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THE INFLUENCE OF INTRAOPERATIVE FLUID MANAGEMENT ON POSTOPERATIVE PULMONARY COMPLICATIONS IN LIVER-TRANSPLANT PATIENTS

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Abstract

Background. Fluid management is one of the key elements for a successful liver transplantation (LT). Perioperative pulmonary complications can contribute significantly to the morbidity and mortality of the patients.
The objective of this study was to assess the influence of intraoperative fluid management on postoperative pulmonary complications.
Methods. We retrospectively analyzed 40 consecutive patients who underwent liver transplantation at Fundeni Clinical Institute, Bucharest, between January 2014 and April 2014. The patients were divided into two groups, based on whether they developed pulmonary complications (group 1) or not (group 2). Analysis of data included perioperative variables, such as volume of intraoperative blood and fluid transfusion, intraoperative blood loss, fluid balance, duration of surgery, postoperative pulmonary complications. Radiographic analysis was standardized in order to assess the presence of pulmonary complications.
Results. Our study included 26 men (65%) and 14 women (35%). Mean (±SD) age was 49.5 (±13.4) years. 23 patients (57.5%) developed pulmonary

Résumé

L'influence de la gestion des liquides administrés en intra-opératoire sur les complications pulmonaires postopératoires chez les patients ayant subi une transplantation hépatique

Objectifs. La gestion des fluides est l'un des éléments clés pour une transplantation hépatique (TH) réussie. Les complications pulmonaires péri opératoires peuvent contribuer de manière significative à la morbidité et à la mortalité des patients. L'objectif de cette étude est d'évaluer l'influence de la gestion des fluides intra-opératoires sur les complications pulmonaires postopératoires
Méthodes. Nous avons analysé rétrospectivement 40 patients consécutifs subissant une transplantation hépatique à l'Institut Clinique Fundeni entre janvier 2014 et avril 2014. Les patients ont été divisés en deux groupes selon qu'ils ont développé des complications pulmonaires (groupe 1) ou non (groupe 2). L'analyse des données comprenait des variables péri opératoires telles que le volume de produits sanguins transfusé en intra-opératoire et la quantité de fluides, la perte de sang intra-opératoire, l'équilibre des liquides, la

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complications after LT. The study revealed that intraoperative fluid administration exceeded 100 ml/kg in patients with pulmonary complications compared to those without pulmonary complications (p=0.02). Plasma transfusion in group 1 was higher than in group 2 (p=0.05) and group 1 received more crystalloid solutions than group 2 (p=0.04). We found that intraoperative fluid balance >45 ml/kg correlates with postoperative pulmonary complications (p=0.01), longer Post Anaesthesia Care Unit (PACU) stay (p=0.01) and longer extubation time (p=0.04). The Meld and Meld Na scores were not significantly different between the two groups (p=0.26).

Conclusion. Excessive intraoperative fluid transfusion was associated with postoperative pulmonary complications, prolonged PACU stay and extubation time.

Key words: liver transplantation, fluid management, pulmonary complications.

durée de la chirurgie, les complications pulmonaires. L'analyse radiographique a été standardisée afin d'évaluer la présence de complications pulmonaires.

Résultats. Notre étude a inclus 26 hommes (65%) et 14 femmes (35%). L'âge moyen (± DE) était de 49,5 (± 13,4). 23 patients (57,5%) ont développé des complications pulmonaires après TH. L'étude a révélé que l'administration de liquides en intra-opératoire dépassait 100 ml / kg chez les patients présentant des complications pulmonaires par rapport à ceux qui n'avaient pas de complications pulmonaires (p = 0,02). La transfusion plasmatique dans le groupe 1 était plus élevée que dans le groupe 2 (p = 0,05) et le groupe 1 a reçu plus de solutions cristalloïdes que le groupe 2 (p = 0,04). Nous avons constaté que le bilan liquidien intra-opératoire> 45 ml / kg est en corrélation avec les complications pulmonaires postopératoires (p = 0,01), le maintien plus long de la PACU (p = 0,01) et le temps jusqu'à l'extubation plus long (p = 0,04). Les scores de Meld et Meld Na n'étaient pas significativement différents entre les deux groupes (p = 0,26).

Conclusion. Une transfusion sanguine intra-opératoire excessive a été associée à des complications pulmonaires postopératoires, à un séjour prolongé de la SRPA et au temps d'extubation.

Mots clés: transplantation hépatique, gestion des liquides, complications pulmonaires.

