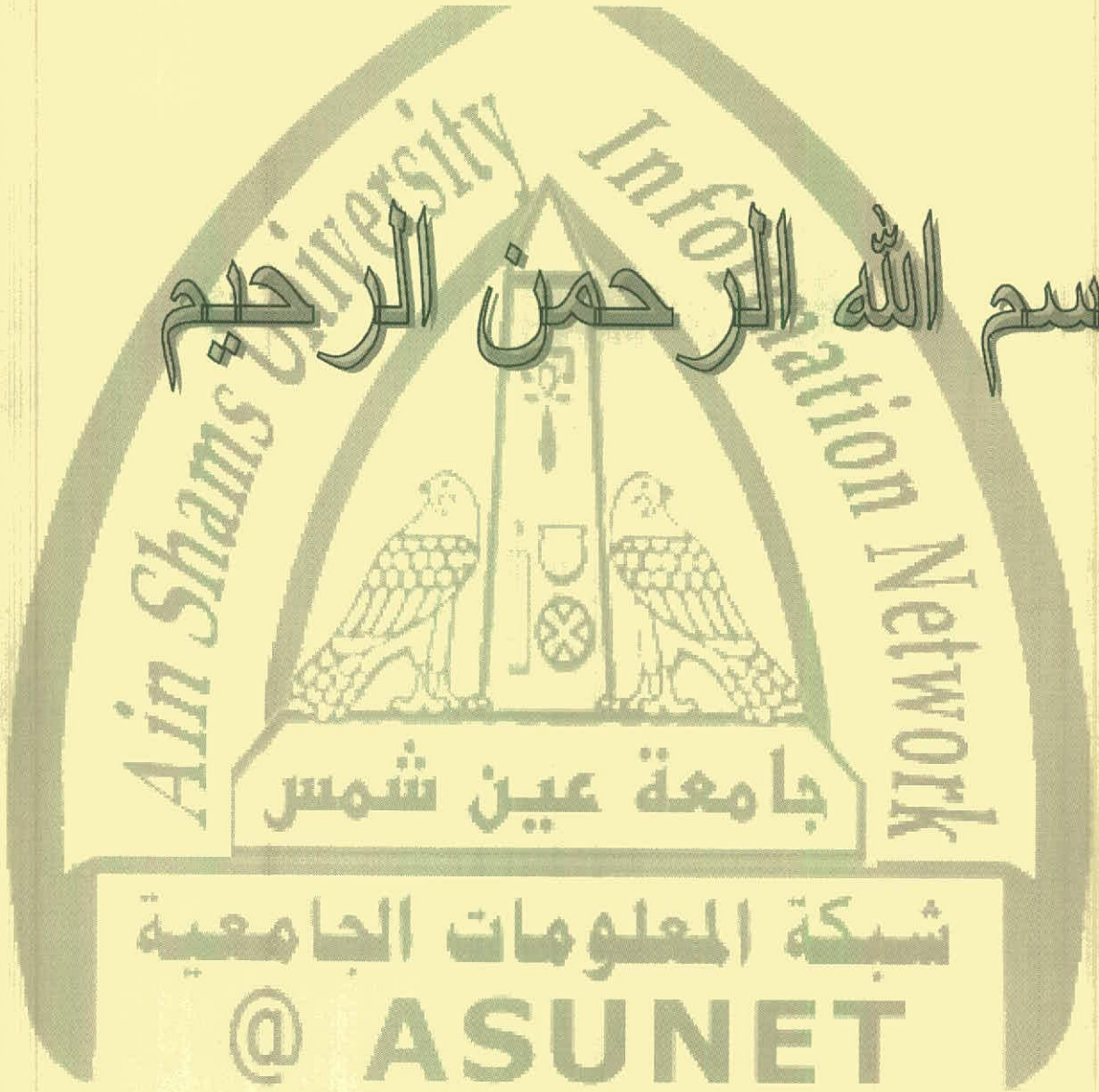
شبكة المعلومات الجامعية



بسم الله الرحمن الرحيم

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

قسم

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بالرسالة صفحات لم ترد بالاصل

A STUDY OF THE ROLE OF ENDOTHELIN-1 IN THE PATHOGENESIS OF PEPTIC ULCER IN PATIENTS WITH LIVER CIRRHOSIS AND RENAL FAILURE

THESIS

Submitted for the Partial Fulfillment of the requirments of the M.D Degree

In

Internal Medicine

By

Tarek Ahmed Talat El-Sharawy

(M.B.,B. Ch.,)

Supervisors

Prof. Dr.

