

# Equivalent efficacy of HES 130/0.4 and Albumin infusions in children

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## Abstract

Human albumin (HA20%) is an expensive blood product, used for infusion therapy in children with nephrotic syndrome and underfill. As recently shown, hypoalbuminemia is not the only cause of oedema in childhood nephrotic syndrome. Therefore other colloidal solutions such as Hydroxy Ethyl Starch (HES) having replaced HA 20% in other pediatric indications may serve as a suitable substitute. Six children with hypoalbuminemic nephrotic syndrome and underfill – defined as a urinary  $((U_K)/(U_{Na+K}) \times 100\%)$  ratio  $> 60\%$  - were randomized to HES 130/0.4 infusion followed HA 20% on the next day or to HA 20% followed by HES 130/0.4 in a cross-over study. Diuresis, body weight and renal function were documented. All children recovered from underfill. There was no difference between the values in both groups, no adverse events were seen. As HES 130/0.4 is less expensive than HA 20% and does not have the risks of a blood product, it may be a suitable alternative for therapy of nephrotic crisis.

## INTRODUCTION

Traditionally, nephrotic crisis in children was explained by a reduced plasma-oncotic pressure in combination with an increased absorption of sodium leading to a vascular "underfill" (1). In the last years it has been shown that low s-albumin-levels are not the only factor for the development of oedema in nephrotic syndrome (1). The main factor seems to be an increased absorption of sodium in the distal tubulus (2). In children with minimal change nephrotic syndrome (MCNS), underfill can be distinguished by the ratio  $[(U_K)/(U_{Na+K}) \times 100\%]$  from "eufill" and "overfill" (3). In all groups, plasmaoncotic pressure is reduced similarly. In cases of underfill and nephrotic crisis, routine therapy is the infusion of HA 20% in a dose of 1 g/kg, followed by iv Furosemide (0.5 – 1 g/kg). By administering HA 20%, intravascular volume and GFR increase followed by increasing diuresis and decreasing edema. However albumin is excreted rapidly and the effect diminishes within a day. The main disadvantage of this therapeutic approach is the repeated use of an expensive human blood product (100 ml HA 20% cost approximately 100€). As administration of HA20% does not lead to a long lasting effect (4), it can be speculated, that infusion of other colloidal solutions such as HES might lead to a similar positive effect, without the disadvantages described. As nephrotic children are not dehydrated, HES infusion is not expected to be followed by acute renal failure

as rarely described in dehydrated adults with chronic renal failure (5). The new preparation HES 130/0.4 has unchanged pharmacokinetics in renal insufficiency (6) and has been licensed for volume therapy in children in 2004 in Germany (7). We therefore compared HES 130/0.4 and HA 20% in children with nephrotic crisis in a cross-over study.

## PATIENTS

Six children (median age 6 years, range 3-8, 4 m, 2 f) with nephrotic crises were randomized either to primary HA 20% (1 g/kg over 2h) or HES 130/0.4 (10 ml/kg over 2h) therapy followed by furosemide 1 mg/kg i.v.. Inclusion criteria were: U-Proteine 1g/l, S-Proteine  $< 25$  mg/dl, oedema and underfill ( $[(U_K)/(U_{Na+K}) \times 100\%] > 70\%$ ). On the following day therapy was switched to the alternative infusion therapy. Urinary output, body-weight, S-Proteine, U-Proteine, S-Creatinine and U-Creatinine were measured daily. The study was accepted by the ethics committee of the Hannover Medical School.

## RESULTS

Three children were randomized to primary HES 130/0.4 therapy followed by HA 20% and 3 to HA 20% followed by HES 130/0.4 on the next day. The mean values of all clinical and laboratory parameters are given in table 1. All children recovered from underfill. Chi square test showed no statistical differences between diuresis or weight loss after

infusion of HA 20% or HAES. Due to the small number of patients in this pilot study, no more extensive statistical evaluations could be performed. No increase of s-creatinine or development of severe adverse effects were documented.

**Figure 1**

Table 1: Course of renal function and body weight before and 24h after infusion of HES 130/0.4 and HA 20% in children with minimal change nephrotic syndrome and underfill (n.a. = not available)

	Before HES	after HES	before HA 20%	after HA 20%	p
Diuresis [ml/kg/24h]	n.a.	46 SD 35	n.a.	50 SD 20	n.s.
Weight-loss [%]	n.a.	3.0 SD 1.8	n.a.	2.3 SD 2.0	n.s.
$[(U_{1d})/(U_{1d+24})] \times 100\%$	78 SD 21	62 SD 63	61 SD 62	53 SD 55	n.s.
S-Albumine [mg/dl]	8 SD 1	10 SD 2	10 SD 8	16 SD 15	n.s.
S-Proteine [mg/dl]	31 SD 12	35 SD 5	30 SD 30	35 SD 33	n.s.
U-Albumine [g/l]	22 SD 14	5 SD 11	10 SD 6	8 SD 4	n.s.
S-Creatinine [µmol/l]	35 SD 10	38 SD 22	38 SD 22	36 SD 33	n.s.

**CONCLUSION**

Our results show that HES 130/0.4 and HA 20% have equivalent effects on diuresis and weight loss of children with nephrotic crisis. No side effects of HES-therapy were documented. As HA 20% is an expensive blood product and as its infusion is associated with all risks known for blood products, our study suggests HES 130/0.4 to be suitable alternative. However, larger randomized trials will have to confirm our clinical observation.

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