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Research Article

Acute normovolaemic haemodilution in cirrhotic patients undergoing major liver resection: Role of ROTEM

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KEYWORDS

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Abstract *Background:* Allogeneic blood transfusion increases the incidence of tumor recurrence and affects survival of patients undergoing liver resection. Acute normovolemic heamodilution (ANH) helps to decrease the exposure to allogeneic transfusion. This technique in cirrhotic patients undergoing major liver resection may compromise the coagulation process. Study of coagulation effects of ANH using rotation thromboelastometry (ROTEM), which provides global evaluation of coagulation function, may add beneficial effects.

Patients and methods: 160 ASAII, Child A cirrhotic patients undergoing major hepatic resection were prospectively randomized into two equal groups; control and ANH group in which ANH was done. ROTEM (extem and fibtem) and conventional coagulation tests (CCT) (INR, fibrinogen level, and platelet count), were measured at baseline, 1 h after start of surgery, at the end of surgery and on 3rd and 5th postoperative days. Also blood lactate level and oxygen consumption were evaluated at the previous measuring points. The number of patients received allogeneic blood transfusion and the amount of blood received blood loss, fluid infused were recorded.

Results: ROTEM parameters of ANH group showed statistically significant changes compared to base line value and corresponding control values at 1 h after surgery. These changes were slightly outside the normal range, 1 h after surgery and within the normal reference range in all the following study points. Conventional coagulation parameters had the same pattern of changes but values were outside normal range all over the study period. ANH decreased the incidence of allogeneic packed red blood cell transfusion by 22.5% (28.75% vs. 6.25% of patients received packed red blood cells in control and ANH groups respectively) and plasma transfusion by 6.25% (13.75%

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vs. 7.5% of patients received plasma in control vs. ANH group respectively). No reported complications related to ANH were detected.

Conclusion: ROTEM added two benefits 1st it gave some clinical evidence of safety of ANH associated coagulation changes which may encourage more degree of haemodilution in this category of patients. Second the use of ROTEM triggered transfusion parameters seemed to help decrease plasma transfusion requirement which serves the aim of ANH.

1. Introduction

The reported rate of allogenic blood transfusion during liver resection varies between centers [1,2]. Allogenic blood transfusion has been associated with an increased incidence of tumor recurrence and decreased survival [3,4] and its avoidance in both cirrhotic and non-cirrhotic patients undergoing liver resection improves survival [5]. Heamodilution has been found as an effective method to decrease intraoperative exposure to allogeneic blood [6]. Hepatic patients are known to have disturbed coagulation profile [7] which would be further disturbed by liver resection surgery with more coagulation derangement [8]. In such situation critical hemostatic levels can become the primary transfusion triggers [9]. In this condition assessment of coagulation changes is mandatory to ensure safety of heamodilution in this category of patients.

Traditionally, evaluation of coagulopathy has been based largely on the platelet poor plasma assessment of the extrinsic and intrinsic pathways which reflects $< 5\%$ of the thrombin generated during clot formation [10]. Previous clinical studies found that up to 35% of the variability in the INR and 20% of the variability of the PTT are unrelated to underlying clotting factor levels [11]. Coagulation research has been redirected to the cell-model of hemostasis, recognizing the central role of platelets, the endothelium, and their interaction with the plasma elements [12]. Thromboelastometry (ROTEM®; Tem International GmbH, Munich, Germany) offers rapid, comprehensive, global, clinical assessment of the patient's coagulation status, from initiation of coagulation to the formation, quality and potential breakdown of the clot [13,14]. ROTEM® test results have also been used to guide coagulation therapy [15,16].

We therefore hypothesized that using ROTEM as a comprehensive assessment of clot integrity may reflect an evidence of safety of ANH associated coagulation changes in this category of patients undergoing such operation.

