Clinical Investigation

The haemodynamic effects of the perioperative terlipressin infusion in living donor liver transplantation: A randomised controlled study

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ABSTRACT

Background and Aims: Liver disease is usually accompanied with a decline in systemic vascular resistance (SVR). We decided to assess effects of the peri-operative terlipressin infusion on liver donor liver transplantation recipients with respect to haemodynamics and renal parameters. **Methods:** After Ethical Committee approval for this prospective randomised controlled study, 50 recipients were enrolled and allotted to control (n = 25) or terlipressin group (n = 25) with simple randomisation method. Terlipressin was infused at 1.0 μg/kg/h and later titrated 1.0–4.0 μg/kg/h to maintain mean arterial pressure (MAP) >65 mmHg and SVR index <2600 dyne.s/cm5/m2 till day 4. Nor-epinephrine was used as appropriate. Haemodynamic and transoesophageal Doppler parameters (intraoperative), renal function, peak portal vein blood flow velocity (PPV), hepatic artery resistive index (HARI), urine output (UOP), liver enzymes, catecholamine support were compared intra-operatively and 4 days post-operatively. Desflurane administration was guided with entropy. **Results:** Terlipressin maintained better MAP and SVR (P < 0.01) during reperfusion versus controls (66.5 ± 16.08 vs. 47.7 ± 4.7 mmHg and 687.7 ± 189.7 vs. 425.0 ± 26.0 dyn.s/cm^5), respectively. Nor epinephrine was used in 5 out of 25 versus 20 in controls. Urea, creatinine and UOP were significantly better with terlipressin. PPV was reduced with terlipressin post-reperfusion versus controls (44.8 ± 5.2 vs. 53.8 ± 3.9 ml/s, respectively, P < 0.01) without affecting HARI (0.63 ± 0.06 vs. 0.64 ± 0.05, respectively, P > 0.05) and was sustained post-operatively. **Conclusion:** Terlipressin improved SVR and MAP with less need for catecholamines particularly post-reperfusion. Terlipressin reduced PPV without hepatic artery vasoconstriction and improved post-operative UOP.

Key words: Haemodynamics, liver, renal, terlipressin, transplantation

INTRODUCTION

Impaired hepatic clearance in the patients with end stage liver disease often causes the levels of endogenous vasodilators to increase.[1,2] This results in a decline in systemic vascular resistance (SVR) and redistribution of the body fluids from the central to the peripheral compartment, reducing effective blood flow to organs as the kidneys.[3]

Surgical manoeuvres can in addition produce marked shifts in body fluids with ischaemia–reperfusion injury in many organs.[4] Rational fluid administration, vasopressor usage and haemodynamic monitoring are crucial during the liver transplantation procedure.[5,6]

Terlipressin (triglycyl-lysine vasopressin), a long-acting synthetic analogue of arginine vasopressin, had been used previously in the treatment of

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paracentesis-induced circulatory dysfunction, hepatorenal syndrome and variceal bleeding in hepatic patients.[7,8]

Terlipressin acts through V1 receptors in the vascular smooth muscle cells found mainly in the splanchnic circulation, which causes vasoconstriction with subsequent reduction in portal pressure and improving renal blood flow.[9] The use of minimally invasive transoesophageal Doppler (TOD) to measure and manage the haemodynamic changes could minimise the risks of invasive manoeuvres.

The primary aim of this prospective hospital-based randomised controlled study was to assess the impact of peri-operative terlipressin intravenous infusion in respect to the systemic and hepatic haemodynamics, with a secondary goal to monitor the effect on the renal functions for recipients undergoing liver donor liver transplantation (LDLT).

METHODS

The study was conducted in specialised tertiary referral hospital with the approval by the Local Ethical Committee (0072/2013). This was a prospective randomised controlled trial and after obtaining written informed consent, 50 recipients were allocated to two groups, control group (C; n = 25) and terlipressin groups (T; n = 25) by simple randomisation technique (sealed opaque envelopes). The study was also registered with the Pan African Clinical Trials registry of South African Cochrane Registry as a RCT (PACTR201402000752252). Inclusion criteria were male and female patients aged 18–55 years with model of end stage liver disease score between 12 and 20, portal vein after transplantation of adequate length for the Doppler beam to allow for high-quality signals. Exclusion criteria included SVR index (SVRI) ≥1700 dyne.s/cm^5/m^2, history of myocardial infarction, renal dysfunction, severe oesophageal varices and irregular heart rhythm.

General anaesthesia was induced with propofol titrated (approximately 20 mg every 10 s, 1–1.5 mg/kg) with Entropy® (GE Healthcare Finland, Helsinki, Finland) and clinical signs. Rocuronium 0.9 mg/kg was used to facilitate endotracheal intubation under neuromuscular monitoring. Anaesthesia was maintained with desflurane (Baxter, Erlangen, Germany) in O_2/air mixture (FiO_2 = 0.4), fentanyl, and rocuronium to keep the entropy between 40 and 60.

An arterial line was placed in the non-dependent hand radial artery, and an ultrasound guided central line was inserted in the right internal jugular vein.