Introduction

Liver transplantation is considered the treatment of choice for patients with End Stage Liver Disease. Since its first success in 1967, liver transplantation has been under continuous progress and despite the newest discoveries, the procedure remains a challenge for both surgeons and anaesthetists[1].

Fluid management is one of the key elements for a successful liver transplantation (LT). Perioperative fluid therapy has proved to be essential for the patient's outcome. Adequate intravascular volume replacement can have a significant impact on organ function, including perioperative pulmonary complications that can contribute fundamentally to the morbidity and mortality of the patients[2]. Postoperative pulmonary complications can appear due to several factors and fluid therapy is one of the most important.

There are many studies in the literature that present the importance of goal directed therapy (GOD) by decreasing the incidence of postoperative organ dysfunction[3]. Inadequate fluid administration can lead to significant oedema, which is associated with different organ dysfunction and death. Prescribing intravenous fluid requires choosing from a variety of fluid types that are now available, each with a background of large randomised controlled trials identifying signs of benefit or harm.

Considering all these, the selection of resuscitation fluid requires a good understanding of the patients' disease, their physiology, the composition of the fluid given, its safety and potential effect. This is one of the reasons we believe our study brings new and important data on this topic.

The aim of this study was to assess the influence of intraoperative fluid management on postoperative pulmonary complications, extubation time, length of Post Anaesthesia Care Unit (PACU) stay and 30 days mortality.

Methods

After obtaining approval and informed consent from the Ethical Committee of Fundeni Clinical Institute, we retrospectively analyzed 40 consecutive patients who underwent liver transplantation at Fundeni Clinical Institute over a 4 months period, between January 2014 and April 2014.

Inclusion criteria were represented by all patients who underwent liver transplantation in our centre between January 2014 and April 2014. We excluded patients who were below 18 years of age.

The patients were divided into two groups, based on whether they developed pulmonary complications or not. Group 1 included liver transplant patients who developed perioperative pulmonary complications and group 2 included those who did not develop pumonary complications.

Anaesthetic management

All the patients in this study underwent LT under general anaesthesia. Induction was obtained using propofol 1.2 mg/kg, fentanyl 2-4 μg/kg and succinylcholine 1mg/kg. Neuromuscular blockade was obtained with atracurium, a loading dose followed by boluses every 20-45 minutes. Maintenance of anaesthesia was achieved using inhaled sevoflurane and fentanyl. Intraoperative monitoring consisted of continuous electrocardiogram, invasive blood pressure (BP) measurement, peripheral oxygen saturation, end-tidal carbon dioxide (ETCO2), diuresis and core temperature. Invasive BP, CVP, cardiac output and derived values (CI, SVRI, SVV, GEDI, GEF, ELWI) were monitored with pulse contour analysis using PICCO Plus®monitor.

Data collection

Preoperative data collection from the patients' medical files included: age, gender, etiology of liver disease, assessment scores for the severity of liver disease (MELD and MELD-Na scores). Intraoperative data were: duration of surgery, blood loss and blood transfusion, fluid administration, fluid balance, mean blood pressure (MAP), central venous pressure (CVP), vasopressor requirements and hemodynamic parameters measured with PiCCO Plus System. We also recorded postoperative data such as: postoperative pulmonary complications, extubation time, length of PACU stay and 30 days mortality.

Radiographic and inflammatory markers (C reactive protein and procalcitonin) analysis were standardized in order to assess the presence of pulmonary oedema, acute respiratory distress syndrome or pneumonia. Chest radiography was done routinely in each patient, as follows: the day before the surgery, immediately after the surgery has finished and the patient was brought to PACU, at day 1, day 3 and after that, anytime we suspected a pulmonary complication. C reactive protein (CRP) was tested before the surgery, at day 1 and day 3 after surgery. The chest radiography and CRP, when abnormal, were analysed together with clinical findings to diagnose pulmonary complications. The acute respiratory distress syndrome was diagnosed according to Berlin definition[4] and pneumonia according to the American Thoracic Society and Infectious Diseases Society of America[5].

Variables recorded

During the intraoperative period, we analyzed a series of different variables concerning the amount of fluid adminstered during the surgery. We recorded the volume of packed red blood cell (RBC) transfusion, volume of plasma transfusion, total intraoperative bleeding volume, fluid balance, diuresis. Fluid balance determination did not include insensitive loss.

Statistical analysis

Data are presented as a mean ± standard deviation of the mean, median [min, max] and percentage (%). Data distribution was examined in order to ensure the proper statistical examination. Group means were compared using Student's *t* test or the Mann-Whitney *U* test as appropriate. In order to assess subgroup differences we used the Pearson correlation test. A P value < 0.050 was considered significant. Statistical analysis was performed using Microsoft Office Excel 2007.

