بسم الله الرحمن الرحيم

EFFECTS OF HETASTARCH ON HAEMODYNAMIC AND HAEMATOLOGIC PARAMETERS IN MANAGEMENT OF HYPOVOLAEMIC SHOCK DURING MAJOR SURGERY

THESIS

Submitted in partial fulfillment of the

M.D. Degree in Anaesthesia

By

SHERIF AHMED ELEWA

M.B., B.Ch., M.S. Anaesthesia - Ain Shams University

Under the supervision of

PROF. DR.

NABIL MOHAMED ABDEL MOOTY

Professor of Anaesthesia

Faculty of Medicine

Ain Shams University

PROF. DR.

NEHAL GAMAL EL-DIN NOUH

Professor of Anaesthesia

Faculty of Medicine

Ain Shams University

DR. MANAL HASHEM AHMED

Lecturer of Clinical Pathology

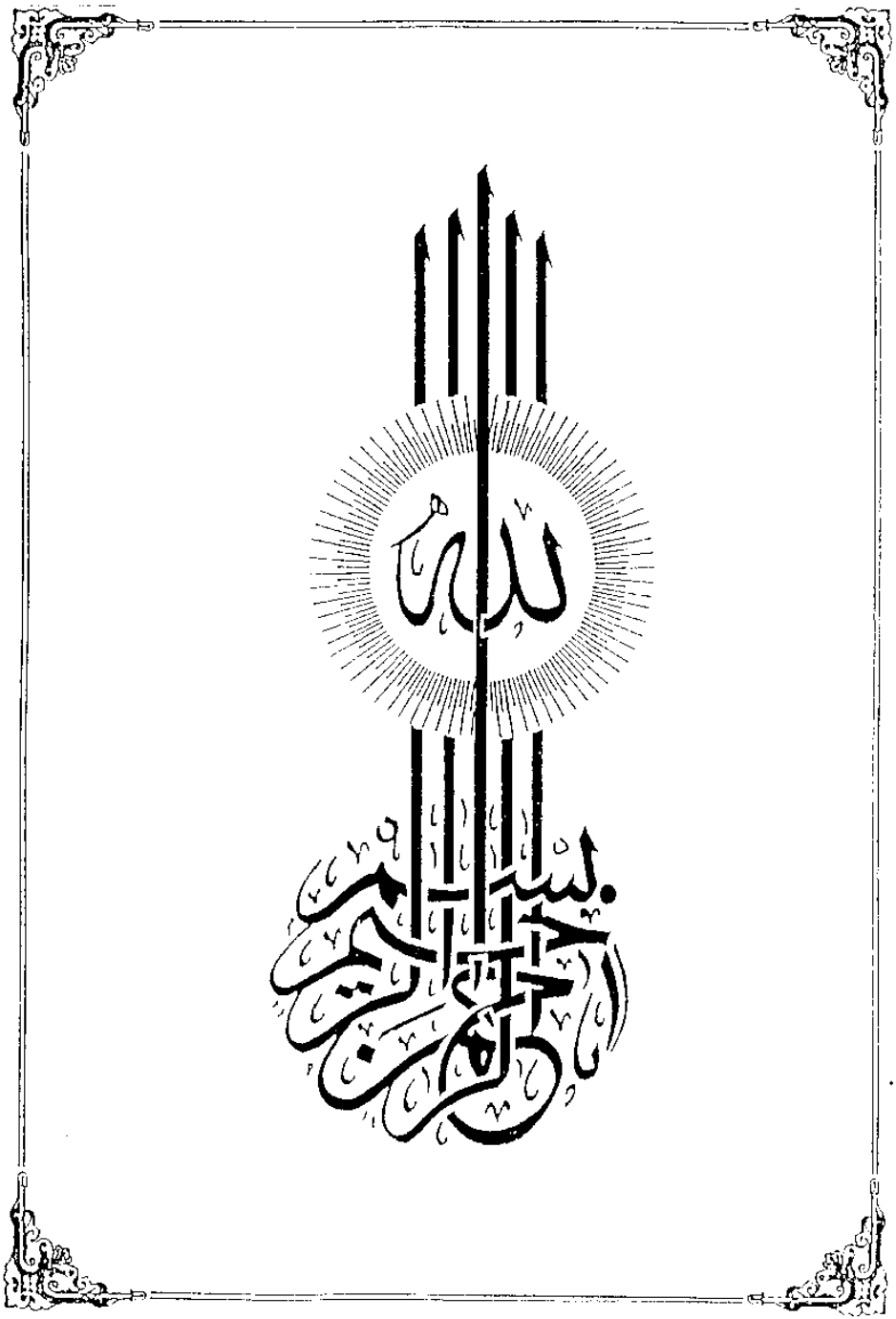
Faculty of Medicine

Ain Shams University

Faculty of Medicine

Ain Shams University

1994



ACKNOWLEDGMENTS

My thanks start by my appreciation to ***Prof. Dr. Nabil Mohamed Abdel Mooty****, Professor of Anaesthesiology, Faculty of Medicine, Ain Shams University, for his help, support and assistance throughout the preparation of this thesis. His valuable supervision and advice were extremely valuable to me in achieving this thesis.*

