بسم الله الرحمن الرحيم

﴿ وقل رب زدني علما ﴾

صدق الله العظيم

EFFECT OF PRIMING WITH HYDROXY ETHYL STARCH ON COAGULATION PROFILE AND HEMODYNAMICS OF CHILDREN UNDERGOING OPEN HEART SURGERY

THESIS

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By

Dr. Abdel Rahman A. Showky
M. B. B.Ch. & MSc.

Supervised By

Prof. Dr. Nabil M. Abdel Moatey
Prof. of Anesthesia & Intensive Care.,
Faculty of Medicine,
Ain Shams University

Prof. Dr. Mahmoud S. Mostafa
Prof. of Anesthesia & Intensive Care.,
Faculty of Medicine,
Ain Shams University

Prof. Dr. Ezz El-Din A. Mostafa
Prof. of Thoracic and Cardiovascular Surgery
Faculty of Medicine
Ain Shams University

Faculty of Medicine
AIN SHAMS UNIVERSITY
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TO MY MOTHER , MY WIFE

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#ABSTRACT

Objective: A prospective non-randomized non- blinded study to evaluate the effect of priming with hydroxyethyl starch on coagulation profile and hemodynamics of children undergoing open heart surgery.

Patients and Methods:

Sixty patients 26 are males and 34 are females were included in the study. Their age ranged from one and eleven years (mean 6±0.3 years) and their weight ranged from eight and twenty eight kg (mean 18±1.03 kg). They had underwent the following operations, ventricular septeal defect closure (21 patients), atrial septal defects closure (17 patients), fallot's tetralogy correction (11 patients),mitral valve replacement (8 patients) and aortic valve repair (3 patients). They were subdivided into two groups.

Group I: were primed with Ringer's solution and mannitol 20% (0.5 gm/kg).

and **Group II:** were primed with hydroxyethyl starch 6% (5 ml/kg), mannitol 20% (0.5 gm/kg) and Ringer's solution.

The followinbg parameters have been assessed:

a) Coagulation profile: bleeding time, prothrombin time, partial thromboplastin time, platelet count, activated clotting time, hemoglobin level and plasma fibrinogen level.

b) Hemodynamic monitoring: heart rate, mean blood pressure, central venous pressure, urinary output, arterial blood gases analysis and serum creatinine. All these measurements have been measured in 3 phases; before cardiopulmonary bypass, immediate postoperative and 24 hours postoperative.

Results: All the coagulation parameters did not show any statistical difference in the both groups except platelet count and prothrombin time. The platelet count had significantly decreased in group II (mean preoperative value $357.0 \times 10^3/mm^3$ and mean immediate postoperative value $253.13x10^3/mm^3$, p-value <0.05). The prothrombin time showed significant prolongation in group II (mean preoperative value 12.61 seconds and mean immediate postoperative value 16.62 seconds, p-value <0.05). Although the mean blood pressure, the heart rate and the central venous pressure values were higher in group II in the immediate postoperative and 24 hours postoperative periods, they were statistically insignificant.

Conclusion

Hydoxyethyl starch is an effective colloidal blood expander that can be used as a priming solution . Inview of its safety and low cost , it proved to be superior to standard priming solution [Ringer solution and Mannitol] for use during cardiopulmonary bypass in children undergoing open heart surgery

Key Words: Hydroxyethyl starch, priming solution for C.P.B., coagulation abnormalities during C.P.B., effect of HES on coagulation profile, hemodynamic changes during and after CPB, effect of HES on hemodynamics during CPB and HES is a safe priming solution.

