The Use of Two Modern Hydroxyethyl Starch Solutions in Major Urological Procedures: Effect on Acid-Base Status and Renal Functions

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Abstract

This study showed that both balanced 6% HES 130/0.4 (Tetraspan) and saline-based 6% HES 130/0.4 were equally effective for hemodynamic stabilization of patients undergoing major urologic procedures without any significant impact on acid base or renal functions. In the context of safety concerns that has been raised recently regarding the use of HES in critically ill patients, it is time to reevaluate the safety of using HES intraoperatively and whether we still need to continue using these solutions or not.the third generation of tetrastarches shows a significantly improved safety profile without any loss of volume effect compared to first- and second- generation HES preparations.

Keywords

ARF, CMDh, AKIN, Hydroxyethyl, ADQI,AKI,

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List of Abbreviations

ADQI	**Acute Dialysis Quality Initiative**
AKI	**Acute kidney injury**
AKIN	**Acute kidney injury network**
ALT	**Alanine transaminase**
ARF	**Acute renal failure**
ASA	**American Society of Anesthesiologists**
AST	**Aspartate transaminase**
AUC	**Area under the plasma concentration curve**
BEST	**Beginning and Ending Supportive Therapy**
BUN	**Blood urea nitrogen**
C	**Carbon atom**
CKD	**Chronic kidney disease**
C_{max}	**Maximum plasma concentration**
CMDh	**The Coordination Group for Mutual Recognition and Decentralised Procedures – Human**
CPB	**Cardiopulmonary bypass**
CrCl	**Creatinine clearance**
CVP	**Central venous pressure**
d	**Day**

dl	**Deciliter**
DM	**diabetes mellitus**
DS	**Degree of substitution**
ELAM	**Endothelial leukocyte adhesion molecule**
ESRD	**End Stage Renal Disease**
FFP	**Fresh frozen plasma**
FiO_2	**Fraction of inspired oxygen**
g	**Gram**
GFR	**Glomerular Filtration Rate**
G_s	**Number of substituted anhydroglucose residues**
G_t	**Total number of anhydroglucose residues in the polymer**
h	**Hour**
HCO_3	**Bicarbonate**
HES	**Hydroxyethyl starches**
ICAM	**Intercellular adhesion molecule**
ICU	**Intensive care unit**
IHD	**Ischemic heart disease**
IL	**Interleukin**
INR	**International Normalized Ratio**
kDa	**KiloDalton**

kg	**Kilogram**
l	**liter**
m^2	**Square meter**
MAP	**Mean arterial blood pressure**
MDRD	**Modification of Diet in Renal Disease**
mg	**Milligram**
min	**Minute**
ml	**Milliliter**
mmHg	**Millimeter of mercury**
mmol	**Millimole**
Mn	**Number averaged MW**
MS	**Molar substitution**
MW	**Molecular weight**
Mw	**Weight averaged MW**
na	**Value not stated in source publication**
NaCl	**Sodium Chloride**
ng	**Nanogram**
NGAL	**Neutrophil Gelatinase-Associated Lipocalin**
PCO_2	**Partial Pressure of Carbon Dioxide**
pg	**Picogram**
PICARD	**Program to Improve Care in Acute Renal Disease**

PO_2	**Partial Pressure of Oxygen**
ppm	**parts per million**
PRAC	**Pharmacovigilance Risk Assessment Committee**
PRAC	**Pharmacovigilance Risk Assessment Committee**
RRT	**Renal Replacement Therapy**
SAPS	**Simplified Acute Physiology Score**
SCC	**Squamous cell carcinoma**
sCr	**Serum creatinine**
SD	**standard deviation**
sELAM	**Soluble Endothelial leukocyte Adhesion Molecule**
sICAM	**Soluble intercellular adhesion molecule**
SPO2	**Oxygen saturation**
$T_{½central}$	**Elimination half-life from the central compartment**
$T_{½\alpha}$	**Initial/distribution half-life**
$T_{½\beta}$	**Terminal/elimination half-life**
TCC	**Transitional cell carcinoma**
ug	**Microgram**
VISEP	**Efficacy of Volume substitution and Insulin therapy in Severe Sepsis study**

vs	**Versus**
W_H	**Weight fraction of hydroxyethyl groups in the polymer**
yr	**year**
α	**Alpha**
µmol	**Micromole**

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Hydroxyethyl Starches

With the development of a new generation of hydroxyethyl starches (HES), there has been renewed interest in their clinical potential. High doses of first- and second-generation HES were associated with adverse effects on renal function, coagulationand tissue storage, thereby limiting their clinical applicability. Newer HES products have lower molar substitution and in vivo molecular weight, resulting in more rapid metabolism and clearance.

A recent systematic review of randomized clinical studies on the use of fluid therapy in various types of surgical procedures found no evidence to recommend one type of fluid therapy over another. Neither was there sufficient evidence to provide guidance on the optimal amount of fluid to use in elective surgical procedures. [1] It was therefore concluded that guidelines for perioperative fluid management must be procedure specific; in the absence of firm evidence for one approach or another, individualized, goal-directed fluid administration should be used.[2]

Despite the absence of clear recommendations for anyparticular fluid therapy, there is plentiful debate aboutthe relative merits of crystalloid or colloid, and evenabout different types of colloids.[3]

Development of HES: Hetastarch to Tetrastarch

The first HES product, i.e., Hespan® (DuPont Pharmaceuticals,Wilmington, DE), was made available in theUnited States in the 1970s. Since then, further generationsof HES have been developed, differing in their mean molecular weight (MW), molar substitution (MS),and C2/C6 ratio. Hydroxyethylstarches are identified bythree numbers, e.g., 10% HES 200/0.5 or 6% HES 130/0.4.[4]

The first number indicates the concentration of the solution,the second represents the mean MW expressed inkiloDalton (kDa), and the third and most significant oneis MS. These parameters are highly relevant to the pharmacokineticsof HES(table 1).[4]

Concentration

Concentration mainly influences the initial volume effect: 6% HES solutions are iso-oncotic in vivo, with 1:l replacing about 1:l of blood loss, whereas 10% solutions are hyperoncotic, with a volume effect considerably exceeding the infused volume (about 145%).[4]

Molecular Weight

In common with all of the synthetic colloids, HES are polydisperse systems containing particles with a wide range of molecular mass. In polydisperse systems, the determination of particle mass or relative molecular mass gives averages, which depend on the method used. The MW can be described in one of two ways: weight averaged MW (Mw) and number averaged MW (Mn).[4]

Table 1: Characteristics of Hydroxyethyl Starch (HES) Preparations

	Concentration andSolvent	MeanMolecular Weight,kDa	Molar Substitution	C_2/C_6 Ratio	MaximumDaily Dose,ml/kg
HES670/0.75	6%balancedsolution	670	0.75	4.5:1	20