CLINICAL STUDY

Individual goal-directed intraoperative fluid management of initially hypovolemic patients for elective major urological surgery

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Abstract: Background: The impact of different approaches to fluid management during intraoperative volume resuscitation in patients undergoing major elective surgery is poorly defined. We compared volume effectiveness of crystalloid and colloid substitution aimed to maintain the cardiac index (CI) between 2.6 and 3.8 l/min/m² as measured by transesophageal Doppler (TED).

Methods: A total of 115 urological patients were enrolled in the prospective randomized trial and then randomized into 2 groups, one with volume therapy based on crystalloids (n = 57) and the other with colloids (n = 58). A TED probe was inserted and then hemodynamic optimization (therapy with Ringer’s solution or hydroxyethyl starch 6 % 130/0.4 and administration of vasoactive drugs) was started according to TED variables to maintain the CI between 2.6 and 3.8 l/min/m².

Results: We observed high incidence of CI < 2.6 l/min/m² after induction of anesthesia (75 %) in both groups. There were no significant differences in demographic characteristics, ASA classification, length of surgery, estimated blood loss and the CI during surgery. To maintain the CI within the requested interval, significantly different amounts of crystalloids were needed as compared to colloid (median: 5000 ml vs 1500 ml). In the CRY group, more patients were treated by vasodilatators (40.4 vs 20.7 %).

Conclusions: The study confirmed that crystalloids and colloids are effective in correcting flow-related perfusion abnormalities. The significant difference between volumes of crystalloids and colloids proved their different characteristics such as unequal distribution between compartments. The expansion of therapeutic algorithm by using vasoactive drugs allows us to avoid adverse events resulting from fluid overload (Tab. 1, Fig. 5, Ref. 35).

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Key words: perioperative fluid management, crystalloids, colloids, transesophageal Doppler.


The main goals of fluid therapy are volume expansion and restoration and maintenance of adequate perfusion and oxygen delivery; this therapy should always be adjusted to individual hemodynamic goals. However, there are some clinical conditions in which volume therapy could be harmful, such as fluid overload, followed by tissue edema formation and increased cardiac filling pressure. A common practice is co-administration of fluids and vasoactive agents, which is supposed to reduce the above risk.

Crystalloid and colloid solutions have, according to their pharmacokinetics, different distribution between body compartments. Older studies, which included patients with trauma and hemorrhagic shock, described the need to use approximately three times the amount of crystalloids compared with colloids for restoration of effective tissue perfusion during emergency fluid resuscitation (1, 2, 3). These findings correspond with the traditional view of the fluid shift between the intravascular and interstitial spaces (4). However, some recently published studies comparing volume effectiveness of these solutions questioned some of the conclusions. According to the SAFE study, 1.16 to 1.3 times more saline solution than 4 % albumin is needed to reach the same values of mean arterial pressure (MAP) in the first four days of hospitalization (5). Another study (major cardiac and vascular surgery) performed in the early postoperative period comparing volume effectiveness of crystalloids and different colloids observed that the adequate volume ratio would be 1.2 : 1 (6). Influence of the used vasoactive agents on global perfusion was not evaluated in these studies. Based on these results, some authors recommended reviewing the traditional opinions related to the ratio of crystalloid and colloid solutions used during volume resuscitation.
The aim of this study was to compare volume effectiveness of colloids and crystalloids during major elective urological surgery using flow-related values derived by transesophageal Doppler (TED) monitoring. The therapeutic algorithm included the use of titrated doses of vasoactive agents in case there were some abnormalities in myocardial contractility and afterload values. Another goal was to find out if the type of solution used has influence on the frequency of postoperative complications and prognosis of the patient.

Patients and methods

A total of 115 consecutive patients undergoing elective major urological surgery have been enrolled in a prospective randomized clinical study (Fig. 1). The study was approved by the Institutional Research Ethics Committee and was carried out in operating theatres and an intensive care unit (ICU) of a tertiary hospital. Statement of the Ethics Committee confirms that all the activities and the structure of members of the Ethics Committee is in compliance with the international rules of conducting clinical trials. The exclusion criteria were age under 21 years, emergency surgery, pregnancy, severe cardiac or respiratory failure and expected duration of surgery less than 90 minutes. Informed consent was obtained from all patients enrolled in the study.