Faiza Foad Lashin

Prof. & Head of Internal Medicine
Faculty of Medicine
Tanta University

Prof. Dr.

Thoraya El-Sayed Badawy

Prof. & Head of Clinical Pathology
Faculty of Medicine
Tanta University

Dr.

Mabrouk Ramadan El-Shikh

Ass. Prof. of Internal Medicine
Faculty of Medicine
Tanta University

FACULTY OF MEDICINE
TANTA UNIVERSITY
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بسم الله الرحمن الرحيم

قَالُوا سُبْحَانَكَ

لَا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَا

إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ

صدق الله العظيم

آيه ٣٢ سورة البقرة

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INTRODUCTION

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Since first reported by Yanagisawa in (1988), there has been a surge of publication on the newly identified vasoconstrictive peptide endothelin. Endothelin-1 (ET-1)is a 21 amino acid peptide that was originally purified from cultured porcine aortic endothelial cells[1].

The endothelins are a family of three isopeptides that are extremely potent vasconstrictors both in vivo and in vitro. At least three isoforms of endothelin have been described, each consisting of 21 amino acids and four cystine residues that form two disulfide bonds. ET-1 is the only isoform produced by endothelium. It inhibits renin release from juxta glomerular cells and exerts a positive inotropic effect on the heart[1].

Two distinct endothelin receptors have been cloned and are members of G protein-coupled receptors family. The ET-A receptor specifically binds ET-1 where as ET-B receptor binds either of three endothelin peptides with equal affinity. ET-A receptor appears to predominate in the heart muscle. some physiologic actions has been demonstrated for this family peptides, including potent and sustained vasoconstriction, positive inotropic and chronotropic effects on myocardium and contraction of vascular smooth muscles of lung and intestine.

Previous studies suggested that endothelin is not stored in endothelial cells. In culture of endothelial cells as well as in isolated blood vessels, the peptide can be detected only after several hours of incubation, indicating that de novo protein synthesis is required[2].

REVIEW OF LITERATURE

REVIEW OF LITERATURE

ENDOTHELIUM

Is a simple squamous epithelium, resting on a basement membrane. The entire cardiovascular system is lined by endothelium.

a- In the heart, endocardial endothelium lines the chambers and coats all structures projecting into these chambers (e.g. ventricular trabecular muscles, valves).

b- In major vessels, endothelium exists at the lumina and is continuous with cardiac endothelium. Capillaries consist solely of endothelium and basement membranes and perhaps, a small number of adventitial connective tissue fibers[3].

* Normal endothelial cell function :

The most obvious function of endothelium is the mechanical separation of blood products from collagen and smooth muscle of the vascular wall. This interface between intra and extra vascular compartments must simultaneously allow transport of nutrients, waste products, regulatory molecules and phagocytotic cells, across cellular basement membranes[4].

Normally, vascular endothelial surfaces resist platelet aggregation and coagulation, by activation of protein C, a potent circulating anticoagulant ,preventing thrombus formation under normal conditions[5].

Healthy endothelial cells, modify the contractile responses of subjacent vascular smooth muscles, an action that was demonstrated in previous studies which showed that the removal of vascular endothelium reversed the response of aortic strips to acetychloine from relaxation to contraction[6].

Disruption of vascular endothelium, eliminates the source of the potent vasodilator prostacyclin (PGI2) and other less well characterized agents. These include an agent that leads to relaxation of vascular smooth muscle, endothelial derived relaxing factor (EDRF) and another that enhances vasospasm, endothelial derived contracting factor (EDCF). Another potent vasoconstrictor of vascular smooth muscles, endothelin (ET), has been identified in some media from cultures of vascular endothelium [1].

***Relaxing and contracting factors of endothelium :**

Endothelium dependent relaxation of blood vessels is produced by a large number of agents (e.g. acetylcholine, ATP, ADP, bradykinin, histamine, thrombine, serotonin).

Relaxation results from release of a very labile non-prostanoid endothelium-derived relaxing factor (EDRF) or factors. EDRF stimulates guanylate cyclase of the vascular smooth muscles, with the resulting increase in cyclic GMP which has a good correlation with acetylcholine and other agents. EDRF is rapidly inactivated by hemoglobin which inhibits the increase in cyclic GMP and by superoxide anion generated from reduction