Extracorporeal Albumin Dialysis using microparticle charcoal for albumin recycling is superior to using MARS macroparticle Adsorbents in removing albumin bound toxins (ABT)

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Background: In liver failure, albumin bound toxins (ABT) are associated with hepatic encephalopathy (HE), renal failure (RF) and pruritus (PR). Albumin dialysis using MARS has been shown to remove ABT, especially those limiting the albumin binding capacity (ABiC) for *phosphatidylcholine*. However, efficacy is limited because of the limited capacity of the MARS Activated Charcoal (AC250) to adsorb albumin stabilizer caprylate and ABT. The Hepalbin Adsorbent (HA) consists of micro particle pharmaceutical charcoal embedded within a micromesh forming three dimensional scaffold, designed to improve the clearance of albumin bound molecules from albumin solutions.

Aim: To compare in vivo reduction of ABT during ECAD using HA versus Mars AC250.

Table 1

ID	Age	G	Primary Diagnosis	Comorbidities	ECAD Mars	ECAD Hepalbin	Alloc.	Out-come	Out-Come Day
1	4	m	Liver Cirrhosis	AKI on Dialysis HE Post OP Colon-Ca	7	1	Amb.	alive	30
2	72	f	Acute Liver Failure	AKI Pneumonia Arterial Hypertension HE HRS	2	7	ICU	fatal	20
3	46	f	Liver Cirrhosis	Aspiration Pneumonia On Ventilator Hemodynamic Instability (Pressor) AKI, Anuria	None (Drop out)	None, Drop out	ICU	n.a.	n.a.
4	56	m	Liver Cirrhosis	PBC AKI, Anuria Pulmonary Metastasis Hepatitis B	1	2	ICU	fatal	4
5	47	f	Liver Cirrhosis	Esophageal Varices II Aszites	Drop out	3	Hosp /ICU	alive	30
6	37	f	Multiorgan Failure	Liver Cirrhosis Autoimmunhepatitis Esophageal Varices Bleeding/TIPS HE,AKI	4	3	ICU	fatal	8
7	68	m	Liver Cirrhosis	AKI	1	3	ICU	alive	30
8	22	m	BRIC I661T-Mutation	Refractory Pruritus	3	1	Hosp	alive	30
9	50	m	Liver Cirrhosis	AKI Pneumonia on Ventilation Ascites Sepsis	3	2	ICU	fatal	12
10	45	f	Liver Cirrhosis	HRS Esophageal Varices Bleeding Ovarial Tumor	2	1	ICU	fatal	26
11	56	m	Fatty Liver Hepatitis	AKI Ascites	1	2	ICU	fatal	24
12	59	m	Fatty Liver Hepatitis	HE Pruritus AKI on ESRD Metabolic Syndrome	1	2	Hosp	alive	30

Method: In a prospective randomized controlled study, subjects with progressive jaundice and/or HE and/or RF and/or PR were treated first with one ECAD pro and after wards crossed over to the other. Subjects were not made aware of which adsorbent they had been treated with, the machine platforms were identical. Pre- and post-values of markers for ABT were measured. Safety and other clinical parameters were compared.

Results: After obtaining consent, 12 subjects (6 females, 1 acute 11 acute on chronic liver failure, 10 with progressive jaundice-bilirubin>16 mg/dl, 2 of those had intractable pruritus) were randomized consecutively. Baseline comorbidities, total number of ECAD treatments (both modes) and outcome are listed in Table 1.

Figure 1

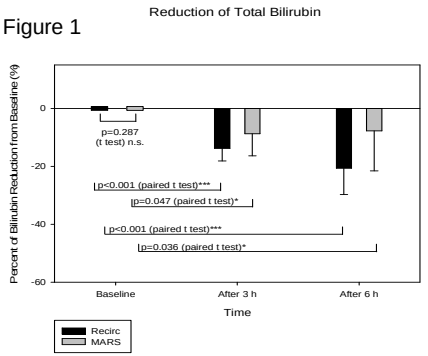
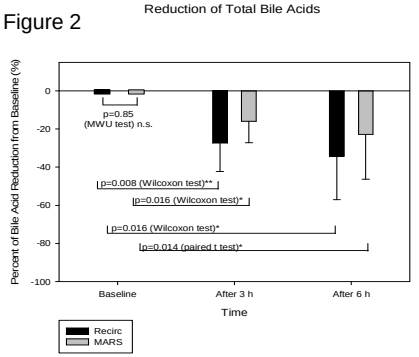


Figure 2

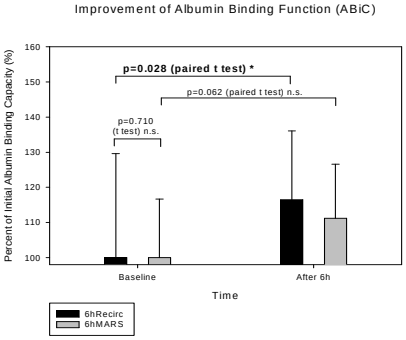


Within 6 hours of treatment, MARS AC resulted in reduction of bile acids by 22.76 (± 23.57) %, fig.2, whereas Hepalbin AC resulted into a reduction by 34.21 (±22.73)%. With respect to total bilirubin, MARS AC resulted in reduction of bilirubin by 7.7 (±13.76)%, whereas Hepalbin AC resulted into a reduction by 20.7 (+9.08)%, fig. 1.

Patients ABiC at the binding site for phosphatidylcholine was non-significantly increased by 11.17 (±15.42)% for MARS, while the improvement was significant (p<0.028; paired t) for the improvement observed for Hepalbin AC by 16.44 (±19.6)%, fig. 3. In parallel, the two subjects with intractable pruritus reported more profound reduction when treated with Hepalbin AC.

Hemoglobin, Platelets, MAP, Prothrombine time index), with the exception that the Shock-Index and Clot formation time (thromboelastography) normalized on Hepalbin AC but not on MARS AC.

Figure 3



Discussion: ABiC has been suggested as a prognostic marker for the effect of albumin dialysis on 28 day survival (Klammt et al. *Liver Transplantation 2008,Vol 14).* In this reference it took between 5-10 Mars treatments to improve ABiC. This study suggests, that in order to be more effective, ECAD needs to be done using more effective adsorbents, a fact that has been shown recently in vitro (Dominik et al., Therapeutic Apheresis and Dialysis, in press 2017). The binding site characterised by ABiC is also the binding site for the pruritugen Phosphatidylcholine, a potential reason, why patients with cholestatic pruritus have claimed more profound response after ECAD using Hepalbin (Soo et al. *Pediatric Nephrol 2016 Nov;31(11)). A multicenter study is currently conducted to confirm these data EUDAMED: CIV-13-04-010642)*