Peri-operative fluid regimens consisted of Ringer's acetate solutions (6 ml/kg/h). Albumin 5% was administered in the presence of hypoalbuminemia related to ascites. Packed red blood cells were transfused to keep haematocrit concentration above 25%. Rotational thromboelastometry (ROTEM) guided intraoperative blood transfusion protocol was undertaken.[10]

Transoesophageal Doppler® (Cardio QP; Deltex Medical, Chichester, UK) was placed at mid-oesophagus level till aortic blood flow signals were identified. The time measured by TOD for blood to flow within the aorta was the systolic flow time, and when corrected for the heart rate, the corrected flow time (FTc). Boluses of colloids were guided by an algorithm depending on stroke volume (SV) and FTc, similar to that used by Sinclair *et al*.[11] 200-ml of 6% hydroxyethyl starch in saline (6% HES 130/0.4 Voluven®; Fresenius-Kabi, Bad Homburg, Germany) was given when FTc reached <0.35 ms.

In the terlipressin treated group, the infusion (Glypressin®) was started at the beginning of surgery at a dose of 1.0 μg/kg/h and later titrated (1.0–4.0 μg/kg/h) to maintain a mean arterial pressure (MAP) >65 mmHg and SVRI <2600 dyne.s/cm^5/m^2 calculated by the TOD. Post-operatively the Doppler probe was removed, and the terlipressin infusion was guided only by the MAP. Controls received a placebo of crystalloids in place of terlipressin. In both groups, noradrenaline was infused when MAP fell to <65 mmHg despite adequate volume resuscitation, particularly post-reperfusion. Same surgeons and piggyback technique was used in all cases. Portal vein anastomosis was performed first, and then followed by hepatic artery anastomosis and bile duct reconstruction in all cases. No veno-venous bypass or temporary portocaval shunt were used. All patients were admitted to the Intensive Care Unit.

Continuous intraoperative data collection included heart rate (beat/min), arterial blood pressure (BP) (mmHg), central venous pressure (CVP) (mmHg) and Doppler parameters (FTc [330–360 ms], SV [50–100 cc/beat], cardiac output [COP] [4–8 L/min] and SVR [1900–2400 dyne.s/cm^5]), at 15 min after induction of anaesthesia (T1), 60 min after T1 (T2), 30 min after clamping of the portal vein (T3), 10 min after reperfusion (T4) and T5, 60 min after reperfusion.

The mean daily post-operative haemodynamic data [heart rate, arterial BP and CVP (mmHg)] were calculated from the averaged 24 h measurements of each day (for 4 days).

Only intraoperative Doppler values were assessed as the probes were removed during the weaning process in haemodynamically stable recipients. TOD probe were continued in place if the recipient was not successfully weaned. Abdominal Doppler ultrasonography monitoring was only applied after transplanting the liver with portal vein and hepatic artery anastomosis completed. Ultrasonography indices included portal venous blood flow (PVBF) ml/s, hepatic artery resistive index (HARI). Urine output (UOP) (ml/kg/h), conventional renal and liver function laboratory and blood concentration of lactate were also reported.

Sample size was calculated as 25 per group based on anticipated 25% change in the SVRI. The SVRI at 60 min after the terlipressin infusion was estimated to be 1472 ± 284 dyne.s/cm^5/m^2 to detect a mean difference of 20% in a previous study[4] (α at 0.05, and maximum β =20% with a power of 80%). IBM SPSS® and Lenth Java applets were used for power and sample size calculation. Kolmogorov–Smirnova test revealed that the variables were normally distributed, and parametric statistics were carried out.[15] Data were described using mean and standard deviation. Comparisons were based on the independent *t*-test. Within the group, comparisons were carried out using repeated measures ANOVA. Box and whiskers graphs were done. Chi-square test and Fisher exact test measured association between qualitative variables. After the end of the study, a correction of *P* value for multiple testing was set to 0.01 for significance (Bonforroni correction of multiple comparisons). Data were statistically analysed using Statistical Package for Social Science (IBM, SPSS 20).

RESULTS

A total of 53 patients were included, and only 50 recipients could be assessed. They were divided equally into terlipressin treated group and control group (placebo). Two of the three recipients excluded had significant intraoperative arrhythmias, and the third patient had a portal vein thrombosis discovered during surgery. Of the 50, 47 were weaned successfully in the immediate post-operative period. Two recipients in the control group and one in the terlipressin group required further ventilation until graft functions and acid-base status improved to allow weaning.

Baseline demographic and clinical characteristics of patients in the both groups were comparable [Table 1]. Arterial BP was better preserved with terlipressin treated group (T) compared to controls (C) during the anhepatic phase (30 min after closure of portal vein) (70.85 ± 18.60 vs. 61.5 ± 2.96 mmHg, $P < 0.05$) and immediately after reperfusion (66.5±6.08 vs. 47.75 ± 4.78 mmHg, $P > 0.01$) [Figure 1]. Terlipressin was associated with a better preserved SVR compared to controls during the anhepatic phase (857.2 ± 263.3 vs. 551.5 ± 45.91 dyne/s/cm^5, respectively; $P < 0.01$) [Figure 2].

This improvement in SVR was sustained till the end of the procedure, and was reflected in the requirement for nor epinephrine; 20 patients out of 25 needed nor epinephrine infusion in controls compared to only 5 in the terlipressin treated group. The median (interquartile range) norepinephrine consumption for the recipients in the control group (patients who required norepinephrine, $n = 20$) was 28,800 (28,650–28,800) μg, while for terlipressin treated recipients (patients who required norepinephrine, $n = 5$), the median was 19,300 (19,200–19,300) μg. The number of recipients who required norepinephrine was significantly lower in the terlipressin group ($\chi^2 = 18.00$, $P = 0.000$). Statistical comparison between the two groups regarding the dose of norepinephrine could not be done because the number of patients required in the terlipressin group was only 5.

