Effect of Estrogen on Basal, Charbacol Stimulated Acid Secretion and Indomethacin Induced Ulcer in Female Albino Rats

Thesis

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Abstract

In the present study, the effect of estrogen on gastric acid secretion and peptic ulcer and whether it acts through alpha or beta estrogen receptors has been investigated in a total number of 90 female albino rats divided into five groups with 18 rats allocated in each group.

Results showed that gastric acid secretion and number of ulcers were significantly higher among ovariectomized group than in control group when estimated within the basal acid secretion, carbachol induced acid secretion and indomethacin induced ulcer sub groups ($P<0.05$).

Key Words:

Gastric Acid Secretion, Gastrointestinal barriers, Peptic ulcer, Estrogens

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List of Abbreviations

AE	Anion exchanger isoform
ANOVA	Analysis of variance
ANP	Atrial natriuritic peptide
cAMP	Cyclic adenosine mono phosphate
CFTR	cystic fibrosis transmembrane conductance regulator
cGMP	Cyclic guanosine mono phosphate
CGRP	Calcitonine gene related peptide
Cl	Chloride
CNQX	6-cyano-7-nitroquinoxaline-2,3-dione
CO_2	Carbone dioxide
COMT	catechol O-methyl transferase
COX	Cyclooxygenase
Da	Dalton
DIDS	4,4′-diisothiocyanostilbene-2,2′-disulphonic acid
DMSO	Dimethyl sulphoxide
DNA	Deoxy riboneucleic acid
DPN	2, 3-bis (4-Hydroxyphenyl) Propionitrile
DRG	Dorsal Root Ganglions
ECL	Enterochromaffine like
EGF	Epidermal growth factor
EGFR	Epidermal growth factor receptor
EP receptors	E series of prostaglandins receptors
ER	Estrogen receptor
EST	Estradiol
EST	Estradiol
FSH	Follicular stimulating hormone
GABAA	g-amino-butyric acid A receptor
GIT	Gastro intestinal tract
GLP	Glucagon like peptide
GPR30	G protein-coupled receptor
GRP	gastrin-releasing peptide
GSK	Glycogen synthesis kinase
H.PYLORI	Helicobacter pylori
H_2O	Water
Hcl	Hydrochloric acid
HCO_3	Bicarbonate
HDL	High density lipoproteins

HSV	High selective vagotomy
ICMJE	International Committee of Medical Journal Editors
IGF	Insulin like growth factor
IM	Intra muscular
IV	Intra venous
Kcl	Potassium chloride
LDL	Low density lipoproteins
LH	Luteinizing hormone
MAPK	mitogen-activated protein kinase
MBS	Mucosal bicarbonate secretion
Na cl	Sodium chloride
NBC	Sodium bicarbonate co transport
NMDA	N-methyl-D-aspartate
NO	Nitric oxide
NOS	Nitric oxide synthesase
NSAID	Non steroidal anti inflammatory drugs
OCD	Obsessive compulsive disorders
OV	Ovariectomy
OVX	Ovariectomized
OX1R	Orexin receptor one
OX2R	Orexin receptor two
PG	Prostaglandins
Pl3K	phosphoinositide 3-kinase
PPT	1, 3, 5-tris (4-hydroxyphenyl)-4-propyl-1H-pyrazole
PUD	Peptic ulcer disease
RNA	Ribonucleic acid
SD	Standard deviation
TFF	Trefoil factor family
TRH	Thyrotropine releasing hormone
TRPV1	Transient receptor potential vanilloid receptor 1
USA	United states of 0America
VIP	Vasoactive intestinal peptide

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قَالُوا سُبْحَانَكَ
لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا
إِنَّكَ أَنْتَ

Introduction

Originally identified as reproductive hormones, estrogens are now generally thought to play an important roles in bone, cardiovascular, gastrointestinal and in the central nervous system. This expanded view of estrogen action reflects the findings of a large number of clinical studies and huge body of empirical observational data gathered on the effect of exogenous estrogen administration on the health of menopausal women. Parallel studies reporting the distribution of estrogen receptors and others describing specific estrogenic responses in functionally related tissues have led to an appreciation of the sphere of influence of this hormone ***(Mc Donnell, 2003).***

Aim of the work

This study aims to investigate the effect of estrogen on basal, charbacol stimulated acid secretion and also its effect on indomethacin induced ulcer and whether it acts through alpha or beta estrogen receptors.