The patients were randomized and allocated according to the sequentially numbered, sealed opaque envelope technique. There were no restrictions or stratification in the randomization process. The research nurse assigning the patients to either the crystalloid (CRY, n = 57) or colloid (COL, n = 58) groups opened the allocation envelope immediately before induction of general anesthesia. After the induction, each patient obtained a TED probe (Hemodynamic™ 100®, Arrow International, Inc., Reading, PA, USA). Then hemodynamic optimization (fluid therapy with Ringer’s solution or hydroxyethyl starch 6% 130/0.4 and administration of vasoactive drugs) was started according to TED variables to maintain the cardiac index (CI) between 2.6 and 3.8 l/min/m². In each patient from any of the groups, the probe was inserted through the mouth to the distal third of the esophagus. According to the predefined therapeutic management algorithm (Fig. 2), fluids, inotropic support with dobutamine (Dobutamin Lachema 250, Pliva-Lachema a.s., Brno, Czech Republic), and vasoactive support with noradrenaline (Noradrenalín Leciva, Zentiva, Czech Republic) or isosorbide dinitrate (Isoket roztok 0.1 %, Schwarz Pharma AG, Monheim, Germany) were used. To compare the volume efficacy of maintaining the CI in the normal range with crystalloids or colloids, Ringer’s solution (Ringer’s injection, Fresenius Kabi, Verona, Italy) for volume re-suscitation was used in the CRY group and hydroxyethyl starch (HES, Voluven®, Fresenius Kabi AG, Bad Homburg, Germany) in the COL group. Concentration of hemoglobin lower than 90 g/l was an indication to start blood substitution. The supplementation of immeasurable fluid losses in the COL group was performed.
Szturz P et al. Individual goal-directed intraoperative fluid management with Ringer’s solution 0.05 ml/kg/min. None of the patients was excluded after randomization.

All patients had their bowels prepared by enema and/or using phosphate solution in the evening before surgery. This therapy was extended by administration of bisacodyl (Fenolax®, ICN Polfa, Rzeszow, Poland) and colonoscopy preparation diet in case of planned radical cystectomy. The patients were encouraged to drink water until midnight. Intravenous fluids, usually used overnight to minimize dehydration before surgery, were not administered due to local urological recommendations.

General anesthesia was induced with propofol and maintained with a balanced technique incorporating mixed nitrous oxide and oxygen, isoflurane with cisatracurium providing muscle relaxation. Sufentanil was used for analgesia at the anesthetist’s discretion. The patients were intubated and ventilated to normocapnia throughout the operation. Standard monitoring included ECG, pulse oxymetry, capnography, and measurement of invasive arterial blood pressure. Prior to the operation, central venous catheter was introduced in 50 patients (88 %) in the CRY group and 49 patients (84 %) in the COL group. Intraoperative epidural analgesia was never used.

All patients enrolled in the study were admitted to a surgical ICU after the procedure and followed until discharge from the hospital. The following parameters were recorded: length of ICU stay, length of hospital stay, rate of postoperative complications and in-hospital mortality. The evaluation of postoperative complications was similar to the method used by Bennett-Guerrero and colleagues (7).

Primary endpoint was defined as the comparison of volume replacement efficiency of crystalloids and colloids during major urological surgery. This efficiency was measured by flow-related perfusion parameters derived by transesophageal Doppler (TED) monitoring. Secondary endpoints included postoperative complications, ICU length of stay, length of stay in hospital and mortality related to the type of used fluids.

For sample size estimation, 750 ml difference in the amount of administered fluids (with a 5 % significance level and 80 % power, SD 1250 ml) was considered clinically important. A sample size of 45 patients in both groups (i.e. 90 patients) was necessary. For the particular sample size, variability and difference in the mean volume of intraoperatively administered fluids between the colloid and crystalloid groups, the power of the test was found to be almost 100 %. This power of the test is sufficient with respect to differences found by the study.

Data on patient characteristics, complications, and Doppler measurement were extracted from the (electronic) patient records. To ensure a proper execution of the trial and to monitor the progress, outcome, and patient safety during the trial, its progress and any occurring adverse events were discussed regularly with an expert team that was not involved in the randomization procedure or postoperative treatment of the patients.

Statistical analysis was carried out by an independent statistical institution. The Mann-Whitney U test was applied to compare continuous variables and the chi-square or Fisher’s exact tests were used for categorical variables. The Wilcoxon matched pairs

Fig. 2. Therapeutic algorithm.
A p value of less than 0.05 was considered statistically significant.