Table 1: Patient's clinical characteristics differences between terlipressin group and control group

Variables	Groups	Mean±SD	*P*
Age (year)	T	43.9±7.01	
	C	45.2±4.84	
Weight (kg)	T	79.75±9.78	
	C	78.3±8.31	
Height (cm)	T	171.65±4.79	
	C	173.6±6.69	
BMI (kg/m^2)	T	27.66±3.09	
	C	26.84±2.98	
MELD	T	14.6±2.56	>0.05
	C	14±2.12	
GFR (ml/min)	T	96.57±24.93	>0.05
	C	92.65±12.67	

Data were presented as mean±SD, tested by paired *t*-test. *P*<0.05 is considered statistically significant. BMI: Body mass index, MELD: Model of end stage liver disease, GFR: Glomerular filtration rate, SD: Standard deviation, T: Terlipressin, C: Control

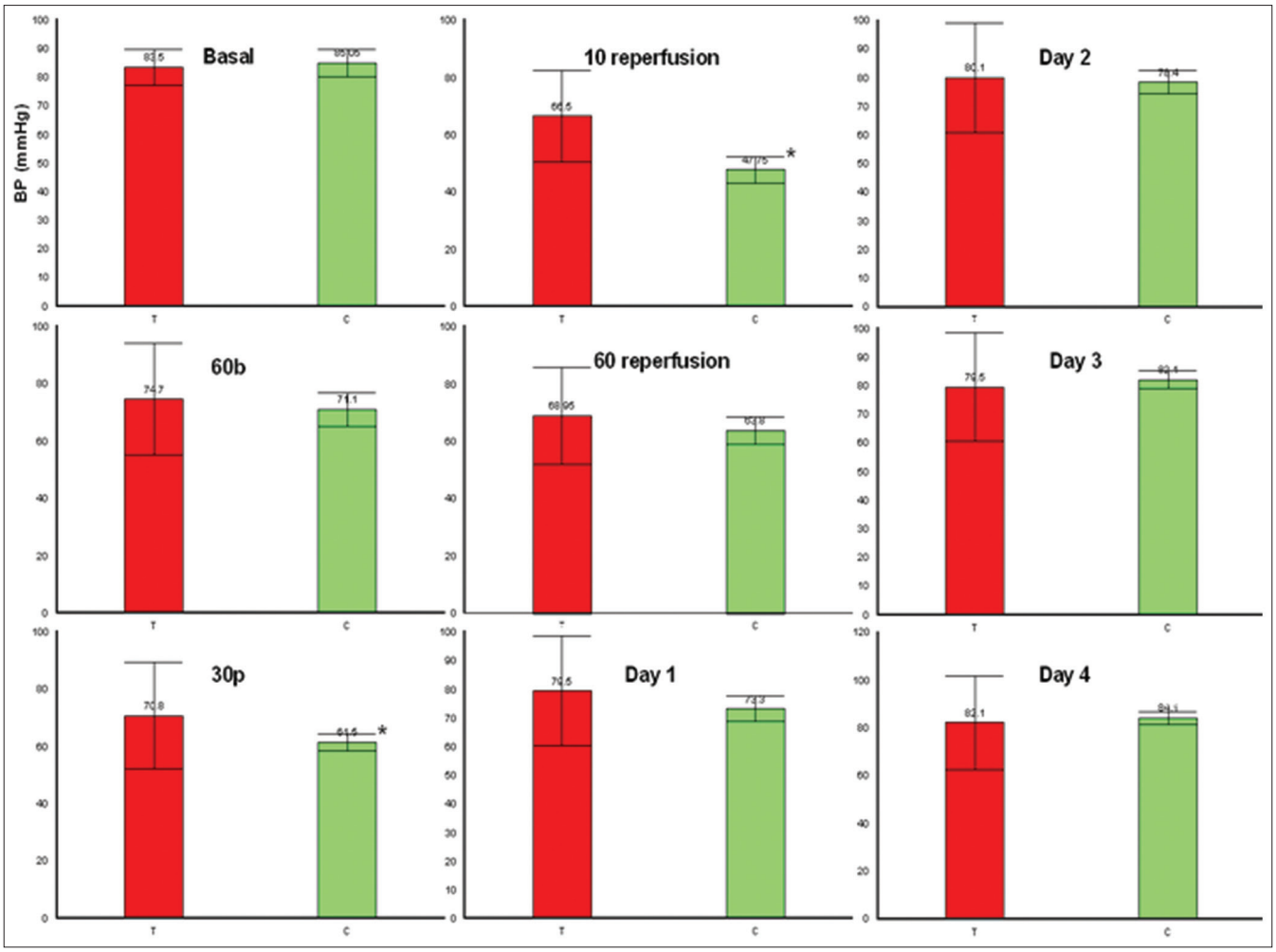

Figure 1: Mean ± standard deviation for blood pressure (BP) differences between terlipressin group (T) and control group (C), tested by paired *t*-test, *indicates $P < 0.05$ statistically significant. Basal: after induction. 60b: 60 min after induction. 30p: 30 min after closure of the portal vein. 10 reperfusion: 10 min after reperfusion. 60 reperfusion: BP 60 min after reperfusion. Days 1, 2, 3, and 4: Post-operative at day 1, 2, 3 and 4