Results

Our study included 40 patients, 26 men (65%) and 14 women (35%). Mean (±SD) age was 49.5 (±13.4). From the total number of patients studied, 23 patients (57.5%) developed pulmonary complications after LT. Pulmonary complications presented as follows: 7 patients developed pneumonia (17.5%), 4 patients developed pulmonary oedema (10%) and 2 patients developed acute respiratory distress syndrome (ARDS, 5%). 2 patients died during the first month after liver transplantation.

Table 1 presents variables which are compared between the two groups of patients: patients from group 1 (with pulmonary complications) and patients from group 2 (without pulmonary complications). Some variables were found to be significant between the two groups. Patients from group 1 had a longer duration of surgery compared to those in group 2 (p=0.13). The intraoperative plasma transfusion in group 1 was significantly higher (11 units) than plasma transfusion in group 2 (5.1 units) (p=0.05). Total intraoperative fluid administration was higher in patients who developed pulmonary complications (7600 ml) compared to patients who did not develop pulmonary complications (5085 ml) (p=0.01). Total intraoperative bleeding was not significantly different between the two groups (p=0.18).

Table 1. The comparison of variables between the two groups of patients studied

Variables	Group 1 (With pulmonary complications)	Group 2 (Without pulmonary complications)	P value
Age (yr)	52.5 ± 10.1	45.3 ± 16.3	0,06
Hb (g/dl)	10.5 ± 2.1	10.3 ± 2.1	0,37
BUN (mg/dl)	40.8 ± 24.9	36.8 ± 17.4	0,27
Creatinine (mg/dl)	1.1 ± 0.3	0.8 ± 0.3	0,04
MELD score	18.2 ± 5.5	17.4 ± 5.8	0,33
Duration of surgery (min)	425 ±68	373 ± 56	0,13
Anhepatic phase (min)	52 ± 16	44 ± 21	0,15
Intraoperative total fluid transfusion (ml)	7609 ± 3762	5085 ± 2437	0,01
Packed red cells (units)	6.6 ± 5.4	4.2 ± 4.4	0,07
Fresh frozen plasma (units)	11 ± 6.8	5.1 ± 4.5	0,05
Crystalloids (ml)	1509 ± 907	1088 ± 572	0,04
Colloids (ml)	1386 ±1381	1282 ± 1012	0,39
Intraoperative bleeding (ml)	4526 ± 3451	3505 ± 3534	0,18
PACU stay	6.3 ± 2.1	4.3 ± 1	0,01
Pulmonary complication (cases)	23	17	na
Pleural effusion	10	0	na
Pneumonia	7	0	na
Pulmonary edema	4	0	na
ARDS	2	0	na

Hb= Hemoglobin; BUN= Blood urea nitrogen; MELD= Model for end-stage liver disease; PACU= Post anaesthesia care unit; ARDS= Acute respiratory distress syndrome.

Both crystalloid and colloid solutions were used as fluid replacement therapy. Patients with pulmonary complications received more crystalloid solutions than those without pulmonary complications (p=0.04) (Figure 1). The use of colloid solutions and the number of packed red cells were not different between groups 1 and 2.

The Meld and Meld – Na severity scores between the two groups were not significantly different (p=0.26) (Figure 2).

The study revealed that intraoperative fluid volume exceeded 100 ml/kg in patients who developed pulmonary complications compared to those without pulmonary complications (p=0.02) (Figure 3).

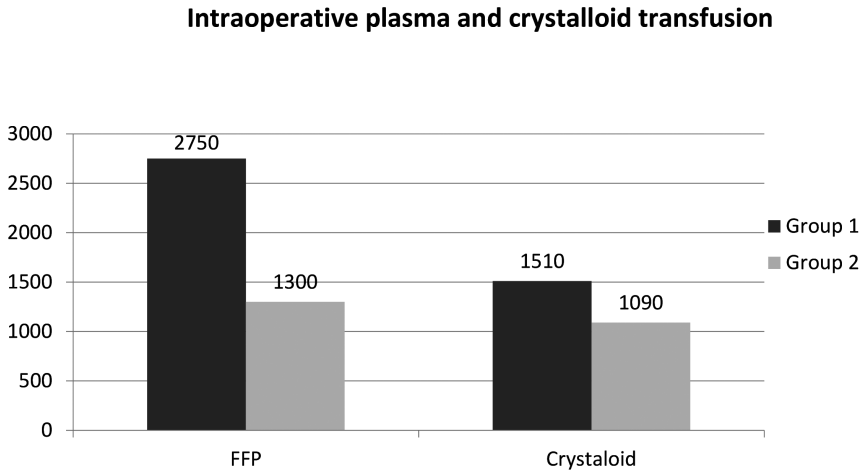

Figure 1. Volume of intraoperative transfusion in patients with pulmonary complications vs those without complications

