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بالرسالة صفحات
لم ترد بالأصل

THE ROLE OF PROPHYLACTIC METHYLENE BLUE IN MANAGEMENT OF POST CARDIOPULMONARY BYPASS VASOPLEGIA IN HIGH RISK PATIENTS

Thesis
Submitted for partial fulfillment
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CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF GRAPHS

ABBREVIATIONS

(ACLS)	Adult cardiopulmonary life support
(ADH)	Antidiuretic hormone
(AVP)	Arginine vasopressin
(cno)	Constitutive nitric oxide
(CPB)	Cardiopulmonary bypass
(EC)	Endothelial cell
(ECP)	Extracorporeal circulation
(ENA)	Endothelial cell neutrophil attractant
(GMP)	Cyclic guanisine monophosphate
(ICAM)	intracellular adhesion molecule
(IFN)	Interferon
(INOS)	Inducible nitric oxide synthesases
(LVAD)	Left sided assisted device
(NAP)	Neutrophilc activating protein
(NF-KB)	Nuclear factor KB
(NO)	Nitric oxide
(OHS)	open heart surgery
(PAF)	Platlet activating factor
(PSGL-1)	P-selectin glycoprotein-1
(TNF)	Tumour necrosis factor
(VCAM)	vascular adhesion molecule
(vs)	vasoplegic syndrome

INTRODUCTION

The English surgeon John Hunter first recognized the malignant systemic spread of inflammation as an abnormal response to injury two centuries ago . The early pioneers in cardiac surgery recognized a similar pattern of systemic injury they encountered after cardiopulmonarybypass (CPS). Kirklin hypothesized that the deleterious effects of CPB were secondary to the exposure of blood to abnormal surfaces in the bypass circuit, which initiated a "whole body inflammatory response." He noted that this response is characterized by activation of coagulation, the kallikrein system, fibrinolysis,. and complement, all of which are now recognized as the mediators of the disseminated intravascular post-pump syndrome(***kirklin et al, 1991)***

Many of the components currently used to perform cardiovascular operations lead to systemic insuIts that result from cardiopulmonary bypass circuit-induced contact activation, circulatory shock, and resuscitation, and a syndrome similar to endotoxemia. Experimental observations have demonstrated that these events have profound effects on activating endothelial cells to recruit neutrophils from the circulation. Once adherent to the endothelium, neutrophils release cytotoxic proteases and oxygen-derived free radicals, which are responsible for much of the end-organ damage seen after cardiovascular operations. Recently the cellular and molecular mechanisms of endothelial cell activation have

become increasingly understood. It is conceivable that once the molecular mechanisms of endothelial cell activation are better defined, therapies will be developed allowing the selective or collective inhibition of vascular endothelial activation during; the perioperative period. **(*Edward et al,1997)***

Within the body the endothelial cell, the only surface in contact with circulating blood, simultaneously maintains the fluidity of blood and the integrity of the vascular system. This remarkable cell maintains a dynamic equilibrium by producing anticoagulants to maintain blood in a fluid state and by generating procoagulant substances to enhance gel formation when perturbed. Coagulation proteins circulate as inert zymogens, which convert to active enzymes when stimulated. Likewise, blood cells remain quiescent until activated to express surface receptors and release proteins and enzymes involved in the coagulation equilibrium. The continuous exposure of heparinized blood to the perfusion circuit and to nonendothelial cell tissues of the wound during clinical cardiac surgery produces an intense thrombotic stimulus that involves both the tissue factor pathway (extrinsic coagulation pathway) in the wound and the contact and intrinsic coagulation pathways in the perfusion circuit. Heparin does not block thrombin formation; during extracorporeal perfusion (ECP) heparin partially inhibits thrombin after it is produced. Thrombin is continuously generated and circulated despite massive doses of heparin in all applications of extracorporeal perfusion, **(*Spanier et al 1996)***

AIM OF THE WORK

The aim of the study is to detect the effect of prophylactic administration of methylene blue in high group for vasoplegic syndrome and its effect on morbidity,mortality, Intensive care and vasopressor requirement.

SYSTEMIC INFLAMATORY RESPONSE

(1) Endothelial cells

Endothelial cells are activated during CPB and, open heart surgery (OHS) by a variety of agonists, The principal agonists for endothelial cell activation during CPB are thrombin, C5a, and the cytokines IL-1B and TNF . Other agonists, such as endotoxin, histamine are less important during CPB, and endothelial cells are largely unresponsive to chemokines . ***(Francis et al2001).***

IL-1B and TNF induce the early expression of P-selectin and the later synthesis and expression of E-selectin, which are involved in the initial stages of neutrophil and monocyte adhesion.The two cytokines also induce expression of intracellular adhesion molecule(ICAM-1) and vascular adhesion rnolecule(VCAM1), which firmly bind neutrophils and monocytes to the endothelium and initiate leukocyte trafficking to the extravascular space (Fig. 1).Experimentally ICAM-1 is upregulated during CPB in pulmonary vessels' and there is evidence that P- and E-selectins are upregulated during CPB and in myocardial ischemia-reperfusion sequences. IL-1B and TNF-, induce endothelial cell production of the chemotactic proteins IL-8 and MCP-1, and induce production of prostacyclin by the cyclooxygenase pathway and nitric oxide(NO) by NO synthase. These two vasodilators reduce shear stress and increase vascular permeability and therefore enhance leukocyte adhesion and transmigration. Lastly, IL-1βand TNF, stimulate endothelial cell production of proinflammatory cytokines, IL-1, IL-6, IL-8, and platlet