Heart rate, COP, CVP and FTc were comparable between two groups at different intervals [Table 2]. No significant difference were observed between T and C groups concerning intraoperative colloids infusion (hydroxyethyl starch), (2500 ± 500 vs. 2520 ± 489.04 ml, respectively, $P = 0.887$). No major haemodynamic incidents were seen peri-operatively. The use of packed red blood cells and fresh-frozen plasma were comparable between the two groups (4 [0–5.5] and 3 [0–5.5] units in terlipressin group vs. 4 [0–4] and 4 [2.25–6.75] units, in control group). There was a significant decrease in urea and creatinine blood levels associated with an improvement in UOP with terlipressin compared with controls ($P < 0.01$) [Table 3], [Figure 3]. PVBF after reperfusion decreased significantly in the T group compared with controls (44.85 ± 5.22 vs. 54.3 ± 3 ml/s, respectively, $P > 0.01$) and this change was sustained at all-time points measured, but with no significant differences between both groups regarding the hepatic artery blood flow reflected in the HARI [Table 4].

Serum lactate changes were comparable between both groups. ($P > 0.05$), but aspartate aminotransferase (AST) and alanine aminotransferase demonstrated significant differences at different measuring points ($P < 0.05$) [Table 4].

The median days of Intensive Care Unit stay were longer with controls (7 days) than terlipressin treated group (6 days), ($P < 0.01$).

DISCUSSION

Terlipressin was previously suggested to have a beneficial effect on haemodynamics and related peri-operative outcome in LDLT,[4,8] but few studies

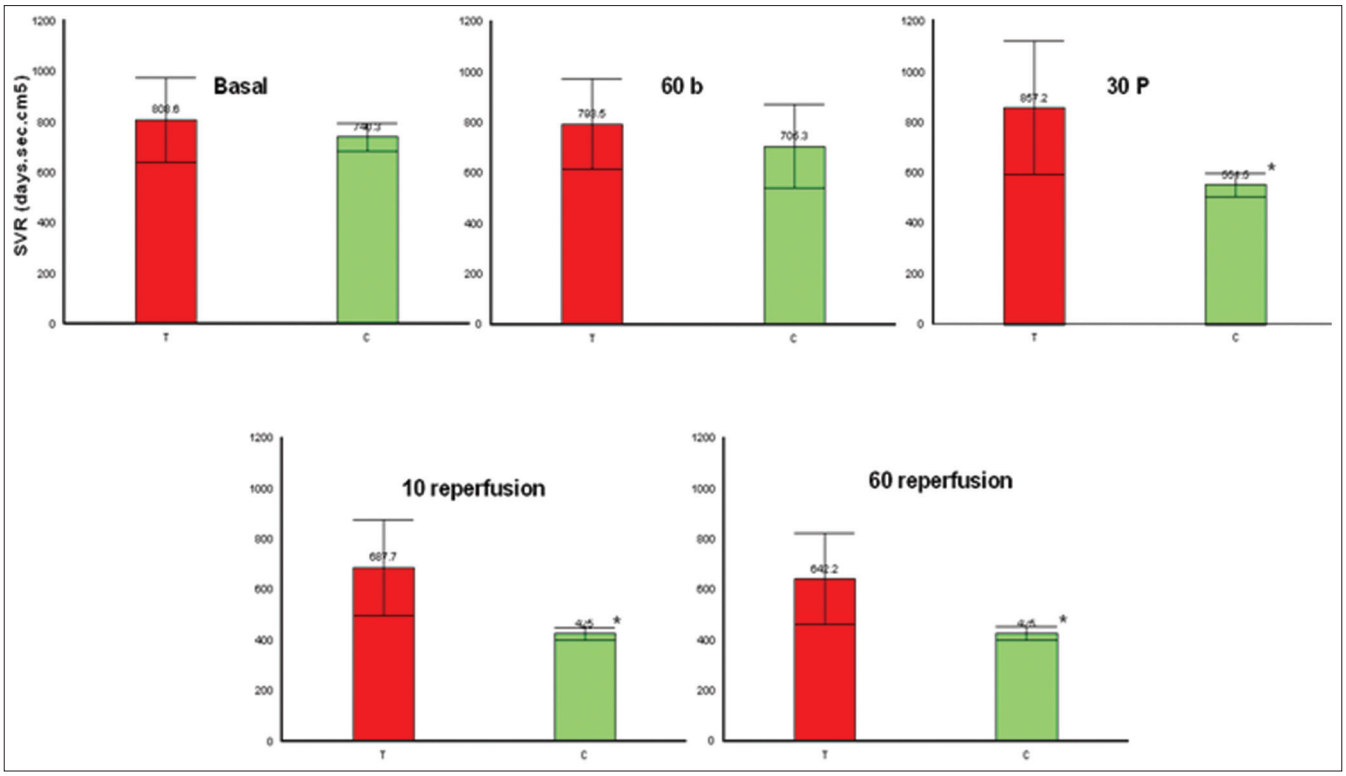

Figure 2: Mean ± standard deviation of systemic vascular resistance differences between terlipressin group (T) and control group (C), tested by paired *t*-test, *indicates $P < 0.05$ statistically significant. Basal: After induction. 60b: 60 min after induction. 30p: 30 min after closure of portal vein. 10 reperfusion: 10 min after reperfusion. 60 reperfusion: 60 min after reperfusion

