 1.0, whereas the index is regarded as failing if the SD still exceeded 1.0.

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FRI can be converted into a body fluid deficit by using a reference curve described by the equation Fluid deficit (litres)=0.20 $FRI^{1.86}$, which has been validated by comparing changes in body weight with urine analyses in eight previous dehydration studies in sportsmen and in 57 subjects aged 17–69 years when performing recreational exercise [4]. A FRI value of ≥ 4.0 corresponds to the degree of renal conservation of fluid that accompanies dehydration to 3% of the body weight (specific gravity ≥ 1.020, creatinine ≥ 12 mmol/L, colour ≥ 4 and osmolality ≥ 600 mosmol/kg) [4].

Statistics

The results were reported as mean and standard deviations (SD). Differences in the continuous parameters between groups were assessed by an analysis of variance (ANOVA) and changes were studied by repeated-measures ANOVA. The correlations between continuous parameters were analysed using simple and stepwise multiple regression analysis.

The urine and blood volumes were reported as the median (25th–75th percentiles) because they showed a skewed distribution, and the data were compared using the Mann-Whitney U test. A logistic regression analysis was used to assess the correlations between dichotomous parameters, and risk estimates were expressed as an odds ratio with a confidence interval of 95%. $P< 0.05$ was statistically significant.

The study was originally intended to differentiate between the haemodynamic responses to post-induction bolus infusions with starch and Ringer´s lactate [10] and has also yielded data on the effects of these fluids on the postoperative food intolerance time [11]. The post hoc analysis showed that a statistically significant difference of 0.6 in the FRI between the two smallest groups (22 and 30 patients) was determined to be 93%. This calculation is based on the SD of 1.39 for the determination of FRI, which supports the findings of previous work [4].

Results

Data were incomplete in 3 patients, leaving 108 to analyse (Figure 1). Their mean (SD) age was 60 (12) years and the body weight 59 (8) kg. The operating time was 201 (71) min and the surgical blood loss 187 (115) ml.

Fluid retention index (FRI)

The results showed statistically significant ($P < 0.05$) correlations between the four markers of fluid retention. The creatinine concentration had to be square root-transformed to show a linear correlation with the other markers (Figure 2).

The final evaluation was based on 301 of the 324 samples. Exclusion of FRI values were due to occasional missing data, but most often that the SD>1.0 even after removal of an outlier.

Before volume loading, the mean FRI was 3.4 (1.1) and it remained at 3.4 (1.0) after the bolus infusions. After one hour of surgery, the index had only decreased to 3.1 (1.2; $P<0.03$) despite the total administration of more than 20 ml/kg of fluid.

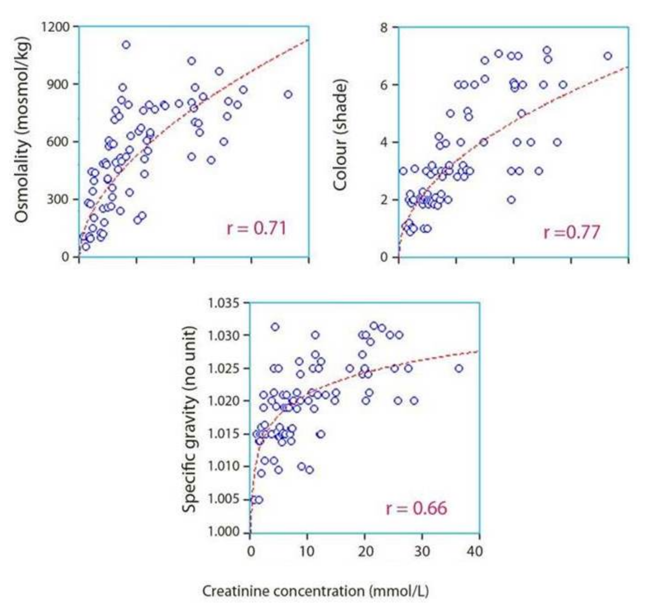

Figure 2: Correlations between urinary markers of dehydration. Data from the infusions of hydroxyethyl starch (HES) are shown.

