The effects of preoperative use of terlipressin in patients undergoing liver resections

Khoronenko V., Baskakov D., Varvarin V., Malanova A., Mandryka E.
P.A. Herzen Moscow Cancer Research Institute, Russia

Introduction. A number of investigators have identified that terlipressin reduces portal blood flow [1]. Terlipressin, a long-acting synthetic analogue of arginine vasopressin, acts through V1 receptors mainly in the splanchnic circulation, which causes vasoconstriction with subsequent reduction in portal pressure [2]. The objective of this study was to evaluate the safety of preoperative use of terlipressin and its impact on the blood loss in patients undergoing liver resections.

Materials and Methods. This was a prospective, randomized study. 60 patients (20-79 years) undergoing left or right hemihepatectomy, liver segmentectomy and atypical resections were randomized via computer-generated random numbers into 2 groups: 1) control group (CON) n=30 2) terlipressin group (TER) n=30. Patients in TER group were given IV bolus of terlipressine 1 mg in 30 minutes before anesthetic induction. In CON group patients received at the same time saline solution.

All the patients received conventional hemostatic therapy including ethamsylate 500 mg and tranexamic acid 5 mg/kg intravenously 30 min before surgery. Patients in both groups received combined general-epidural anesthesia. Epidural catheter was placed at Th8-T9 interspace, then the intraepidural infusion of ropivacaine 0,375% was started with rate 4-8 ml/h. Anesthesia was induced with propofol 2 mg/kg; fentanyl 0,002 mg/kg; ketamine 25 mg, rocuronium 0,6 mg/kg. Ventilation was mechanically controlled and adjusted to maintain end-tidal CO2 at 30–35 mmHg, FiO2 - 35%. After endotracheal intubation anesthesia was maintained in all groups with sevofluran (0,8-1 MAC), fentanyl, ropivacaine (0,375% through epidural catheter 4-8 ml/h). Rocuronium was used for muscle relaxation. The BIS value was maintained at 50–60.

The low central venous pressure (LCVP) assisted technique was used for all patients. LCVP consists of two phases: a pre-hepatic transection which takes advantage of strict fluid restriction and the vasodilatory effect of anesthetic agents to provide LCVP. Fluid boluses and/or vasoactive drugs are administered at the discretion of the anesthesia care team to maintain systolic blood pressure (SBP) of ≥ 90 mmHg and urine output of >25 ml/h while maintaining the CVP at <5 mmHg. The second phase, at post-hepatic resection, begins once the specimen has been delivered and haemostasis secured. During this phase, an attempt is made to return the patient to normovolaemia, crystalloid infusion at 6 ml/kg/h of total operative time to restore the calculated insensible losses and maintenance requirements. Blood loss is replaced volume-to-volume with Gelatin succinylated or at a ratio of 3:1 with crystalloid. The trigger hemoglobin level for packed red blood cells (PRBC) transfusion was less than 80 g/l, fresh-frozen plasma (FFP) or platelets were given in selected patients, at the request of the surgeon, either during the resection if hemostasis was felt to be inadequate.

Results. Patients in the 2 groups were comparable with respect to age, sex, body weight, height, ASA status, type and duration of surgery. Preoperative laboratory tests were not different between the groups.

Analysis of the intraoperative hemodynamics showed that, mean arterial pressure (MAP) during anesthesia did not differ between the groups. (Table 1.)

Table 1. Mean Arterial Blood Pressure (mmHg)

Time	CON (n=30)	TER (n=30)
Preoperative	86±9,42	84±10,19
After laparotomy	90±10,87	91±9,68
End of resection stage	77±8,78	80±9,96
End of operation	80±9,56	84±10,16

CON: control group, TER: terlipressin group

But the perioperative heart rate (HR) in TER group was significantly reduced versus CON group at the time after laparotomy ($p<0,05$). (Table 2.)

Table 2. Heart Rate (beats/min)

Time	CON (n=30)	TER (n=30)
Preoperative	78±11,25	74±10,14
After laparotomy	69±12,26	62±11,2*
End of resection stage	69±8,05	66±7,76
End of operation	71±13,39	70±10,69

CON: control group, TER: terlipressin group, * - $p<0,05$

Estimated blood loss was significantly lower in the TER group than in the CON group, therefore patients in the TER group needed greater volume of the colloids solutions. At the same time we did not find significant differences in transfusion of packed red blood cells and FFP (fresh frozen plasma). Urinary output during anesthesia was significantly decreased in TER group versus CON group. (Table 3.)

Table 3. Compensation of the blood loss

Variables	CON (n=30)	TER (n=30)
Estimated blood loss, ml	1562,5±854,88	648,75±841,67*
Crystalloids, ml	2570±513	2323±462
Colloids, ml	866±346	633±225*
Packed red cells, ml	270±288	170±258
Fresh frozen plasma, ml	220±201	142±193
Urine output, ml/h	75,12±3,02	71±1,41*

CON: control group, TER: terlipressin group, * - $p<0,05$

At the first postoperative day the level of hemoglobin in group TER was significantly higher than that in CON group. There were no other differences in the postoperative laboratory tests between the groups. (Table 4.)

Table 4. Postoperative laboratory tests

Tests	CON (n=30)	TER (n=30)
Hemoglobin, g/l	93,4±4,17	108,56±8,83*
Leukocytes, $10^9/l$	11,5 ±2,65	10,65±2,8
Trombocytes, $10^9/l$	213,3±45,09	224,1±43,72
Total bilirubin, mmol/l	26,5±5,69	24,16±0,17
AST, U/l	478,3±82,2	434,2±78,2
ALT, U/l	434,4±80,9	415,7±81,3
ALP, U/l	124±14,61	125,8±13,66
BUN, mmol/l	34,56±11,3	32,78±12,4
Creatinine, $\mu\text{mol/l}$	107,72±12,75	102,1±15,50
aPTT, sec	33,7±1,63	32,1±1,03
Prothrombin time, sec	14,4±1,46	11,0±0,98
Prothrombin by Quick, %	83,9±9,61	95,6±9,8
INR	1,1±0,004	1,05±0,003

CON: control group, TER: terlipressin group, * - $p<0,05$

Discussion. In our study intraoperative use of terlipressin significantly reduced mean blood loss, as a result postoperative level of hemoglobin was higher in group TER than in group CON. Intraoperative use of terlipressin did not impact on hemodynamics parameters and other laboratory tests. According to data of the other investigations the use of terlipressin can improve renal function without any detrimental effect on hepatosplanchnic gas exchange and lactate metabolism [3], and an infusion of terlipressin perioperatively has no effect on the creatinine values postoperatively[4]. In our study terlipressine incricased intraoperative urine output, but did not impact on postoperative creatinine level.

References.

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