2. Patients and methods

After approval of the local ethical committee and written informed consent, 160 ASAII patients with Child A cirrhosis undergoing major liver resection ($>$ or $=3$ segments) were prospectively randomized studied. Exclusion criteria included significant history of cerebrovascular disease, cardiovascular disease, pulmonary disease, renal dysfunction (creatinine $\geqslant 1.5$ mg/dL), platelet count $< 100{,}000$, presence of active infection, evidence of hepatic metabolic disorder (bilirubin > 2 mg/dL or ALT > 75 U/L), drug therapy affecting coagulation within 14 day before and preoperative hemoglobin less than 11gm/dl. Patients were divided randomly into two groups; ANH group ($n = 80$) in which patients underwent ANH and control group ($n = 80$), without ANH. After standard monitoring had been placed, anesthesia was induced using propofol 2 mg/kg and 0.9 mg/kg rocuronium to facilitate endotracheal intubation. Anaesthesia was maintained with isoflurane in O_2: air mixture ($FiO_2 = 0.4$), fentanyl , and rocuronium keeping entropy reading between 40% and 60%. Two wide bore peripheral venous cannulae , an arterial line , and central line were inserted. For ANH group, hemodilution process was initiated immediately after tracheal intubation via the internal jugular catheter to a target Hematocrit of 27%. the allowable blood withdrawn was determined using the established formula: VL = EBV *H0 – HF/HAV, where VL is the allowable blood loss, EBV is the estimated blood volume, H0 is the patient's initial Hgb, HF is the patient's minimal allowable Hgb, and HAV is the average of the initial and minimal allowable Hgb.12,19,20. The blood, removed into standard citrate–phosphate–dextrose adenine blood storage bags, was simultaneously replaced by equal volume of 6% hydroxyl ethyl starch 130/0.4 (HES 130/0.4).

Transfusion threshold for erythrocytes was hematocrit less than 24%. Haemostatic products are transfused using ROTEM based protocol, shown in the index [17]. Autologous blood was reinfused when a target hematocrit value was reached or after completion of liver resection and hemostasis, in the reverse order of collection.

All Patients received Ringer's acetate: 6 ml/kg/h as a continuous infusion. Intraoperative fluid optimization managed by the Cardio Q_ oesophageal Doppler monitor (ODM) using the following protocol adopted by Sinclair and colleagues [18].

For patients with a FTc less than 350 ms, suggesting hypovolaemia, the protocol consisted of a fluid challenge HES 130/0.4 (3 ml/kg) over 5–10 min.

There were three possible outcomes:

(i) SV same or increased, FTc < 350 ms—repeat fluid challenge;
(ii) SV increases by $> 10\%$, FTc > 350 ms—repeat fluid challenge till no increase in SV; and
(iii) FTc $>$ 400 ms—no further fluid till FTc or SV decreased by 10%.

Invasive blood pressure, heart rate, central venous pressure (CVP), arterial oxygen saturation, end tidal CO_2 tension and esophageal temperature were monitored continuously. INR, fibrinogen level, platelet count, and ROTEM extem CFT, MCF, alpha angle and fibtem MCF were done preoperative as base line, 1 h after start of surgery , at the end of surgery, and 3rd and 5th postoperative days. ODM parameters include including cardiac output, corrected flow time, systemic vascular resistance, Oxygen consumption and Serum lactate were recorded; base line, 1 h after start of surgery and at end of surgery. Urine output, blood loss, fluids and allogeneic blood products administered were recorded. Liver and kidney function tests were done at base line and on postoperative day 1, 3.

3. Statistical procedure

Data was statistically analyzed using SPSS (statistical package for social science) program version 13 for windows for all the analysis a p value < 0.05 was considered statistically significant: – data are shown as mean, range or value and 95% confidence interval (95% CI) and frequency and percent. All data are tested with Kolmogorov-Smirnov Z test and most of them were found normally distributed and so presented with mean ± SD. And using both parametric and non-parametric testes on doing associations. Repeated measures ANOVA test was performed to differentiate changes in different follow up results of normally distributed studied variables.

4. Results

Patient's data and clinical characteristics given in (Table 1). There were 3 patient in control and 5 in ANH group with preoperatively controlled hypertension and 4 patients of type II diabetes on oral hypoglycemic treatment 2 in each group.