I wish also to express my thanks to ***Prof. Dr. Nehal Gamal El-Din Nouh****, Professor of Anaesthesiology, Faculty of Medicine, Ain Shams University, for her extensive devotion in the preparation and review of the text and for her wise recommendations in the layout of the thesis.*

To ***Dr. Manal Hashem Ahmed****, Lecturer of Clinical Pathology, Faculty of Medicine, Ain Shams University, I wish to express my deepest gratitude for her great efforts in the practical work of this thesis. She has spared no effort in processing the samples as soon as they were obtained. She has*

provided me with numerous knowledge about the haematologic parameters measured in this work.

Also, I wish to thank very much ***Dr. Ahmed Omar Ahmed****, Lecturer of Anaesthesiology, Faculty of Medicine, Ain Shams University, for his good help and guidance throughout the preparation of this thesis. His scientific knowledge has helped me to understand difficult points in may research.*

Lastly, I cannot miss to express my thanks to all ***the members*** *working in the Scientific Office of both Dupont and Fresenius Companies for their help and supply with material and references despite the difficulties they met.*

CONTENTS

Introduction

INTRODUCTION

Starch is the energy storage polysaccharide of plants and is analogous functionally and structurally to glycogen, the energy storage polysaccharide molecule of animals. Starch is composed of two types of glucose polymers: amylase, a linear molecule and amylopectin, a highly branched molecule which structurally resembles glycogen. Amylopectin is compatible with various biologic systems and is well tolerated when infused intravenously into animals. But, it is rapidly hydrolyzed by natural amylase, with a half life of only about 20 minutes. So, a hydroxy-ethyl group was attached to the sixth carbon of the glucose unit, the resulting substance: Hydroxy-ethyl starch, originally shown by: Wedersheim, 1957, was stable, non-toxic, non-allergic and effective as plasma volume expander in animals (*Metcalf,* 1970).

There are three commercially available preparations: high molecular weight (HES 450/0.7), medium molecular weight (HES 200/0.5) and low molecular weight (HES 40/0.5). These figures refer respectively to the molecular weight and the degree of substitution. So, HES 450/0.7 means that the molecular weight is: 450,000 Daltons and seven of the glucose units are substituted by hydroxy-ethyl groups. The

degree of substitution determines the rate of hydrolysis by natural amylase in the body. The more substitution, the more stabilization (*Thompson et al.,* 1970). On the basis of studies on toxicology, bleeding volume indices, bleeding times, haemodynamics, acid-base balance, among other parameters, it was shown that hydroxy-ethyl starch is effective and long acting colloid for plasma volume expansion (*Ballinger,* 1966 and *Lee et al.,* 1968).

Thompson et al. (1978) concluded that hydroxy-ethyl starch is an effective plasma substitute, with no recognizable histamine release, non-allergic, minimally interfering with coagulation and remains stable in solution without flocculation on storage.

The Aim of the Present Work

Is to evaluate the clinical efficacy of hydroxy-ethyl starch (HES 450/0.7) in terms of haemodynamic and haematologic parameters during resuscitation of patients suffering from hypovolaemia and shock during major surgical operations in different branches of surgery.

Review of Literature

Hydroxy-Ethyl Starch

HYDROXY-ETHYL STARCH "HES: 450/0.7"

Presentation

6% hydroxy-ethyl starch in 0.9% sodium chloride solution, 500 ml in glass bottle or plastic bag with an additive port. It is marketed as: Hespan (DuPont Pharmaceuticals U.S.) or plasmasteril (*Fresenius*, W.G.).

