Effects of balanced hydroxyethyl starch 6% (130/0.4) and albumin 5% on coagulation: a prospective randomized trial using thrombelastometry and platelet function tests

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Background and Goal of Study:

The use of artificial colloids is still very common in perioperative medicine, but decreasing in critical care patients. The effects on coagulation are widely analyzed in different in vitro and in vivo studies. The negative effects of colloids results not only from haemodilution but also from direct impairment of coagulation factors. The influence on coagulation is seen not only in artificial colloids but also in albumin. Albumin, like every other intravenous fluid, can lead to haemodilution and decrease fibrinogen levels. In clinical trials, a relevant impairment of coagulation is often seen in cases of severe haemodilution.

The effects on coagulation are often not seen in global lab parameters like aPTT and prothrombin time. Modern bedside point-of-care diagnostic tools can give important information to the clinician. The thrombelastometric ROTEM® system is a quick and easy usable method to evaluate the clot formation and stability. The Multiplate® system can give information about the function of platelets and the influence of potentially present platelet inhibitors.

The aim of this prospective randomized trial was to evaluate the effects of a modern balanced artificial colloid and albumin on coagulation and to detect differences between both groups.

	Albumin (n=28)	HES (n=28)	
ASA classification	2.57 (±0.69)	2.57 (±0.63)	
Age [ys]	64.5 (±9.39)	70.3 (±9.24)	<i>p</i> =0.024*
Calculated blood loss [ml]	1245 (±709)	1557 (±825)	<i>p</i> =0.042*
Crystalloid amount [ml]	2384 (±808)	2059 (±648)	<i>p</i> =0.257
Colloid amount [ml]	1144 (±430)	1474 (±591)	<i>p</i> =0.026*
Red cell transfusion rate	25 %	21.4 %	<i>p</i> =0.628
FFP transfusion rate	3.6 %	3.6 %	<i>p</i> =1.0

Tab.1: Demographic data , calculated blood loss, intraoperative fluids and transfusion rate (mean values).
* = significant differences between both groups. FFP=fresh frozen plasma.

	Albumin (n=28)	HES (n=28)	
Fibrinogen (Clauss)	-28.2%	-27.8%	<i>p</i> =0.93
Quick (prothrombin time)	-16.7%	-20%	<i>p</i> =0.99
aPTT	+4.9%	+9.5%	<i>p</i> =0.461
A10 INTEM	-2.4%	-5.7%	<i>p</i> =0.004*
A20 INTEM	-1.7%	-5.1%	<i>p</i> =0.002*
MCF INTEM	-1.7%	-4.8%	<i>p</i> =0.005*
MCE INTEM	-1.7%	-4.8%	<i>p</i> =0.006*
A10 FIBTEM	-23.2%	-42.9%	<i>p</i> =0.001*
A20 FIBTEM	-23.1%	-41.7%	<i>p</i> =0.002*
MCF FIBTEM	-23.1%	-41.7%	<i>p</i> =0.001*
MCE FIBTEM	-23.9%	-50%	<i>p</i> =0.001*

Tab.2: Percentage change of global lab parameters and ROTEM Tests. All values given as median. * = significant differences between both groups. aPTT=activated partial thromboplastin time; A=amplitude; MCF=maximum clot formation; MCE=maximum clot elasticity.

Materials and methods:

Presented data are from a subgroup analysis of a monocentric, open-label, randomized, comparative trial with two parallel patient groups, comparing human albumin 5% versus balanced HES 6% 130/0.4. Patients between 18 and 85 years undergoing surgical cystectomy were included. Exclusion criteria were i.a. bleeding tendency or platelet dysfunction. Global coagulation parameters (prothrombin time (PT), partial thromboplastin time (aPTT), fibrinogen level (Clauss method)), rotational thrombelastometry (ROTEM®), PFA-100 and the Multiplate® analyzer were used to evaluate the effects on coagulation. Wilcoxon's test was used to detect intragroup changes and Mann-Whitney-U test for differences between groups. The perioperative application of infusions, vasoactive medics and transfusions was done according to a goal directed protocol with different target parameters depending on the ASA classification and cardiovascular comorbidities. Fluid losses (urine, perspiratio insensibilis) were replaced with a balanced crystalloid Ringer's acetate solution (Jonosteril®) in a ratio of 1:1. Blood and protein losses were replaced with either albumin 5 % or balanced hydroxyethyl starch 6 % 130/0.4 in a ratio of 1:1 up to a specific transfusion trigger point or to a maximum dose of 30 ml/kg/d. The intraoperative blood loss was calculated using a modulated formula published by our department in 1998¹.

Fig.1: Percentage change of global lab parameters. All values given as median. * = significant differences from baseline levels. aPTT=activated partial thromboplastin time; Quick=prothrombin time

Fig.2: Percentage change of INTEM parameters. All values given as median. * = significant differences from baseline levels. # = significant intergroup differences. A=amplitude; MCF=maximum clot formation; MCE=maximum clot elasticity.

Fig.3: Percentage change of EXTEM parameters. All values given as median. * = significant differences from baseline levels. # = significant intergroup differences. A=amplitude; MCF=maximum clot formation; MCE=maximum clot elasticity.

Results and discussion:

56 patients were randomized to receive either human albumin 5% (n = 28) or balanced HES 6%/130/0.4 (n = 28). Risk factors and comorbidities were similar in both groups, whereas the age was statistically different (see **tab.1**). intraoperative crystalloids amount was also similar, whereas the colloid amount and the calculated blood loss was significant higher in the HES group (see **tab.1**). The transfusion rate for red blood cells and fresh frozen plasma was statistically not different (see **tab.1**). In both groups aPTT increased significantly (*p* = 0.004; Wilcoxon) whereas prothrombin time and fibrinogen levels decreased (*p* < 0.001; Wilcoxon) without differences between the groups (see **tab.2** and **fig.1**). ROTEM® parameters A10, A20, MCF (maximum clot formation) and MCE (maximum clot elasticity) were significantly more compromised in the HES than in the albumin group (INTEM and FIBTEM; *p*≤0.005) (see **tab.2** and **figures 2** and **3**). No intergroup differences were detected by Multiplate® or PFA-100 (data not shown). Both colloids, balanced HES 6% and albumin 5%, compromise coagulation factors, presumably due to dilutive effects. Thrombelastometric values, measured by FIBTEM and INTEM, were significantly more impaired by HES whereas the platelet function, measured by Multiplate® analyzer and PFA-100, was not different between both groups.

Conclusions:

Although significant changes of the global coagulation parameters were found in both groups, we found significant differences between albumin and hydroxyethyl starch only by rotational thrombelastometry. Interestingly, the platelet function, measured by Multiplate® and PFA-100, was not different in both groups. Additionally we've seen a higher blood loss in the HES group compared to albumin as well as a higher intraoperative colloid amount. Further studies in a perioperative setting are needed to examine the correlations of thrombelastometry, platelet function and clinical parameters like blood loss and hemodynamic changes.