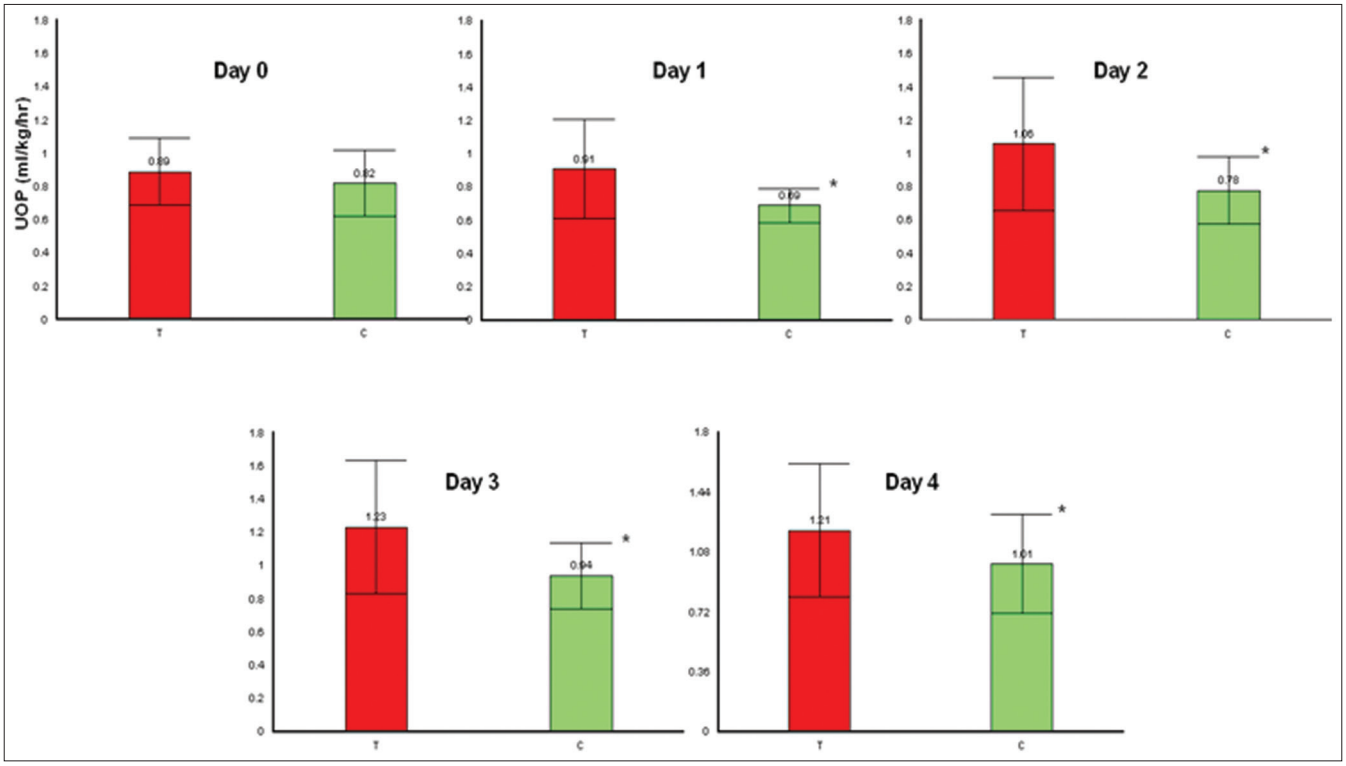

Figure 3: Urine output mean ± standard deviation differences between terlipressin group (T) and control group (C), tested by paired *t*-test, *indicates $P < 0.05$ statistically significant. Day 0: During day of operation. Days 1, 2, 3, and 4: post-operative days 1, 2, 3 and 4

Table 2: Differences in HARI, PPV, (ml/s), urea (mg/dl), creatinine (mg/dl) and lactate (mg/dl) differences between terlipressin group and control group

Variables	Measuring point	Mean±SD	
		Terlipressin	Control
HARI	Post-graft reperfusion	0.63±0.06	0.64±0.05
	Day 1	0.62±0.04	0.63±0.05
	Day 2	0.62±0.05	0.64±0.04
	Day 3	0.62±0.05	0.64±0.05
	Day 4	0.62±0.05	0.64±0.05
PPV0	Post-graft reperfusion	44.8±5.2	54.3±3.4*
	Day 1	39.6±4.3	53.8±3.9*
	Day 2	39.1±3.8	54.4±2.5*
	Day 3	39.7±3.4	53.7±2.8*
	Day 4	39.7±3.3	54.6±2.2*
Urea (mg/dl)	Before operation	22.4±6.8	20.5±6.4
	After operation	31.7±12.6	48.7±13.9*
	Day 1	45.0±16.7	75.0±19.8*
	Day 2	66.5±26.5	100.2±18.5*
	Day 3	71.1±29.8	111.5±24.9*
	Day 4	70.4±30.7	116.9±39.2*
Creatinine (mg/dl)	Before operation	0.6±0.2	0.6±0.2
	After operation	0.8±0.2	0.9±0.3
	Day 1	1±0.3	1.3±0.6
	Day 2	1.0±0.4	1.7±1.0*
	Day 3	0.9±0.5	1.7±0.9*
	Day 4	0.8±0.4	1.7±0.8*
Lactate (mg/dl)	Before operation	18.2±6.36	16.8±3.34
	After operation	79.55±39.43	61.60±12.29
	Day 1	37.71±21.05	28.70±7.19
	Day 2	23.60±16.16	20.70±4.81
	Day 3	16.60±11.82	17.54±4.99
	Day 4	15.80±15.14	15.25±4.03