LIST OF ABBREVIATION

ACT :	Activated clotting time
ADP :	Adenosine diphosphate
ANS :	Autonomic nervous system
AT III :	Antithrombin III
B.T. :	Bleeding time
CAMP :	Cyclic adenosine monophosphate
CHD :	Cogenital heart disease
CNS :	Central nervous system
CO2 :	Carbon dioxide
COP :	Cardiac output
CPB :	Cardiopulmonary bypass
CVP :	Central venous pressure
DIC :	Disseminated intravascular coagulopathy
DCG :	Electrocardiogram
EEG :	Electroencephalogram
FDPs :	Fibrin degradation products
HES :	Hydroxy ethyl starch
HITS :	Heparin induced thrombocytopenia syndrome
HS :	Hypertonic saline solution
hrs :	hours
LD :	Lethal dose
LMW :	Low molecular weight
LMWH :	Low molecular weight heparin
LR :	Lactated Ringer's solution
IPPV :	Intermittent positive pressure ventilation
K :	Potassium
min :	minutes
MW :	Molecular weight
Na :	Sodium
O2 :	Oxygen
PCOP :	Plasma colloid osmotic pressure
PEEP :	Positive end expiratory pressure
PGI2 :	Prostacyclin
P.T. :	Prothrombin time
P.T.T. :	Partial thromboplastin time
u/L :	unit / litre
T.B.T. :	Templete bleeding time
T.T. :	Thrombin time
WBCT :	Whole blood clotting time

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AIM OF THE WORK

The aim of this work is to evaluate the effects of priming with hydroxyethyl starch on coagulation profile and hemodynamics in children undergoing open heart surgery.

INTRODUCTION

A proportion of children undergoing open heart surgery need volume expansion in the pre-bypass period because of the vasodilator effects of the anesthetics or surgical blood loss **(Quoncy et al , 1988).**

A varicty of fluids are recommended to enhance blood volume and improve haemodynamics in this situation including homologus blood and blood products, plasma expanders and crystalloids. **(Linkok, et al , 1959).** Hydroxy ethyl starch (HES) could be used safely as a volume replacement. It improves coagulation profile in children undergoing open heart surgery **(London et al., 1988).**

Volume replacement is given after induction of anesthesia until, the start of cardiopulmonary bypass. HES is either; low molecular weight (M.W. 20,000 dalton), medium molecular weight (M.W. 200,000 dalton) or high molecular weight (M.W. 450,000 dalton).

HES is superior to lactated ringer, dextran or albumin as a volume expander **(Thompson et al , 1970).**

HES has a potent hemodynamic action as it improves blood flow, microcirculation and organ perfusion and oxygen transport. It also has a medium term volume effect for upto 4 hours. **(Mishler et al , 1975).**

HES has no histamine release nor allergic reactions **(Thompson et al , 1970).** Low molecular weight HES has minimal interference with coagulation mechanism and significantly less effects on hemostasis and platelet function, so HES leads to less blood loss both intraoperatively and postoperatively and the need for blood and blood products is comparably less **(Tachow et al , 1983).**

LMW HES appears less likely to cause fluid accumulation in tissues than other HES preparations. Although the outcome is not a good variable for assessing the importance of HES accumulation in reticulo-endothelial system, there is no changes in organ function **(Quoncy et al., 1988).**

REVIEW OF LITERATURE

HYDROXY ETHYL STARCH (HES)

Physical and chemical proporties of HES:

HES is made from wax corn starch more than 95% of which consist of high molecular weight amylopectin. **(Cech et al , 1987).**

The molecular weight (M.W.) of the native amylopectin molecule is first reduced by acid hydrolysis.

In alkaline solution, ethylene oxide is used to introduce hydroxyethyl groups to obtain a molar substitution of 0.5. The need for hydroxy ethylation arises from the fact that native amylopectin is subjected to very rapid hydrolysis by endogenous alpha-amylase, so that its intravascular residence time would be only about 10 minutes. **(Sommermeyer et al., 1987).** The molecular weight of the substituted amylopectin molecule is then reduced acidolytically to approximately 200,000 dalton.

The resulting product is then filtered, extracted with acetone and spray dried. **(Cech et al , 1989).**

The structure of the end product, HES is similar to that of glycogen and consist of D-glucose units linked via linear alpha-1,4 bonds and branching off from about one in every 17 glucose via alpha 1,6 bonds **(Weidler et al , 1987).** The remarkably low incidence of anaphylactoid reactions to HES can be explained by the structural similarities between HES and glycogen molecules. While native amylopectin is rapidly hydrolyzed in the blood by serum amylase.

Hydroxyethylation increases the resistance of amylopectin to enzymatic hydrolysis. In fact, the greater the number of hydroxyethyl groups that are introduced, the more resistant is HES to enzymatic degradation and the longer it's intravascular residence time **(Lohmann et al , 1991).** Hydroxyethylation at the same time enhances the water-binding