Composition

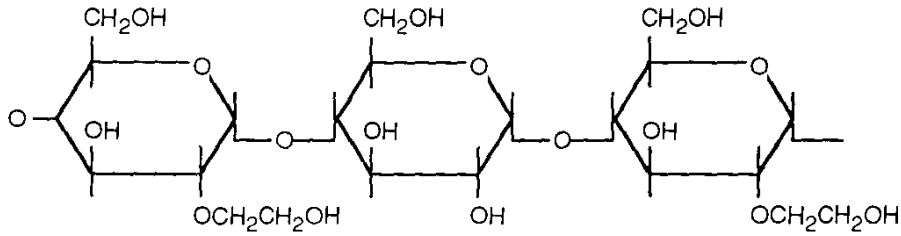
– Hetastarch:		6.0 gm/100 ml.
– Sodium chloride:		0.9 gm/100 ml.
– Water for injection BP.		
– PH adjusted with sodium hydroxide to:		5.5.
– Osmolarity:		310 mosm/L.
– Electrolytes:	Sodium:	154 mEq./L.
	Chloride:	154 mEq./L.
– Molecular weight:		450,000 Daltons.
– Molecular number:		70,000.
– Degree of substitution:		0.7.

(*Courtesy of Am. Cr. Care, Illinois, U.S.A.*, 1980).

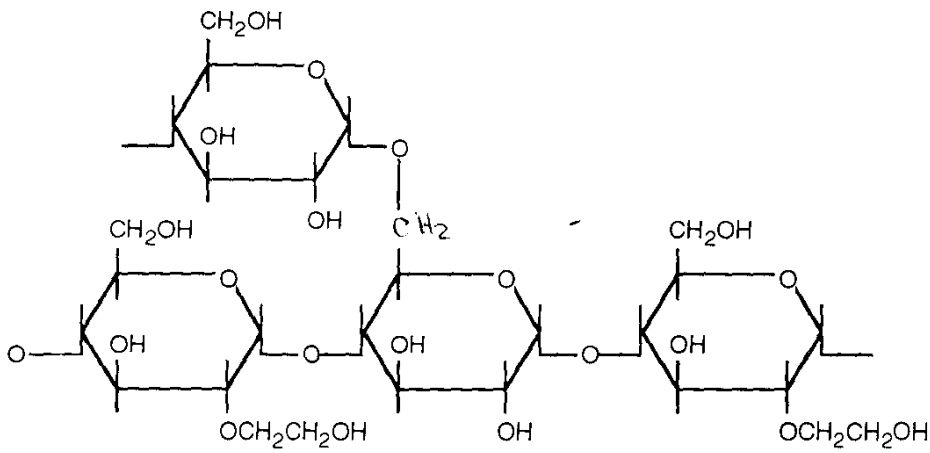
Description (Fig. 1)

Hetastarch is an artificial colloid derived from a waxy material (starch), composed almost entirely of amylopectin. Hydroxy-ethyl groups are introduced into the glucose units of starch and the resulting material is hydrolyzed to yield a product with a molecular weight suitable for use as a plasma volume expander. The infusion form is a clear pale yellow solution, exposure to prolonged bad storage conditions (temperature above 40° C or below freezing) may result in change in colour to turbid deep brown, or may result in the formation of a crystalline precipitate, in such conditions the solution should be discarded (*Rackow et al.,* 1983).

The molecular weight of the native amylopectin is first reduced by acid hydrolysis. The resulting substance is filtered, extracted with acetone and spray-dried in alkaline solution, ethylene oxide is used to introduce hydroxy-ethyl groups to obtain a molar substitution of 0.7. Hydroxy-ethylation increases the resistance to enzymatic degradation and hence, increases the half-life in the plasma, it also enhances the water binding capacity and colloid osmotic pressure for effective plasma volume expansion (*James et al.,* 1984).



Linear portion of hydroxy-ethyl starch molecule.



Branching in hydroxy-ethyl starch molecule.

Fig. (1): (Courtesy of Am. Cr. Care, Illinois, U.S.A., 1980).

Hydroxy-ethyl starch is soluble in water and physiologic solutions e.g. 0.9% sodium chloride, but it is insoluble in alcohol (*Rackow et al.,* 1983).

Pre-Clinical Pharmacology

Isovolumic substitution by hetastarch in dogs with haemorrhagic shock (they were bled to a mean arterial blood pressure of 35 mmHg), it was as effective as the whole blood, plasma or dextran as measured by animal survival (*Simeone et al.,* 1965).

Isovolumic substitution of hetastarch in splenectomized dogs to a haematocrit of 10%, 100% survival has been reported (*Jesch et al.,* 1975).

In rats bled to 20% of their baseline haematocrit and infused with equal volume of hetastarch, they survived without significant deviations from the initial blood volumes. Haemoglobin and haematocrit values were close to normal range 14 days after infusion, reticulocytosis was noted on the third day and was maximum at the seventh day. There were no pathological changes of the kidneys of these animals (*Holscher et al.,* 1976).