Data were presented as mean and SD, tested by Mann–Whitney test, **P*<0.05 statistically significant. HARI: Hepatic artery resistant index, PPV: Peak portal vein velocity, SD: Standard deviation, T: Terlipressin, C: Control

Table 3: Liver enzymes difference for terlipressin group and controls

(AST levels U/L)	Groups	Mean±SD
AST basal	T	55.2±35.4
	C	56.4±31.6
AST0	T	305.2±236.1*
	C	639.4±485.0
AST1	T	247.2±146.8*
	C	467.9±269.7
AST2	T	264.2±215.8*
	C	422.5±279.4
AST3	T	171.3±117.4
	C	214.4±79.0
AST4	T	106.1±69.0
	C	143.3±76.9
ALT basal (U/L)	T	33.8±19.0
	C	35.7±20.6
ALT0	T	278.0±203.2*
	C	632.2±491.1
ALT1	T	323.1±279.4*
	C	696.4±396.5
ALT2	T	343.1±337.6*
	C	727.6±541.9
ALT3	T	286.8±254.5*
	C	464.8±273.3
ALT4	T	228.1±186.2*
	C	343.7±166.5

Data were presented as mean±SD, tested by Mann–Whitney test, **P*<0.05 statistically significant. AST basal and ALT basal: AST and ALT the day before operation, AST0 and ALT0: AST and ALT immediately after operation. AST 1, 2, 3, 4 and ALT 1, 2, 3 and 4; postoperative AST and ALT at day 1, 2, 3 and 4. AST: Aspartate amino-transferase, ALT: Alanine amino-transferase, SD: Standard deviation, T: Terlipressin, C: Control

monitored these haemodynamic changes with TOD during the procedure.[2] The results of this study demonstrated that with terlipressin, the TOD calculated SVR was significantly better preserved during the a hepatic phase and immediately after reperfusion compared to controls. This was reflected in a better mean arterial BP without any significant reduction in COP and heart rate during the immediate post-operative period as seen in a study by Mukhtar *et al*.[12] Fayed *et al*.[13] in a similar study demonstrated significant improvement in MAP but with an associated decrease in COP and heart rate. Kalambokis *et al*.[14] studied the effects of terlipressin on haemodynamics in patients with cirrhosis and observed increases in SVR. Normalising low SVR in cirrhotic patients with portal hypertension helps to return the hepatosplanchnic blood to the central compartment and improves perfusion into major organs. Compromised COP during clamping of the inferior vena cava without veno-venous bypass must be supported by an increase in the SVR, since excessive compensation by fluids might lead to a right heart dysfunction after reperfusion.[3]

In the current study, the requirements for norepinephrine support were significantly lower among patients treated with terlipressin, as evidenced in other studies.[12,13]

Terlipressin administration can also improve renal functions by decreasing plasma concentrations of rennin, aldosterone and nor epinephrine. This reduction in the vasoconstrictors leads to an increase renal blood flow.[16,17] In our study, patients treated with terlipressin not only showed improvement in renal function tests but also demonstrated a significant increase in UOP compared with controls without any sign of splanchnic hypoperfusion. Terlipressin increases UOP not only due to improvement in renal function, but also by stimulating V1a receptors.[18] In the present study, terlipressin was associated with a decrease in PVBF velocity. Portal hyperflow carries risk of increasing vascular injury to the graft, contributing to the dysfunction. Portal decompression after blood

Table 4: HR, CVP, SV, SVR and FTC in terlipressin group and control group

	10 min after induction	60 min after induction	30 min after portal vein reperfusion	10 min after reperfusion	60 min after reperfusion	Post-operative at day 1	Post-operative day 2	Post-operative day 3	Post-operative day 4
HR (beat/min)									
T	79.05±20.043	80.45±21.099	87.75±23.300	91.50±26.613	89.40±26.014	86.21±9.198*	81.42±7.0*57*	76.42±6.167*	74.15±6.121*
C	84.80±7.244	87.90±5.910	94.10±4.733	102.55±4.628	100.85±4.923	95.95±4.019	90.95±3.691	86.05±4.904	81.80±5.156
HR (beat/min)									
T	83.50±6.353	74.70±19.647	70.85±18.607*	66.50±16.086*	68.95±16.928	79.50±19.033	80.10±19.111	79.55±19.035	82.15±19.647
C	85.05±4.762	71.15±5.976	61.50±2.964	47.75±4.788	63.85±4.923	73.35±4.579	78.45±4.071	82.15±3.150	84.10±2.531
CVP (mmHg)									
T	10.30±1.657	10.10±3.143	10.20±2.764	10.35±2.870*	11.00±3.583	11.60±3.377	11.05±3.086	11.90±3.354	10.70±3.163
C	10.65±1.755	11.35±1.348	10.00±1.169	12.75±0.966	12.00±1.450	12.45±1.234	12.10±1.252	11.35±1.496	11.45±1.316
SV (ml/beat)									
T	77.45±15.595	79.05±12.411	74.75±10.100	82.55±18.729	88.65±18.904				
C	74.80±3.562	75.10±2.954	79.50±3.953	85.55±4.058	86.35±3.731				
SVR (dyn.s/cm^5)									
T	808.65±167.984	793.50±178.750	857.20±263.301*	687.70±189.715*	642.20±182.739*				
C	740.30±53.677	705.30±165.539	551.50±45.914	425.00±26.056	425.00±26.056				
FTC (ms)									
T	357.60±28.538	364.50±28.836	356.00±34.378	371.70±70.684	367.04±46.042				
C	342.20±12.219	339.20±12.219	342.60±7.836	348.85±6.930	349.50±6.411				