There were no statistically significant hemodynamic differences between both groups at all measuring points. However the hemodynamics in both groups changed significantly compared to base line after resection and towards the end of surgery (Table 2).

Regarding allogeneic transfusion requirement 5 out of 80 patients in ANH group required packed red blood cell unites compared to 23 out of 80 patients in control group also plasma transfusion showed statistically significant decrease in ANH group 6/80 compared to control group 11/80 (Table 3). None of both groups received platelets or cryoprecipitate.

ROTEM parameters showed statistically significant change compared to base line in ANH, 1 h after start of surgery and at end of surgery while control group showed statistically significant difference only at the end of surgery compared to the base line. The comparison between both groups showed statistically significant difference 1 h after surgery and no significant change between both groups after that. Almost all studied ROTEM parameters were within normal range values (apart from slight changes at 1 h after surgery in ANH group) (Table 4). CCT parameters showed the same pattern of changes in both groups when compared to base line values and when compared to each other but the values were outside the normal range values (Table 5). There was significant increase in lactate level compared to base line in both groups while the there was no significant differences between both groups at all measuring points. Oxygen consumption showed significant reduction in both groups compared to base line values and the comparison of both groups was insignificant (Table 6). All patients were extubated at the end of surgery in the operation room except 5 patients (2in control and 3 in ANH GROUP) who were extubated within 4 h in surgical ICU. One patient in control group suffered from postoperative bleeding due to surgical causes and re-explored.

5. Discussion

The challenge in this study was the disturbed coagulation profile of cirrhotic patients which was further stressed by both ANH and liver resection hence critical haemostatic levels may become the primary transfusion triggers. Singbartl et al. [9] demonstrated that in normal volunteers during profound haemodilution, haemostasis disturbed before the supply of oxygen to tissues, i.e., the limiting factor for haemodilution would be the changes in haemostasis caused by dilution of platelets and coagulation factors. Although we followed milder degree of haemodilution compared to Singbartl et al., the compromised coagulation reserve of cirrhotic patients and the effect of liver resection may impair the haemostatic process to a critical level that makes it logic to seek for a more firm proof of safety of this maneuver in such operation.

ROTEM has gained wide acceptance for monitoring of acquired perioperative coagulopathy and compared with PT/PTI and aPTT, thrombelastometry yields additional information regarding clot firmness and stability [19,20]. On the other hand, INR and PTT failed to correlate with clinical bleeding [21,22] and were not sensitive in detecting coagulation defects, compared with TEG which differentiated the mechanism re-

Table 1 Patients clinical characteristics.

Studied variables	ANH (N = 80)	Control (n = 80)
Age (years)	50 ± 6	48.5 ± 1
Weight (kg)	71 ± 12	69 ± 12
Height (cm)	160 ± 4	159 ± 4.67
Gender (M/F)	65/15	60/20
Operation time (min)	302 ± 54	286 ± 44
Volume of blood withdrawn (ml)	1750 ± 550	0
Initial HCT (%)	40.82 ± 2.94	41.11 ± 3.21
Final HCT (%)	30.55 ± 3.31	29.55 ± 2.88
Estimated blood loss (ml)	1240 ± 776	1322 ± 834
Intraop urine output (ml)	919 ± 651	833 ± 604
Intraoperative fluids (ml)	5011 ± 1340*	3486 ± 1344
Colloids (ml)	2718 ± 526*	1294 ± 415
Crystalloids (ml)	2293 ± 736	2152 ± 799
RLV (%)	39.5 ± 4.6	39 ± 4.8

Values are mean ± SD, ANH = acute normovolemic hemodilution, RLV% = remaining liver volume %.
* Denotes statistical significant between both groups.

Table 2 Haemodynamic changes.