Gastric Acid Secretion

Hydrochloric acid (HCl) is the best-known component of the parietal (oxyntic) cell secretion which is known as the gastric juice. The capacity of the stomach to secrete HCl is directly proportionate to the parietal cell number, which on stimulation secretes HCl at a concentration of roughly 160 millimol (mM)/liter that is equivalent to a pH of 0.8. Gastric acid facilitates the digestion of protein and absorption of iron, calcium, and vitamin B12, and prevents bacterial overgrowth and enteric infection ***(Wei and Mitchell, 2006)***.

Functions of Gastric Acid:

Hydrochloric acid (HCl) secretion assists protein digestion by activating pepsinogen to pepsin, renders the stomach sterile against orally-ingested pathogens,prevents bacterial or fungal overgrowth of the small intestine, encourages the flow of bile and pancreatic enzymes, and facilitates the absorption of a variety of nutrients, including folic acid, ascorbic acid, beta-carotene, non-heme iron, and some forms of calcium, magnesium, and zinc.Moreover normal gastric acid secretion is necessary for effective absorption of thyroxine ***(Centanni etal 2006)***.

Mechanism of Acid Secretion:

Hydrogen ions are generated within the parietal cell from electric dissociation of water. The hydroxyl ions formed in this process rapidly combine with carbon dioxide to form bicarbonate ion, a reaction cataylzed by carbonic anhydrase.

Bicarbonate is transported out of the basolateral membrane in exchange for chloride. The outflow of bicarbonate into blood results in a slight elevation of blood pH known as the "alkaline tide". This process serves to maintain intracellular pH in the parietal cell. Chloride and potassium ions are transported into the lumen of the cannaliculus by conductance channels, and such is necessary for secretion of acid. Hydrogen ion is pumped out of the cell, into the lumen, in exchange for potassium through the action of the proton pump; potassium is thus effectively recycled. Accumulation of osmotically-active hydrogen ion in the cannaliculus generates an osmotic gradient across the membrane that results in outward diffusion of water. The resulting gastric juice is 155 mM HCl and 15 mM KCl with a small amount of NaCl ***(Yao and Forte, 2003)***.

Phases of acid secretion:

The physiologic stimulation of acid secretion has classically been divided into three interrelated phases: cephalic, gastric, and intestinal .The cephalic phase is activated by the thought, taste, smell and sight of food, and swallowing. It is mediated mostly by cholinergic/vagal mechanisms. The gastric

phase is due to the chemical effects of food and distension of the stomach. Gastrin appears to be the major mediator since the response to food is largely inhibited by immunoneutralizing or blocking gastrin. The intestinal phase accounts for only a small proportion of the acid secretory response to a meal; its mediators remain controversial. The observation that H2 receptor antagonists block the cephalic and gastric phases underscores the importance of histamine mediation of the stimulatory response, and illustrates the interdependence of the different phases ***(Lloyd et al., 1994).***

Regulation of Acid Secretion:

The regulation of gastric acid secretion is complex and involves a multitude of neural, hormonal, and paracrine pathways that act directly on the parietal cell and indirectly by modulating secretion of the hormone gastrin and the paracrine agents histamine and somatostatin in the stomach.

I) Central mechanisms for gastric acid secretion:

The dorsal motor nucleus of the vagus in the medulla and the paraventricular nucleus in the hypothalamus play key roles in the integration of afferent and efferent information. Various neurotransmitters and neuropeptides in the brain regulate gastric acid secretion. Central vagal stimulation induced by cold exposure or intracisternal injection of thyrotropin-releasing hormone activates cholinergic neurons in the stomach that increase gastric acid secretion ***(Yuan et al., 2005)***.