FRI responses to infusion fluids

The FRI values for the fluid groups are shown in Table 2. Preloading with Ringer´s lactate before the surgery resulted in a lower initial FRI compared to the other patients (mean 2.8 versus 3.6; $P<0.001$) but infusing Ringer´s during the volume loading procedure after the induction of general anaesthesia did not reduce FRI (mean before 3.6; after 3.5; P=0.70). Administration of Ringer´s during the first hour of surgery reduced FRI from 3.3 to 2.9 (n=83, $P<0.01$). Volume optimization with starch did not reduce FRI at any point in time.

Group	Preloading	Volume loading	Fluid Retention Index (FRI)			
			Volume loading		First hour of surgery	
	500 ml of RL	9 ml/kg	Before	After	HES	RL
A, C	No	HES	3.6 (1.1)	3.5 (1.1)	3.6 (1.0)	3.0 (1.4)
B	Yes	HES	2.8 (1.0)	3.0 (1.0)		2.8 (1.2)
D	No	RL	3.6 (0.9)	3.5 (0.9)		3.1 (1.1)

The number of patients in each group is given in Figure 1, HES = hydroxyethyl starch 130/0.4; RL = Ringer´s lactate.

Table 2: Fluid Retention Index (FRI) in the different fluid treatment groups.

Excretion during 1 hour of surgery

Blood loss during the first hour varied between 20 and 100 ml (median, 50 ml). The markers of fluid retention showed lower values at

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the end of the one-hour period if the urinary excretion was > 100 ml (Figure 3).

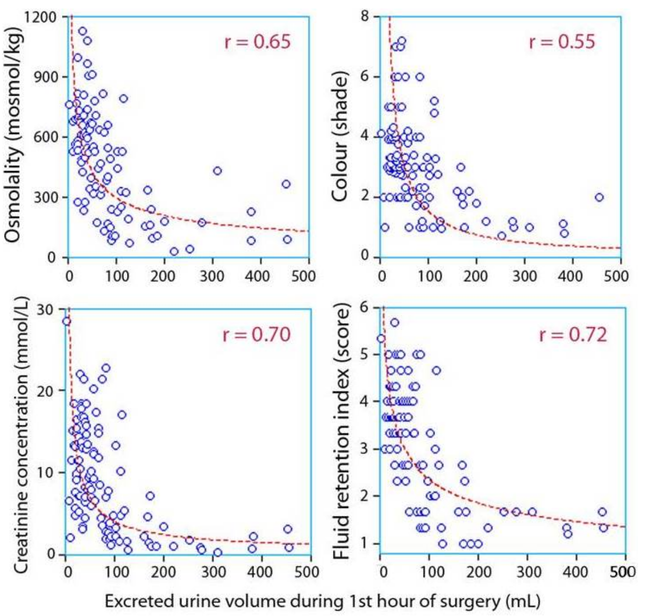

Figure 3: Correlations between the urinary excretion during the first hour of surgery and urinary markers of dehydration. Correlation coefficients are based on power transformation of the data.

The creatinine clearance during the first hour of surgery was 84 (52–163) ml/min and increased with the preoperative urinary creatinine concentration (r=0.40; P<0.0001) but did not correlate with the urine flow, type of fluid used, or with the preoperative serum creatinine concentration.

Postoperative serum creatinine

After the surgery, serum creatinine was available in 88 patients. Fifteen of them showed an increase. The mean increase was 8%, and the highest increase was 19%. Patients with an increase in serum creatinine had a higher preoperative FRI than the other patients did (Table 3). If a patient fulfilled the criterion for dehydration (FRI score of ≥ 4.0) [4], which occurred in 32% of the patients, the odds ratio for a postoperative rise in serum creatinine was 6.4 (95% confidence interval, 1.7–22.7).