	Baseline	After haemodilution	After resection	End surgery
CVP (mm Hg)				
ANH	7.3 ± 2.0	6.8 ± 1.7	7.2 ± 0.8	6.4 ± 1.3
Control	7.1 ± 2.1	6.7 ± 1.5	6.9 ± 1.1	6.1 ± 1.4
MAP (mm Hg)				
ANH	87.33 ± 14.5	74.2 ± 11.2*	71.8 ± 10.4*	70.8 ± 11.1*
Control	88.29 ± 13.7	76.1 ± 12.4*	73.9 ± 11.2*	71.6 ± 12.3*
FTC (ms)				
ANH	361 ± 16.8	369 ± 9.7	370 ± 14.6	375 ± 39
Control	365 ± 36	377 ± 45	367 ± 45	372 ± 35
COP (L/min)				
ANH	5.6 ± 1.8	6.17 ± 1.5	7.15 ± 15.8*	7.5 ± 1.8*
Control	5.9 ± 1.9	6.04 ± 1.5	7.04 ± 1.5*	7.7 ± 1.9*
SVR (dynes sec/cm^5)				
ANH	1100 ± 355	985 ± 344	862 ± 284*	808 ± 320*
Control	1187 ± 340	1010 ± 298	850 ± 290*	790 ± 340*

No statistical significant difference between both groups, FTC = corrected flow time; COP = cardiac out put; SVR = systemic vascular resistance; MAP = mean arterial blood pressure.
* Denoting statistically significant difference compared to base line values ($P < 0.05$).

Table 3 Allogenic transfusion requirement.

	ANH ($n = 80$)	Control ($n = 80$)
Allogenic packed red blood cells		
Number of patients (%)	5/80 (6.25)	23/80 (28.75)
Units/patient	0.7 ± 1.68*	1.55 ± 1.8
Allogenic fresh frozen plasma		
Number of patients (%)	6/80 (7.5)	11/80 (13.75)
Units/patient	0.8 ± 1.64*	1.7 ± 1.95

Values are mean ± SD, ANH = acute normovolemic hemodilution.
* Denoting statistically significant difference ($P < 0.05$).

lated to clotting abnormalities in experimental trauma and hemorrhagic shock [23].

This study assessed ROTEM extem clot formation time (CFT), which is the time (in seconds) until a definite clot is formed (defined as an amplitude of 20 mm), extem maximum clot firmness (MCF; given in millimeters), which measures the clot strength and depends primarily on platelet and fibrinogen function. And extem α angle that measured between the midline of the tracing and a straight line drawn from the 1-mm point tangential to the curve, indicates the rate of fibrin polymerization, and fibtem MCF which monitor the firmness of fibrin clot when the contribution of platelets is removed.

These selected ROTEM parameters are are used primarily to evaluate overall clot stability and fibrin polymerization [24] and should be performed simultaneously as first-line ROTEM tests in bleeding surgical patients [25]. Also, CFT and MCF are the most interesting parameters to be considered for clinical studies to assess bleeding-risk in cirrhotic patients [26].

In this study markers for clot strengthening (α-angle and MCF), MCF of fibtem, and extem CFT changed significantly after 1 h of start surgery and at end of surgery compared to baseline with ANH. In normal healthy volunteers, TEG parameters R, K, angle alpha, and MA changed exponentially and in contrast to our study it has been found that the effects were significant only at dilutions 60% for R, K, and angle alpha, while MA decreased significantly at dilution 30% [27]. In current study the significant changes on ROTEM parameters were observed at milder dilutions which may be attributed to the type of our patients with impaired coagulation reserve. The results of Bang et al. [28] supported this explanation as they concluded that: haemodilution with 6% HES (130/0.4) results in TEG abnormalities even with 11% hemodilution, in ESLD patients undergoing liver transplantation and the more the dilution the higher the increasing in the significance of TEG deterioration. Kim et al. [29] stated that coagulopathy was not observed at mild 25% or moderate 50% hemodilution, highlighting the important functional reserve of coagulation factors in the setting of trauma and hemorrhagic shock.

In spite of the recorded statistical significant difference of ROTEM parameters in ANH group, compared to their base line values and to corresponding values of control group, after ANH and even they were sometimes slightly outside the normal range, these changes were only indicating unimpaired haemostasis with reduced reserve according to Andreas Calatzis et al. [30] clinical interperitation of ROTEM parameters in acute haemostatic disorders. This is in agreement with a study by Wohlauer et al. [31] who found that hemodilution does not have a significant impact on coagulation and clot integrity is maintained following fluid resuscitation.