Positive intraoperative fluid balance that exceeded 45ml/kg correlates with postoperative pulmonary complications (p=0.01) (Figure 4). Patients in group 1 had a longer PACU stay (6.5 days) than patients in group 2 (4.3 days) (p=0.01)(Figure 5).

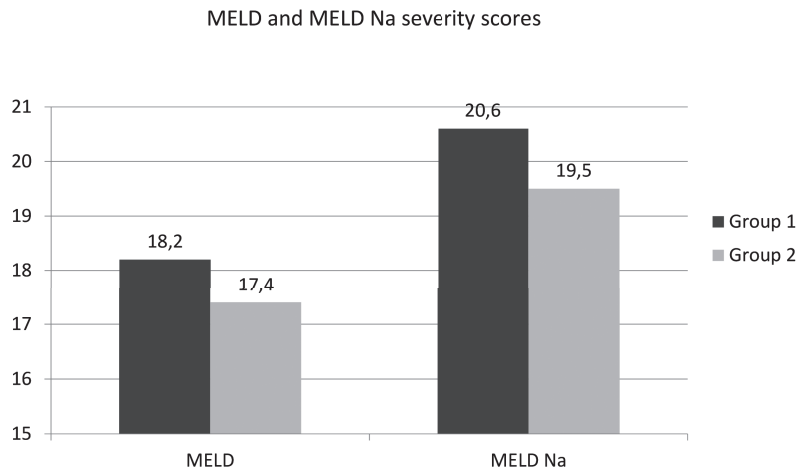

Figure 2. The difference in Meld and Meld Na severity scores between the two groups

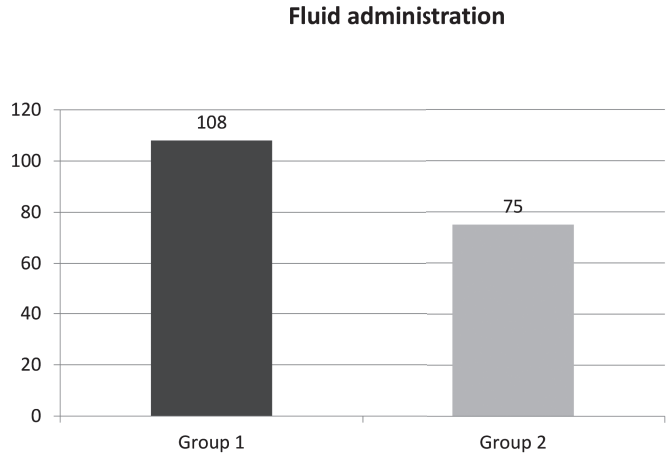

Figure 3. Total intraoperative fluid administered in group 1 vs group 2

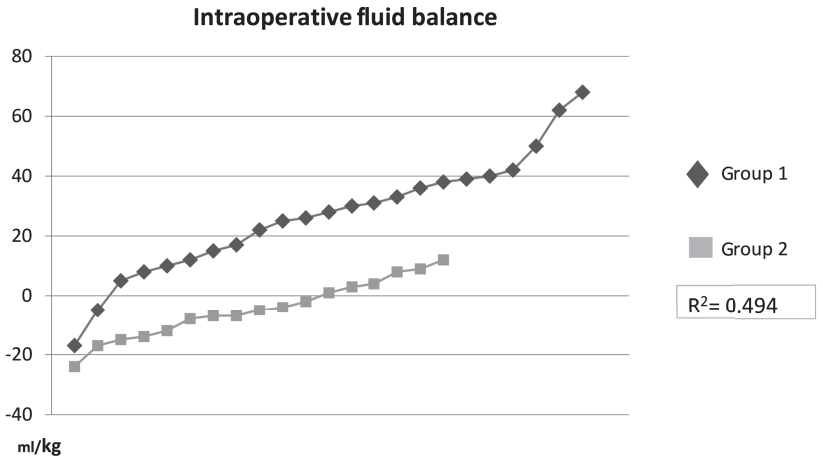

Figure 4. The correlation between fluid balance and postoperative pulmonary complications