Results

During the inclusion period 115 patients were potentially suitable for the study. After screening, all patients match all inclusion criteria. The flow chart of the number of patients at inclusion, during follow-up and available for analysis is shown in Figure 3. We therefore analyzed the results of all 115 patients who were included and had entered the protocol. Demographic data of all patients enrolled in the study are presented in Table 1. Statistical analysis did not show any differences in age (median: 61 years in the CRY group vs 63.5 years in the COL group), gender (males: 71.9 % vs 72.4 %), body surface area (median: 2.0 vs 2.0), and estimated risk of anesthesia according to the ASA classification (median: 2.0 vs 2.0). Most of the patients underwent surgery for a tumor (78.9 % in the CRY group vs  79.3% in the COL group). The most frequent surgery was radical prostatectomy (42.1 % vs 39.7 %), followed by nephrectomy (35.1 % vs 41.4 %) and cystectomy (22.8 % vs 19 %).
between both study groups. Dynamic changes in LVETi, Acc and
TSVRi are shown in Figure 4. The time course of measured values
of the CI describing the actual achievement of the target in both
groups is shown in Figure 5. More than 70 % of patients in both
groups had the initial CI lower than 2.6 l/min/m² (median: 2.17
vs 2.19). However, the rate dropped to 10 % of patients after 20
minutes and always stayed lower than 5 % of patients during the
further course of the procedure.

The dynamics of intraoperative catecholamine dosage also
suggested that the initial higher doses of dobutamine and isosor-
bide dinitrate could be, after achieving the desired cardiac index,
lowered and subsequently even discontinued. Despite the statistic-
ally significant differences in the frequency of isosorbide dinitrate
administration between the two groups, continuous administration
of the infusion was terminated (after achievement of hemody-
namic values according to protocol) in all patients before their surgery
was completed. Besides, there were no significant differences in
the values of mean arterial pressure, central venous pressure and
heart rate between both study groups, with all of them being within
the normal interval (Fig. 5).

With regard to postoperative complications, there was a statisti-
cal significance related only to gastrointestinal tract dysfunction
in the CRY group (31.6 %) vs the COL group (15.5 %; p = 0.05).
The number of complications in hemodynamics, renal, respiratory
and hematological parameters was not statistically significant. The
overall amount of complications during ICU stay was not signifi-
cantly different. Also the length of ICU stay, the length of hospital
stay and mortality were not significantly different.

Discussion

The primary goal of fluid therapy is reduction of plasma vol-
ume deficit and thus to achieve an adequate CI, tissue perfusion
and oxygen delivery. However, fluid overload can cause excess-
ive extravascular fluid retention, pulmonary congestion and other
complications (8, 9). Vasoactive drugs may effectively prevent the
complications. This rules have been derived from complex ap-
proach to Frank-Starling law (not only preload changes, but also
afterload and contractility are responsible for curve shift) (10).
Therefore, optimal management might be a combination of fluid
and vasoactive therapy which maintains the CI index within the
normal interval without excessive elevation of cardiac filling pres-
sure or preventing the development of interstitial edema.

The causes of perioperative hypovolemia are multifactorial,
including preoperative fasting and bowel preparation (11, 12).
Hypovolemia induces peripheral vasoconstriction and microciri-
culatory compromise due to bar receptor reflex-induced increase
in sympathetic activity and release of catecholamine, and is an
important factor contributing to organ failure.

After introduction to general anesthesia, worsening of global
hemodynamic parameters is observed, especially preload, which
causes reduction of the CI and parallel elevation of systemic vas-
cular resistance (13). However, traditional parameters such as
heart rate (HR), mean arterial pressure (MAP) and central venous
pressure (CVP) are often normal (14). Use of anesthetics with

Fig. 4. Proportion of patients with cardiac index < 2.6 l/min/m² during
surgery in both groups of patients.

Fig. 5. Total number of postoperative complications in both groups of
patients. Number of complications (hemodynamic, respiratory, renal,
GIT, coagulation and neurology) did not reach statistical significance
during ICU hospitalization.

Data concerning surgery are presented also in Table 1. All
surgeries lasted at least 90 minutes (median: 155 minutes in the
CRY group vs 150 minutes in the COL group). To maintain the
CI within the requested interval, significantly different amounts
of crystalloids compared to colloids were needed (median: 5000
ml vs 1500 ml, p = 0.001, respectively). Total amount of fluids
(except for red blood cells and fresh frozen plasma) was 5000 ml
in the CRY group vs 2200 ml in the COL group. The number of
intraoperatively administered blood units was also higher in CRY
group than in the COL group (red blood cells: median 0.9 vs 0.3 p
= 0.018; fresh frozen plasma: median 1.0 vs 0.3, p = 0.006, respec-
tively). However, the differences in administered blood units and
fresh frozen plasma within the day of surgery were not significant.
Significant differences were found in the use of vasoactive agents
during the surgery. In the CRY group, more vasodilators (40.4 %
vs 20.7 %) were used. The differences in amounts of administered
inotropic and vasoactive drugs were not statistically significant.
There were no significant differences in the values of left ventricu-
lar ejection time index (LVETi), peak aortic blood flow accelera-
tion (Acc) and total systemic vascular resistance index (TSVRi)
cardiodepressive and vasodilator effects (15) or acute blood loss further enhance the negative impact on tissue perfusion.