All ROTEM parameters improved at the end of surgery (all values were within normal range) and were statistically nonsignificant compared to corresponding control values. This may be attributed to retransfusion of the autologous blood with its contents of coagulation factors and platlets. The 3rd and the 5th day values were statistically insignificant compared to control group and were within normal range. These data came with disagreement to conventional coagulation tests results.

On the other hand the base line values of INR were outside the normal range in both groups and further significantly dete-

Table 4 ROTEM parameters changes of both group.

Variable	Control group	ANH group	*P*
EX CFT baseline (s)	117.15 ± 21.95	116.05 ± 23.4	0.99
EX CFT 1 h after start of surgery (s)	120.45 ± 24.86	155.0 ± 29.76*	0.019
EX CFT at end of surgery (s)	139.15 ± 25.39*	135.1 ± 23.65*	0.13
EXCFT 3rd POD	146.96 ± 21*	145.75 ± 22.78*	0.09
EX CFT 5th POD	129.81 ± 19.98*	128.98 ± 18.81*	0.08
EX MCF baseline (mm)	56.80 ± 7.56	55.45 ± 6.29	0.148
EX MCF 1 h after start of surgery (mm)	54.05 ± 6.81	48.40 ± 4.15*	0.024
EX MCF at end of surgery (mm)	45.25 ± 5.17*	46.00 ± 6.42*	0.144
EX MCF 3rd POD	55.20 ± 6.47	56.50 ± 6.76	0.26
EX MCF 5th POD	56.20 ± 7.56	57.90 ± 7.48	0.167
EX baseline α-angle (°)	58.20 ± 7.19	59.00 ± 8.01	0.934
EX α-angle 1 h after start of surgery (°)	56.35 ± 7.72	51.80 ± 7.3*	0.026
EX α-angle at end of surgery (°)	50.00 ± 6.91*	50.70 ± 7.67*	0.466
EX α-angle 3rd POD	59.89 ± 8.29	59.35 ± 9.19	0.58
EX α-angle 5th POD	60.89 ± 7.29	61.99 ± 8.39	0.12
FIBTEM baseline MCF (mm)	13.90 ± 2.60	14.10 ± 2.90	0.649
FIB MCF 1 h after start of surgery (mm)	12.25 ± 2.52	10.10 ± 2.21*	0.043
FIB MCF at end of surgery (mm)	9.80 ± 2.12*	10.05 ± 2.58*	0.74
FIB MCF 3rd POD	14.5 ± 3.1	14.8 ± 2.9	0.52
FIB MCF 5th POD	15.8 ± 3.9*	15.9 ± 3.4*	0.64

ANH = acute normovolaemic haemodilution.
EX = extem FIB = fibtem CFT = clot formation time MCF = maximum clot firmness POD = postoperative day.
Data are presented as mean ± SD.
P indicating the significance of comparison of both groups.
* Denotes $P < 0.001$ vs. corresponding baseline value.

Table 5 Conventional coagulation changes of both groups.

Variable	Control Group	ANH group	*P*
Fibrinogen level 1 (mg/dl)	224.65 ± 69.50	228.55 ± 63.19	0.854
Fibrinogen level 2 (mg/dl)	213.50 ± 66.03	172.55 ± 43.79*	0.014
Fibrinogen level 3 (mg/dl)	145.75 ± 51.09*	149.9 ± 44.17*	0.365
Fibrinogen level 4 (mg/dl)	246.50 ± 49.91*	250 ± 46.23*	0.312
Fibrinogen level 5 (mg/dl)	228.25 ± 43.62	231 ± 39.91	0.225
Platelet count 1 ($\times10^3/mm^3$)	161.20 ± 41.80	167.55 ± 45.49	0.458
Platelet count 2 ($\times10^3/mm^3$)	151.40 ± 41.03	138.8 ± 37.25*	0.041
Platelet count 3 ($\times10^3/mm^3$)	129.85 ± 20.11*	130.4 ± 25.44*	0.320
Platelet count 4 ($\times10^3/mm^3$)	117 ± 23*	119 ± 21*	0.26
Platelet count 5 ($\times10^3/mm^3$)	124 ± 22*	129 ± 19*	0.14
INR 1	1.43 ± 0.21	1.47 ± 0.19	0.549
INR 2	1.48 ± 0.21	1.64 ± 0.16*	0.041
INR 3	2.19 ± 0.31*	2.03 ± 0.27*	0.078
INR 4	1.67 ± 0.17*	1.66 ± 0.15*	0.15
INR 5	1.54 ± 0.16	1.51 ± 0.11	0.11