Surgical bleeding of ≥ 250 mL was also associated with a greater likelihood of a rise in serum creatinine (odds ratio 4.6, 95% confidence interval, 1.3-16.1), whereas the amount and type of fluid given did not correlate with serum creatinine. The total blood loss during operations and the number of erythrocyte transfusions given to these 88 patients are shown at the bottom of Table 3.

Discussion

The results show that the FRI decreased only slightly during the early perioperative period despite administration of liberal amounts of fluid and only minor surgical hemorrhage. FRI was unchanged in response to 9 ml/kg of either hydroxyethyl starch or Ringer's lactate given for volume optimization.

Parameter	Increase in serum creatinine		Statistics
	No	Yes	
Number of patients	73	15	
Age (years)	60 (11)	61 (13)	p=0.62
Female gender	34%	20%	p=0.48
Body weight (kg)	58 (8)	64 (7)	p<0.02
Fluid retention index, FRI (score)	3.1 (0.8)	3.7 (1.1)	p<0.04
1st hour of surgery*			
Urine flow (ml/min)	0.9 (0.5-1.7)	0.7 (0.5-1.1)	p=0.70
Creatinine excretion (mmol/min)	5.5 (3.1-9.9)	9.9 (4.8-18.2)	p<0.02
Creatinine clearance (ml/min)	80 (49-145)	155 (79-250)	p<0.02
Cardiac index (ml/min/m^2)	2.7 (2.4-2.9)	2.6 (2.3-3.0)	p=0.61
Systolic arterial pressure (mmHg)	120 (11)	118 (12)	p=0.62
Diastolic arterial pressure (mmHg)	67 (9)	67 (8)	p=0.86
Heart rate (bpm)	63 (8)	64 (7)	p=0.48
Whole operation			
Operating time (min)	203 (72)	201 (72)	p=0.91
Infused Voluven® (ml)	902 (318)	867 (297)	p=0.69
Infused Ringer's lactate (ml)	1,655 (657)	1,567 (563)	p=0.63
Blood loss ≥ 250 mL	22%	53%	p<0.04
Erythrocyte transfusion	12%	20%	p=0.43
Urinary excretion (mL)	480 (300-600)	300 (220-245)	p<0.04
Urine flow (mL/min)	1.9 (0.8)	1.4 (0.7)	p<0.03

*patient mean value based on all measurements performed up to the 60th minute of surgery.

Table 3: Surgical parameters in the patients who had a postoperative rise in serum creatinine concentration compared to those who had no rise.

Moreover, FRI did not change when an additional 12 ml/kg of starch was infused during the first hour of the surgery. Because starch alone could not reverse the state of fluid retention in the perioperative setting, the kidneys did not seem to sense that starch was a "fluid". In contrast, several of the subgroups showed that Ringer´s lactate was able to reverse fluid retention.

The patients who fasted overnight were often in a state of fluid retention before the major surgery. At baseline, the FRI of one third reached 4.0, which implicates dehydration [4]. In a previous study, FRI was 2.8 before open abdominal surgery when the patients took oral fluid on demand up to two hours preoperatively [5]. A FRI of 2.8 was also found in our subgroup that was given 500 ml of Ringer´s lactate several hours prior to surgery. In the remaining subgroups, 3.6 was the typical starting value.

The measurements performed during the first hour of surgery demonstrated that FRI was strongly dependent on urine flow. When the amount of excreted urine decreased to below 100 ml per hour, the concentrations of the urinary markers rose dramatically (Figure 3). Kinetic studies have demonstrated that the whole body clearance of infused Ringer´s is only 10% during laparoscopic surgery compared to the conscious state [12,13]. Also in the present study the urine flow was quite low, and amounted only to 5-10% of the infused volume during the first hour of surgery.

