STUDY OF GASTRIC EMPTYING IN AGED RATS

Thesis

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master degree in Physiology

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Summary & Conclusion

The present study was planned to investigate the changes in gastric emptying and motility in aged rats and their contribution to changes in food intake in addition to the role of NO in gastric emptying.

The present study was performed on 42 male Sprague Dawley rats (10 adults, B.W. 160-210 g) and (32 aged, B.W. 300-475 g). The rats were randomly allocated into the following two main groups;

1. **Group I;** 10 adult rats (9-12 months old).
2. **Group II;** comprised of 32 aged rats (18-30 months old) randomized into the following 3 subgroups.
   a) **Aged untreated rats:** 10 aged rats. These rats were given normal saline daily by gavage in a dose of 1ml/Kg B.W. for 14 days, used as control group for L-arginine and L-NAME treated groups.
   b) **Aged L-arginine treated rats:** 11 aged rats treated with the nitric oxide precursor; L-arginine for two weeks. L-arginine was freshly dissolved in normal saline prior to injection (300 mg/1 ml), and then injected intraperitoneally in a dose of 300 mg/Kg B.W.


بسم الله الرحمن الرحيم


وقل رب زدني علما


صدق الله العظيم

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List of Abbreviations

ANOVA	Analysis of variance
ATP	Adenosine triphosphate
BW	Body weight
CART	Cocaine-amphetamine-regulated transcript
CCK	Cholecystokinin
CSF	Cerebrospinal fluid
FBW	Final body weight
FD	Functional dyspepsia
GIP	Gastric inhibitory polypeptide
GLP-1	Glucagon-like peptide-1
IBW	Initial body weight
ICC	Interstitial cells of Cajal
IGP	Intragastric pressure
IL	Interleukin
L-NAME	N omega-nitro-L-arginine methyl ester
LSD	Least significant difference

NAD	Nicotinamide adenine dinucleotide
NANC	Non-adrenergic, Non-cholinergic
nNOS	Neuronal nitric oxide synthase
NO	Nitric oxide
NOS	Nitric oxide synthase
NPY	Neuropeptide Y
NRC	National research council
PYY	Peptide YY
SEM	Standard error of the mean
SIR2	Silent information regulator 2
SPSS	Statistical Program for Social Science
TNF	Tumor necrosis factor
VIP	Vasoactive intestinal peptide

Introduction

As the world's population continues to live longer, studies in physiological changes in aging become increasingly essential for living a longer healthier life. **Aging** is a natural, complex, and multifactorial biologic process characterized by deterioration of homeostatic mechanisms that reduces the capability of the individual to adapt to internal and external environmental changes.

Studies in previous literature suggested that aging is associated with disordered gastrointestinal transit, slowing of solid and/or liquid gastric emptying. The slowing of gastric emptying was reported to be implicated in some aging- associated health problems like anorexia of aging ***(Morley, 2001)*** resulting from early satiation ***(Clarkston et al., 1997).*** Anorexia of aging might be implicated in the development and progression of chronic diseases commonly affecting the elderly like impaired muscle function, decreased bone mass, immune dysfunction, anemia, reduced cognitive function, poor wound healing, delayed recovery from surgery, and ultimately increased morbidity and mortality. ***(Chapman, 2007).***

Rate of gastric emptying is a rate limiting step in the absorption of orally –administered drugs **(Gidal *et al.*, 2006)** and is also a major determinant of the glycemic and cardiovascular response to oral carbohydrate **(Ishii *et al.*, 1997 and Jones *et al.*, 1998).** Glycemic response to oral carbohydrate is important for the dietary management of people with diabetes mellitus and to reduce both the development and progression of microvascular complications **(American Diabetes Association, (2001)**. Cardiovascular response to oral carbohydrate might be relevant to postprandial hypotension, which is an important clinical problem in the elderly **(Jansen and Lipsitz,1995).**

Delayed gastric emptying and disturbed gastric motility are deeply involved in Impaired tolerance to gastric feeding in criticall ill patients in intensive care units (**Heyland *et al.,* 2003)** leading to patient discomfort, increased risk of pulmonary aspiration with the need for post-pyloric feeding, or parenteral nutrition (**Mentec *et al.,* 2001 and Multu *et al.,* 2001)** which would adversely affect patient morbidity and mortality **(Ritz *et al.*, 2000).**

Nitric oxide (NO) is a widespread signaling molecule that participates in virtually every cellular and organ function in the body **(Moncada and Higgs, 2006)**. Nitric oxide (NO) is an inhibitory neurotransmitter of peripheral nonadrenergic noncholinergic (NANC) nerves in the gastrointestinal tract that is involved in the reflex relaxation of the gastric fundus to accommodate food or fluid **(Desai et al., 1991)** and mediate relaxation of the pylorus and upper duodenum, thereby facilitating gastric emptying **(Orihata and Sarna, 1994).** Reports on NO changes with aging were conflicting with some authors reporting decreased neuronal nitric oxide synthase (nNOS) expression in myenteric plexus with aging (**Takahashi *et al.*, 2000)** and others reporting enhancement of neuronal NO synthase, a lowering of endothelial, and no alteration in inducible activity of nitric oxide synthase (**Domek-Łopacińska and Strosznajder, 2010)** with aging.

Thus**,** it was intriguing to design a study to investigate changes in gastric emptying and motility with aging and the contribution of NO to these changes.

Aim of the work

The present study was planned to investigate the changes in gastric emptying and motility in aged rats and their contribution to changes in food intake as well as the effect of stimulation or inhibition of NO synthesis on these parameters.