1 = Base line values, 2 = values 1 h after start of surgery, 3 = values at the end of surgery,4 = postoperative day3, 5 = postoperative day5.
ANH = acute normovolemic hemodilution.
Data are presented as mean ± SD.
P indicating the significance of comparison of both groups.
* $P < 0.001$ vs. corresponding baseline value.

riorated after ANH compared to its base line value and to corresponding value of control group. And continue to deteriorate in both group at the end of surgery and did not reach its base line value at 5th POD. This reflected hypocoagulability is not of clinical significance as the available evidence is notable for a lack of correlation between mild-to-moderate coagulation test abnormalities and the development of procedural bleeding or need for red blood cell administration [32,33].

Chowdary et al. noted that nearly 50% of patients with abnormal coagulation tests (INR > 1.5) had coagulation factor levels generally considered sufficient for adequate thrombus formation [34].

Table 6 Metabolic and laboratory changes.

	Base line	1 h After surgery	End surgery	D1	D3
Lactate(mg/dl)					
ANH	10.8 ± 5.1	17.1 ± 6.51*	22.3 ± 7.3*		
Control	11.08 ± 4.82	16.8 ± 6.12 *	21.9 ± 7.4*		
VO2 (ml/min/m^2)					
ANH	127.7 ± 25.1	91.19 ± 19.3*	88.2 ± 17.8*		
Control	129.2 ± 27.8	89.8 ± 17.9*	92.4 ± 20.2*		
Creatinine (mg/dl)					
ANH	0.85 ± 0.23			0.83 ± 0.2	0.78 ± 0.1
Control	0.78 ± 0.1			0.85 ± 0.17	0.79 ± 0.1
Serum aminotransferase SGPT					
ANH	51.03 ± 27.9			263.9* ± 18*	212.2 ± 49*
Control	54.9 ± 28.4			257.9* ± 293*	215.7 ± 57*

Values are mean ± SD D1 = postoperative day1 D3 = postoperative day 3VO2 = oxygen consumption.
* $P < 0.05$ compared with baseline value.

Patients in the ANH group had 22.5% reduction in the likelihood of requiring allogeneic blood transfusion compared to control group. Previous studies provided strong evidence that ANH technique effectively reduces the need for allogeneic blood transfusions [2,7] in Patients undergoing major hepatic resection and recommended ANH for routine use [35]. As ANH reduces the hemoglobin (Hb) concentration of blood, any surgical blood loss will contain relatively less Hb [36].

The efficacy of ANH to decrease exposure to allogenic blood transfusion in this study was less than that reported by Idit Matot et al. (22.5% versus 26%) respectively, this may be due to the higher transfusion trigger of HCT in this study (24% versus 21%). Although our transfusion trigger was less efficacious, we have chosen this approach, following other investigators [37] as sudden extensive bleeding may occur with an acute and rapid decrease in Hematocrit below the lowest acceptable value. In our study, ROTEM was used to assess the effects of (ANH) on blood coagulation.

Fresh frozen plasma transfusion was higher in control group suggesting that ANH is also effective in preserving coagulation factors. Reinfusion of fresh coagulation factors and platelets is thought to augment a patient's inherent coagulation function [38] as manifested by better (although non-significant) end of surgery ROTEM and CCT in ANH group compared to control group.