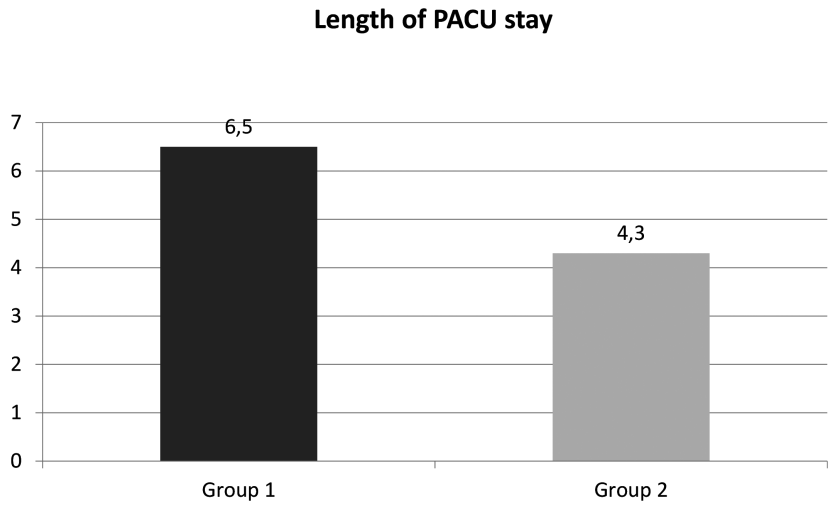

Figure 5. The difference of PACU stay in patients from group 1 vs patients from group 2

Discussion

Liver transplantation outcome has significantly improved over the past decades due to the improvement in both surgical and anaesthetic techniques[6,7]. Despite recent advances, which have decreased blood loss and blood transfusion, LT surgery is still associated with a high risk of important blood loss and need of massive fluid resuscitation[8].

There are many reasons why intraoperative fluid management tends to be aggressive and has been so in transplanted patients for the last decades. Almost all patients who undergo LT suffer from ESLD with important water-sodium retention. There is also the degree of portal hypertension which leads to capillary leak syndrome creating the third space[9] and increasing fluid loss during surgery.

Our study showed that intraoperative blood and fluid transfusion that exceeded 100 ml/kg was an independent risk factor for the appearance of pulmonary complications in patients who underwent LT. The correlation is independent from other preoperative variables, such as recipient's age, duration of surgery, intraoperative bleeding or severity of the disease. The length of PACU stay and extubation time are also prolonged in this group of patients.

These findings support those of the recent studies that suggest we should aim for a restrictive fluid therapy. Recent studies stressed the importance of adequate intraoperative fluid management and reducing the volume of fluid administration[10]. Excessive fluid therapy was associated with higher incidence of postoperative complications[11]. Bozbas et al showed that pulmonary complications led to a worse outcome, a longer extubation time and PACU stay[12]. Restrictive fluid therapy was proved to reduce morbidity and mortality, PACU stay and extubation time[13].

A significant debate has arisen regarding the safety use of hydroxyethyl starches (HES). In 2008, Brunkhorst et al published a large randomised trial presenting the negative impact of HES use in intensive care patients[14]. Four years later, Perner et al found higher risks with HES than with other volume expanders[15]. In a similar study, in 2012, Myburgh et al demonstrated that resuscitation with HES as compared to saline in intensive care patients does not provide any clinical benefit. The use of HES resulted in an increased risk of renal dysfunction and need of renal replacement therapy[16]. In another study, conducted by Perel et al, resuscitation with colloids rather than crystalloids proved no benefit in patients following surgery or burns. They also concluded that the use of HES might increase mortality[17].

All these data demonstrate the fact that intraoperative fluid volume is associated with the incidence of postoperative pulmonary complications. Studies show that a negative fluid balance during the first 3 days after liver transplantation is essential for a positive outcome of patients[9].

The study also revealed that plasma transfusion and crystalloid solutions are independent risk factors for postoperative pulmonary complications. A positive intraoperative fluid balance of more than 45 ml/kg correlates with pulmonary complications and worse postoperative outcome.

Our study has several limitations. A potential weakness of this study is the fact that details of pressor agents were not taken into account. Another weakness could be the patients' comorbidities (renal impairment), which were not taken into consideration

but can affect the fluid management. We should also take into consideration the relatively low number of patients included in the study, compared to other studies on the same subject.

Conclusions

These results are of great importance to our daily practice as we can guide the fluid management during LT and predict the patients' outcome based on the total volume and type of fluid given. Patients with excessive fluid transfusion (more than 100 ml/kg) will have higher rates of organ dysfunction.

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