HR: Heart rate, CVP: Central venous pressure, SVR: Systemic vascular resistance, SV: Stroke volume, FTC: Flow time corrected, SD: Standard deviation, T: Terlipressin, C: Control

flow restoration plays an important role for survival in experimental models.[19]

The decrease in portal flow was not accompanied by changes in HARI; this suggests that terlipressin does not cause hepatic arterial vasoconstriction and maintains the flow in the face of falling portal perfusion. Narahara *et al*.[17] also observed that terlipressin infusion dose did not decrease HARI in cirrhotic patients with ascites. Fayed *et al*.[13] demonstrated that decrease in portal blood flow was associated with a decreased hepatic arterial resistance. Hepatic arterial buffer response (HABR) is an intrinsic regulatory mechanism to maintain total hepatic blood flow (when PVBF decreases, hepatic arterial blood flow increases, and vice versa). HABR can be blunted in some cirrhotic patients, and this may be due to a hyposensitivity of adenosine receptors of the artery.[20,21]

Post-operative liver enzymes were significantly lower in terlipressin group as compared to control, possibly because of the reduction in portal venous pressure. Yagi *et al*.[21] studied the impact of portal venous pressure on graft function after LDLT and demonstrated that peak serum AST, bilirubin levels and international normalised ratio after LDLT were significantly higher with increased portal venous pressures. Reduced blood flow in the splanchnic region with terlipressin was not accompanied with signs of splanchnic hypo perfusion as lactate blood levels, which were comparable between both groups; this was also observed by Wagener *et al*.[22]

Reducing portal vein pressure is expected to decrease the amount of bleeding and transfusion. Blood transfusion requirements were not significantly different between two groups in the present study as in other studies.[4] The refinement of surgical techniques and the use of piggy back technique during transplantation together with ROTEM may have all contributed to the reduction in transfusion requirements. TOD data can also help guide the clinician in fluid administration and titration of vasopressors and inotropes,[23] which was evident in the results of our study where terlipressin use was associated with reduced nor epinephrine usage.[24]

Transoesophageal Doppler was used in the current study intraoperatively; several studies have demonstrated good overall correlation between CO determined by TOD and thermo dilution.[25,26] The pulmonary capillary wedge pressure (PCWP) is often a misleading measurement of left ventricular preload. Many

disorders can alter the relationship between PCWP and left ventricular end-diastolic pressure (LVEDP), and there is often no direct relationship between LVEDP and left ventricular end-diastolic volume due to factors affecting left ventricular compliance, particularly in critically ill patients. In comparison, the FTc has been shown to correlate well with preload.[27] Kincaid *et al*. study concluded that FTc was a better indicator of preload than PCWP when resuscitating hypovolaemic trauma patients.[28] In contrast to pulmonary arterial catheterisation, TOD provides an estimation of contractility by the measurement of peak velocity. Alterations of waveform shapes in both patients and normal subjects can be assessed using TOD when inotropes are used.[23]

One of the limitations of our study was the frequent repositioning of the Doppler probe due to the surgical manoeuvres, together with the diathermy interference.

CONCLUSION

Terlipressin infusion significantly improved the low SVR and BP with reduced need for catecholamine support and with less renal dysfunction in LDLT as assessed by TOD. Peak portal blood flow was reduced with terlipressin without hepatic artery vasoconstriction or signs of splanchnic hypo perfusion. TOD monitoring during the terlipressin infusion helped to frequently guide the dose in order to maintain an adequate SVR and avoid significant elevations. Further studies involving more patients is recommended to study the interrelationship of corrected flow time (FTc of the TOD) and CVP, in order to decide, which one reflects best the patient's fluid requirements. This could lead to the establishment of new TOD guided protocols for fluid replacement in this category of hepatic patients during their peri-operative period.