Mild perioperative changes in serum creatinine occurred, but no patient was diagnosed with kidney injury [14]. However, the data allowed comparisons that outlined the circumstances under which a rise in serum creatinine developed. Two factors that inhibited the kidney´s capacity to retain fluid - a high FRI and a more-than-minimal hemorrhage (≥ 250 mL) - were statistically associated with a rise in serum creatinine. Interestingly, the patients who developed a postoperative rise in serum creatinine had a high creatinine clearance during the first postoperative hour, which shows that the kidneys worked hard to eliminate this waste product but not hard enough to prevent accumulation in the plasma.

Based on our results, the mild postoperative elevations of serum creatinine probably did not indicate kidney injury but were more likely to be caused by marked fluid retention. The finding of a high creatinine clearance is inconsistent with arterial hypotension being responsible for the rise in serum creatinine; if so, the clearance would rather have been on the low side. This view receives support from our measurements of central hemodynamics up to the first hour of surgery, which showed virtually identical data for patients who had and had not a postoperative rise in serum creatinine (Table 3).

A rational approach to report fluid retention is to use the aggregate result of several urinary markers that represent different metabolic mechanisms [4]. A previous study showed the ranges of specific gravity, creatinine, osmolality and urine color, osmolality, specific gravity and creatinine concentrations in subjects aged 17–69 years [4]. Although these markers are normally in reasonably good agreement with each other, there may be occasional outliers because of erroneous measurement or other confounders. Urine color might be increased by urinary tract infection and hemorrhage, creatinine by the excessive consumption of meat, and osmolality by the ingestion of salt. Using a composite index makes it unlikely that several urinary markers of fluid retention would be erroneous at the same time. A mathematical correction was used to exclude apparent outliers from the mean of the four markers. The most commonly excluded marker was urine color, which could be explained by fact that the urine samples were taken using a freshly placed urinary bladder catheter. With this approach to outliers, FRI is likely to be a more robust and valid measure of fluid retention than any one of the four components.

A urine sample clearly shows how the kidneys are set to excrete or conserve (retain) water, and such testing is a potentially helpful tool to detect dehydration. A preoperative urine sample could possibly serve to individualize the perioperative fluid administration in patients where central hemodynamic monitoring is not used.

There seems to be no benefit of repeating the urine test during the perioperative period, as changes from time to time are quite small. The kinetics of crystalloid fluid is fundamentally different when given to the preoperative patient with high urinary concentrations of waste products compared to another patient who has low concentrations. For example, renal fluid conservation prolongs the half-life [5] and greatly increases the plasma volume response [6] to crystalloids, and the urinary concentration of neutrophil gelatinase-associated lipocalin (NGAL) is more likely to increase [15]. An impact on postoperative health needs to be further elucidated, although fluid retention has already been shown to have a negative impact on outcome in elderly patients subjected to hip fracture repair surgery [1] and acute disease [7].

Strength of the present study is that the fluid therapy was strictly standardized. The limitations include that open-labeled trial was used in which all patients received both fluids. The patients were not allocated individually to the fluid programs but in groups of 25-30 subjects. The urine analyses quantify fluid retention by any cause, although renal fluid conservation caused by preoperative dehydration was probably the predominant mechanism as measurements were performed early during the operations. The result must still be interpreted with caution in certain patients where fluid retention is a part of the pathophysiology, such as heart failure.

A continuous infusion of propofol lasting for more than 1 hour might cause a greenish discoloration of the urine, in particular in the presence of liver dysfunction [16]. As only a bolus injection was given in the present study, this confounder is unlikely to be of importance but, if so, our policy of excluding outliers would prevent such discoloration from affecting the final FRI value.

Conclusions

Urinary indices of renal fluid retention could be partly reversed by the liberal infusion of Ringer´s lactate but not by hydroxyethyl starch. Patients with preoperative fluid retention or bled ≥ 250 ml during major abdominal surgery had a higher likelihood of showing a postoperative rise in serum creatinine.

Acknowledgements

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