In our study we observed that the % of plasma transfusion in both groups (7.5% and 13.75% in ANH and control group respectively) was lower than that recorded by Jarnagin et al. [2] (17.5% and 28.4% in ANH and control groups respectively). Actually William et al. depended on INR >1.8 as a trigger for plasma transfusion while we depended on ROTEM triggers together with clinical assessment of the surgical field. It has been found that PT and aPTT are not good for orientating the decision and indication of transfusion of blood products [39]. On the other hand thromboelastography-guided transfusion decreases transfusion plasma in liver transplantation [40] and aortic arch replacement [41].

In ANH group, the mean volume of collected blood was 1750 ± 550 ml. Feldman et al. [42] found that, withdrawal of more than 1000 ml, blood during ANH is accompanied with significant reduction in the likelihood of transfusion.

The overall mean surgical blood loss in ANH group was lower but statistically insignificant compared with control group which comes in agreement with other studies [7].

In the current study, HES 6% (130/0.4) was used for replacement during ANH. Erol and Erdogan [43] found that ANH with HES 6% (130/0.4) did not cause any hemodynamic or blood gas parameters changes and did not have any adverse effect on haemostatic mechanisms that could enhance the risk of bleeding at surgery. While in their study, Konrad et al. [44] demonstrated that hydroxyethyl starch (HES) prolonged the time of clot formation Similarly, Egli et al. [45] demonstrated that HES prolonged CFT at any degree of hemodilution. In our study coagulation parameters significantly changed after heamodilution but the effect of HES 6% (130/0.4) as a contributing factor cannot be confirmed or ruled out as there is another important factor, the hemodilution which may account totally or in part in this effect.

This study depended on ODM for optimal fluid management and the colloid required in ANH group was significantly higher than control group for replacement of withdrawn blood. Also it is used to assess intraoperative heamodynamic changes. It seems that ANH did not affect the hemodynamic condition of the patients as evidenced by the non-significant comparison between both groups. COP and SVR changes after resection and at the end of surgery were attributed to the hemodynamic effect of liver resection [46].

Oxygen consumption remained adequate with no statistically significant difference between both groups and hematocrite kept more than 24% all over the study period. Crystal and Salem [47] reported that patients undergoing hemodilution to hematocrit as low as 20% can maintain oxygen supply to tissues due to compensatory mechanisms .The improvement of the rheological conditions may optimize tissue oxygen delivery and attenuate ischemia–reperfusion injuries [48].

Plasma lactate levels significantly increase compared to base line in both groups and the comparison between both groups was insignificant which rules out the role of ANH as a leading cause. The elevated lactate level is explained by decreased lactate uptake due to decreased hepatic blood flow during compression and mobilization of the liver [49]. Also, a dose-dependent decrease in hepatic blood flow induced by isoflurane might depress liver function significantly in cirrhotic patients, and thus enhance lactate accumulation [50]. There were no adverse cardiac, renal, or neurologic outcomes with ANH. This may be attributed to careful patient selection and exclusion of patients with medical conditions which might be adversely affected by hemodilution. Matot et al. reported similar findings [6].

In conclusion ROTEM in this study added two benefits 1st it gave some clinical evidence of safety of ANH regarding associated coagulation changes in such category of patients which may encourage to go with HCT transfusion trigger to a lower value. Second the use of ROTEM triggered transfusion parameters seemed to help decrease plasma transfusion requirement which serves the aim of ANH.

6. Index of ROTEM guided transfusion protocol

Check surgical field if there is:

1 – Diffuse surgical bleeding
Check and optimize basic conditions.
(Temperature > 35°, ph > 7.2, Cai > 1 mmol/l, HB > 8 gm/dl)
Then if:
Extem MCF < 25 mm give platelets, cryoprecipitate, FFPs
Extem MCF < 45 mm and fibtem MCF < 8mm.give cryprecipitate
Extem MCF < 45 mm and fibtem > 8 mm give platelets
2 – No diffuse clinical bleeding
Then if:
Extem MCF > 35 mm; no haemostatic therapy is indicated
Extem MCF MM < 35 mm and fibtem MCF < 8 mm give cryoprecipitate
Extem MCF < 35 mm and fibtem MCF > 8 mm give platelets
3 – If Extem CT > 80 s give FFPs

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