REFERENCES

1. Hennenberg M, Trebicka J, Sauerbruch T, Heller J. Mechanisms of extrahepatic vasodilation in portal hypertension. Gut 2008;57:1300-14.
2. Hussien M, Refaat E, Fayed N, Yassen K, Khalil M, Mourad W. Use of transesophageal Doppler as a sole cardiac output monitor for reperfusion hemodynamic changes during living donor liver transplantation: An observational study. Saudi J Anaesth 2011;5:264-9.
3. Skagen CL, Said A. Vasoconstrictor use in liver transplantation: Is there evidence for rational use? Minerva Gastroenterol Dietol 2010;56:279-96.
4. Hong SH, Lee JM, Choi JH, Chung HS, Park JH, Park CS. Perioperative assessment of terlipressin infusion during living donor liver transplantation. J Int Med Res 2012;40:225-36.
5. Schroeder RA, Collins BH, Tuttle-Newhall E, Robertson K, Plotkin J, Johnson LB, *et al.* Intraoperative fluid management during orthotopic liver transplantation. J Cardiothorac Vasc Anesth 2004;18:438-41.
6. García-Criado A, Gilabert R, Salmerón JM, Nicolau C, Vilana R, Bianchi L, *et al.* Significance of and contributing factors for a high resistive index on Doppler sonography of the hepatic artery immediately after surgery: Prognostic implications for liver transplant recipients. AJR Am J Roentgenol 2003;181:831-8.
7. Moreau R, Asselah T, Condat B, de Kerguenec C, Pessione F, Bernard B, *et al.* Comparison of the effect of terlipressin and albumin on arterial blood volume in patients with cirrhosis and tense ascites treated by paracentesis: A randomised pilot study. Gut 2002;50:90-4.
8. Abdullah MH, Salah SM, Morad WS. Terlipressin versus nor epinephrine to counteract intraoperative paracentesis induced refractory hypotension in cirrhotic patients. Ain Shams J Anesthesiol 2012;5:89-100.
9. Zhang LP, Li M, Yang L. Effects of different vasopressors on hemodynamics in patients undergoing orthotopic liver transplantation. Chin Med J (Engl) 2005;118:1952-8.
10. Gorlinger K. ROTEM – Erweitertes perioperatives gerinnungs management. J Anaesth Intensive BehandLung 2005;2:S53-8.
11. Sinclair S, James S, Singer M. Intraoperative intravascular volume optimisation and length of hospital stay after repair of proximal femoral fracture: Randomised controlled trial. BMJ 1997;315:909-12.
12. Mukhtar A, Salah M, Aboulfetouh F, Obayah G, Samy M, Hassanien A, *et al.* The use of terlipressin during living donor liver transplantation: Effects on systemic and splanchnic hemodynamics and renal function. Crit Care Med 2011;39:1329-34.
13. Fayed N, Refaat EK, Yassein TE, Alwaraqy M. Effect of perioperative terlipressin infusion on systemic, hepatic, and renal hemodynamics during living donor liver transplantation. J Crit Care 2013;28:775-82.
14. Kalambokis GN, Pappas K, Tsianos EV. Differential effects of terlipressin on pulmonary and systemic hemodynamics in patients with cirrhosis and pulmonary hypertension: An echo study. Angiology 2012;63:199-205.
15. Field A, editor. Discovering Statistics Using SPSS. 2nd ed. London, California, New Delhi: SAGE Publications Ltd.; 2006.
16. Krag A, Møller S, Henriksen JH, Holstein-Rathlou NH, Larsen FS, Bendtsen F. Terlipressin improves renal function in patients with cirrhosis and ascites without hepatorenal syndrome. Hepatology 2007;46:1863-71.
17. Narahara Y, Kanazawa H, Taki Y, Kimura Y, Atsukawa M, Katakura T, *et al.* Effects of terlipressin on systemic, hepatic and renal hemodynamics in patients with cirrhosis. J Gastroenterol Hepatol 2009;24:1791-7.
18. Mutlu GM, Factor P. Role of vasopressin in the management of septic shock. Intensive Care Med 2004;30:1276-91.
19. Man K, Lo CM, Ng IO, Wong YC, Qin LF, Fan ST, *et al.* Liver transplantation in rats using small-for-size grafts: A study of hemodynamic and morphological changes. Arch Surg 2001;136:280-5.
20. Gülberg V, Haag K, Rössle M, Gerbes AL. Hepatic arterial buffer response in patients with advanced cirrhosis. Hepatology 2002;35:630-4.
21. Yagi S, Iida T, Taniguchi K, Hori T, Hamada T, Fujii K, *et al.* Impact of portal venous pressure on regeneration and graft damage after living-donor liver transplantation. Liver Transpl 2005;11:68-75.
22. Wagener G, Gubitosa G, Renz J, Kinkhabwala M, Brentjens T, Guarrera JV, *et al.* Vasopressin decreases portal vein pressure and flow in the native liver during liver transplantation. Liver Transpl 2008;14:1664-70.
23. Singer M, Allen MJ, Webb AR, Bennett ED. Effects of alterations in left ventricular filling, contractility, and systemic vascular

resistance on the ascending aortic blood velocity waveform of normal subjects. Crit Care Med 1991;19:1138-45.
24. Schober P, Loer SA, Schwarte LA. Perioperative hemodynamic monitoring with transesophageal Doppler technology. Anesth Analg 2009;109:340-53.
25. Poutanen T, Tikanoja T, Sairanen H, Jokinen E. Normal aortic dimensions and flow in 168 children and young adults. Clin Physiol Funct Imaging 2003;23:224-9.
26. Dark PM, Singer M. The validity of trans-esophageal Doppler ultrasonography as a measure of cardiac output in critically ill adults. Intensive Care Med 2004;30:2060-6.
27. King SL, Lim MS. The use of the oesophageal Doppler monitor in the intensive care unit. Crit Care Resusc 2004;6:113-22.
28. Kincaid EH, Fly MG, Chang MC. Nonivasive measurements of preload using esophageal Doppler are superior to pressure-based estimates in critically injured patients. Crit Care Med 1999;27:100.

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