Aim of work

The purpose of the present study was to evaluate the effect of acute renal failure on gastric acid secretion, and to measure plasma gastrin level in rats with acute uremic syndrome induced by bilateral nephrectomy or by bilateral ligation of the ureters. Combined results of these two procedures throw some light on the role played by renal mass in acute uremia. Also, the relationship of gastrin level with acid secretion data was investigated.

Gastric Acid Secretion in Experimental Acute Uremia and Circulating Levels of Gastrin

THESIS
Submitted for partial fulfillment of the Master Degree in Physiology

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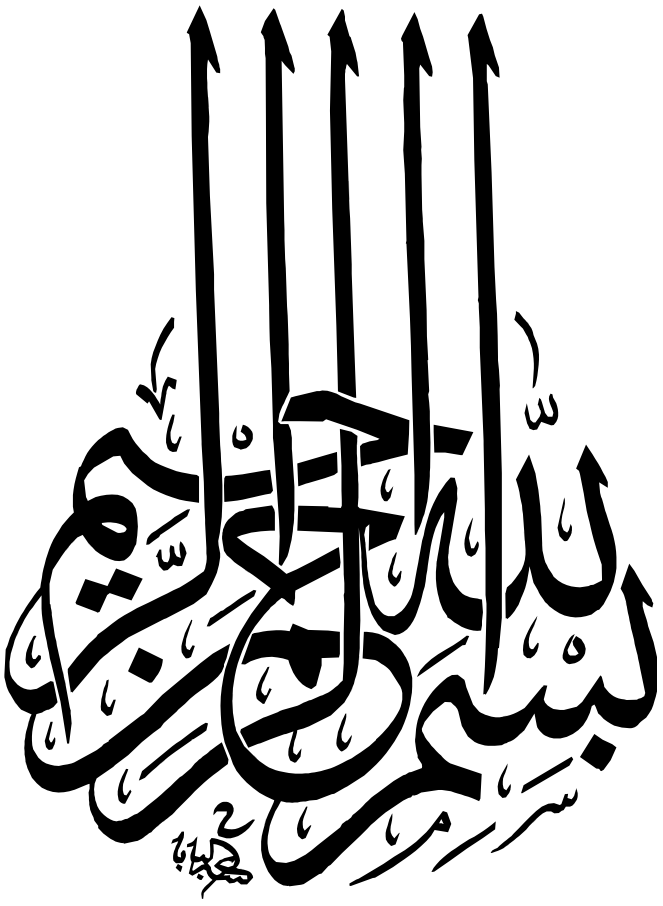
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TO MY

FAMILY

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List of Abbreviations

ARF	Acute renal failure
CAPD	Continuous ambulatory peritoneal dialysis
CaR	External calcium sensor receptor
CCK	Cholecystokinin
CFTR	Cystic fibrosis transmembrane conductance regulator
CLC-2	Chloride channel voltage sensitive 2
CLIC-6	Chloride intracellular channel 6
CRF	Chronic renal failure
CSPP-28	Calcium-sensitive phosphoprotein
DAG	Diacylglycerol
DMNV	Dorsal motor nucleus of the vagus
ECL	Enterochromaffin-like cells
ER	Endoplasmic reticulum
ESRD	End stage renal disease
GFR	Glomerular filtration rate
GIP	Gastric inhibitory polypeptide
GLP	Glucagon-like peptide
GOAT	Ghrelin-O-acyltransferase

GRP	Gastrin-releasing peptide
HD	Haemodialysis
HDC	Histidine decarboxylase
IP3	Inositol-1, 4, 5-trisphosphate
KCNE2	Potassium voltage gated channel, ISK related family, member 2
KCNQ1	Potassium voltage gated channel KQT- like subfamily, member 1
Kir4.1	Inward rectifying K^+ channel
L-NAME	NG-nitro-L-arginine methyl ester
MAPK	Mitogen-activated protein kinases
mGluR	Metabotropic glutamate receptor
MMP	Matrix metalloproteinase
NHE	Na^+/H^+ exchangers
NKCC1	Na^+-K^+-$2C1^-$ cotransporter
NMDA	N-methyl-D-aspartate
PACAP	Pituitary adenylate cyclase-activating peptide
PAM	Peptidyl-alpha-amidating mono-oxygenase
PI_3K	Phosphatidyl inositol 3 kinase
PKA	Protein kinase A

PKC	Protein kinase C
PLC	Phsopholipase c
PPIs	Proton pump inhibitors
PYY	Polypeptide tyrosine-tyrosine
RIFLE	Risk, injury, failure, loss and end stage kidney disease
SLC26A7	Solute carrier family 26 member 7
SLC26A9	Solute carrier family 26, member 9
SLC4A2	Solute carrier family 4, anion exchanger, member 2
SNAREs	Soluble N-ethylmaleimide-Sensitive Factor Attachment Proteins
SPC	Subtilisin-like prohormone convertases
TGN	Translocated to trans-Golgi network
VAMP	Vesicle-associated membrane protein
VMAT2	Vesicular monoamine transporter type 2
VR1	Vanilloid receptors

Introduction

The stomach's main secretory function is the production of hydrochloric acid. Acid facilitates the digestion of protein as well as the absorption of iron, calcium, vitamin B12, and certain medications such as thyroxin **(O'Connell et al., 2005; Hutchinson et al., 2007; Checchi et al., 2008; Den Elzen et al., 2008 and Lahner et al., 2009)**. Gastric acid also prevents bacterial overgrowth and enteric infection **(Zhu et al., 2006; Leonard et al., 2007; Howell et al., 2010 and Lombardo et al., 2010).**

Since too much acid can overcome the mucosal defense mechanisms and cause ulceration **(Dimaline and Varro, 2007 and Nayeb-Hashemi and Kaunitz, 2009)** and too little acid causes bacterial overgrowth **(Williams and McColl, 2006),** gastric acid secretion must be tightly regulated **(Shulkes et al., 2006).**

Gastrointestinal complications are known to commonly occur in patients with renal failure. A lot of studies tried to define the association between renal failure and gastrointestinal complications, however, the results were conflicting **(Etemad, 1998).**

Introduction

The role of gastric acid secretion in the development of gastroduodenal diseases in chronic renal failure (CRF) has been examined **(Ventkateswaren et al., 1972; Reisman et al., 1976 and Gold et al., 1980)**. However, there has been controversy on gastric acidity in CRF. Studies reported increased **(Ventkateswaren et al., 1972)**, normal **(Reisman et al., 1976 and Gold et al., 1980)**, or decreased **(Muto et al., 1985)** acid secretion in CRF.

A number of clinical studies have demonstrated fasting hypergastrinemia in azotaemia **(Shapira et al., 1978; Gold et al., 1980; Taylor et al., 1980 and Muto et al., 1985)** although other researchers have argued against this finding **(Dent et al., 1972 and Reisman et al., 1976)**. It remains undetermined whether hypergastrinemia contributes to accelerated gastric acid secretion or is a consequence of decreased acidity via a feedback mechanism in CRF.

Besides the reported controversy regarding gastric acid secretion associated with chronic uremia, the clinical importance and the biological relevance of altered gastric acidity and gastrin level in acute renal failure are uncertain because of lack of information. Therefore, the present study was designed to investigate the possible changes in gastric acid

secretory parameters in acute renal failure rat model, highlighting the role of gastrin hormone in this respect.