There are no randomized controlled trials which would sufficiently evaluate interaction between the amounts of administered fluids and vasoactive agents used to reduce hypoperfusion abnormalities in relation to outcome of patients undergoing elective major surgery, trauma, sepsis or burns (16). Recommendation for volume resuscitation of early hypoperfusion abnormalities is based on identification of real intravascular volume deficiency and also on knowledge about different biological and physicochemical properties of crystalloid and colloid solutions such as the length of volume-expansion effect, hemorrhheologic properties (with influence on vascular integrity and immunologic response) and simultaneously reduction of potential adverse effects of any administered fluids (8, 17).

Perioperative fluids amount should be directed by reaching individual hemodynamic goals. Administration of crystalloids is sufficient for reaching euvolemia in almost all clinical situations. Administration of colloids (both natural and synthetic) should always be justified by real need of fast volume replacement and measurement of dynamic flow parameters.

From healthy volunteer studies and also from clinical practice, it is clear that for achievement of the same equivalent plasma volume expansion effect, 3–4 times the amount of crystalloids is needed as compared to colloids (18, 19). In the SAFE study, during the first 4 days of hospital stay at an intensive care unit, the crystalloid to 4% albumin ratio was found to range from 1.16 to 1.4:1. Similar results (crystalloid:colloid; 1:1.45) were noted in septic patients in the VISEP study where the goals of hemodynamic optimization were adjustments in HR, MAP, CVP and mixed venous oxygen saturation (5, 20). Nevertheless, a recent study performed in an early postoperative period showed that while using the same amounts of different solutions, colloids are more effective in increasing cardiac filling, output and oxygen delivery than administration of Ringer’s solution (21). Interaction between amounts of administered fluid and vasoactive agents was not evaluated.

The results of our study confirmed the assumption that hypovolemia can be frequently found in patients undergoing major elective surgery (13, 22). We also verified high significance of flow-related parameters for detection of hypoperfusion abnormalities (23, 24, 25) while using TED. The study proved that both crystalloids and colloids are efficient tools correcting early flow hemodynamic abnormalities, but there was no statistically significant difference in some important outcome parameters such as the overall frequency of postoperative complications, length of ICU stay, overall length of hospitalization and in-hospital mortality. On the other hand, statistically significant differences in the amount of administered crystalloid and colloid solutions suggest different expansion characteristics. The extension of the therapeutic algorithm by the use of vasoactive drugs aids in avoiding potential adverse events resulting from fluid overload (26, 27). Effectiveness of therapeutic algorithm was proven in 230 surgical patients. Mortality, rate of perioperative complications, length of hospital stay were all lower in group with optimization of flow parameters compared to the group with standard perioperative monitoring only (28). We also verified their influence on correction of altered parameters of global perfusion, which finally helped us adjust the infused amounts of crystalloid and colloid solutions more effectively. Higher frequency of gastrointestinal tract complications in the group of patients using crystalloids reminds us of possible adverse effects resulting from administration of these solutions (29). Gut edema may be associated with postoperative gastrointestinal dysfunction, impairment of tissue oxygenation and increased intraabdominal pressure (7, 30–33). These results could be affected by different strategy of fluid management in ICU, where no postoperative protocol was standardized.

We are aware of the limits of the study, namely the small number of patients and specificity of major urologic surgery, which do not allow to exactly apply the results to another subpopulation of critically ill patients. Moreover, the used flow parameters to guide hemodynamic optimization could not sufficiently define preload, contractility and afterload. Nonetheless, we assume that these flow parameters are more accurate in titration of the amount of administered fluid and vasoactive drugs in the intraoperative period and have better correlation to outcome, in comparison with the traditional parameters (HR, MAP and CVP) (34, 35).

Conclusion

Despite considerable attention dedicated to perioperative medicine and significant advances in technology of perioperative hemodynamic monitoring devices, there are no standardized procedures and protocols recommending the dosage of fluids and vasoactive drugs. Early detection of intravascular volume deficiency by flow-related parameters is an effective tool in amelioration of hypoperfusion abnormalities. In these situations, both crystalloid and colloid solutions may still be administered together with vasoactive drugs to avoid adverse effects generally related to fluid therapy. To prove this in other groups of patients, more extensive randomized controlled trials are needed. Definition of hemodynamic parameters and creating algorithms allowing early and adequate therapeutic intervention therefore remain a great challenge for future perioperative research.

References


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