EFFECTS OF ω-3 FATTY ACIDS AND ESTROGEN REPLACEMENT THERAPY ON OVARIECTOMY INDUCED OSTEOPOROSIS IN FEMALE ALBINO RATS

Thesis
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Abstract

Fatty acids especially omega 3 unsaturated fatty acids has known anti-inflammatory effects. And there are different mechanisms by which dietary fatty acids may affect bone, but there protective effect against postmenopausal osteoporosis remains a controversial issue. This study was applied on 50 female albino rats that were divided into 5 equal groups: sham operated group, ovariectomy group, ovariectomy + flaxseed oil group (0.4 g per day), ovariectomy + fish oil administered group (0.4 g per day) and ovariectomy + estrogen replacement therapy group (30 µg/kg 5 days a week). The study proceeded for 12 weeks then femurs bone mineral density (BMD) were measured with dual-energy X-ray absorptiometer (DXA) scan and serum osteoprotogerin (OPG), bone specific alkaline phosphatase (ALP-b) and tumour necrosis factor alpha (TNF-α) were measured. There was a significant increase in the BMD of the treated groups compared with the ovariectomy group ($p < .01$). There were a significant differences in the means of serum bone markers measures of the treated groups versus the ovariectomy group in the form of significant increase in OPG ($p < .001$) and a significant decrease in ALP-b ($p < .001$) and TNF-α ($p < .001$) of the treated groups compared with the ovariectomy group. This study showed a significant negative correlation between BMD and ALP-b ($r = - 0.375$, $p < .001$). According to this study the chronic administration of omega 3 fatty acids (flaxseed oil - fish oil) has a preventive effect against osteoporosis and suppression of bone turn over process appears to have a role in this preventive effect.

Key Words : Osteoporosis - Omega 3 fatty acids - Bone mineral density - Osteoprotogerin - Tumour necrosis factor alpha - Alkaline phosphatase

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List of Abbreviations

3β-HSD	**3β-hydroxysteroid dehydrogenase**
15-S-HETE	**15S-hydroxyeicosatetraenoic acid**
17β-HSD	**17β-hydroxysteroid dehydrogenase**
17-HDHA	**17-hydroxydocosahexaenoic acid**
18-HEPE	**18-hydroxyeicosapentaenoic acid**
AA	**Arachidonic acid**
ALA	**Alpha-linolenic acid**
ALP-b	**Bone specific alkaline phosphatase**
ALX	**Lipoxins receptor**
BCAR1	**Breast cancer anti-estrogen resistance protein 1**
BMD	**Bone mineral density**
BMP	**Bone morphogenetic protein**
Cbfa1	**Core-binding factor alpha 1**
COX	**Cyclooxygenase**
CRP	**C-reactive protein**

CYP	**Cytochrome P450**
DBD	**DNA-binding domain**
DDH	**Death domain homologous**
DHA	**Docosahexaenoic acid**
DHEA	**Dehydroepiandrosterone**
DNA	**Deoxyribonucleic acid**
DPA	**Docosapentaenoic acid**
DXA	**Dual-energy X-ray absorptiometry**
EDTA	**Ethylenediaminetetraacetic acid**
EFA	**Essential fatty acids**
EGF	**Epidermal growth factor**
ER	**Estrogen receptor**
ERK	**Extracellular-signal-regulated kinase**
EPA	**Eicosapentaenoic acid**
FA	**Fatty acid**
FasL	**Fas ligand**

FDA	**Food and drug administration**
FGF	**Fibroblast growth factor**
GM-CFU	**Granulocytic-macrophage colony-forming unit**
H&E	**Hematoxylin and eosin stain**
HPETE	**Hydroperoxy-eicosatetraenoic acids**
IGF	**Insulin-like growth factor**
IJO	**Idiopathic juvenile osteoporosis**
IκBα	**nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor alpha**
IKKs	**inhibitor of nuclear factor kappa-B kinase**
IL	**Interleukin**
ITAM	**Immunoreceptor tyrosine-based activation motif**
JNK	**c-jun N-terminal kinase**
LA	**Linoleic acid**
LBD	**Ligand- binding domain**
LDLs	**Low density lipoproteins**
LOX	**lipoxygenase**

LPS	**Lipopolysaccharide**
LRP	**Lipoprotein receptor-related protein**
LX	**Lipoxin**
MAPK	**Mitogen-activated protein kinases**
M-CFU	**Macrophage colony-forming unit**
M-CSF	**Macrophage colony-stimulating factor**
miR-21	**MicroRNA 21**
MMP-13	**Matrix metallopeptidase 13**
MSCs	**Mesenchymal stem cells**
MUFA	**Monounsaturated fatty acid**
NFATc1	**Nuclear factor of activated T cell c1**
NF-κB	**Nuclear Factor kappa B**
OI	**Osteogenesis imperfecta**
OPG	**Osteoprotegerin**
OSCAR	**Osteoclastassociated receptor**
OVX	**Ovariectomy group**

OVX-E	**Ovariectomy + Estrogen**
OVX-FS	**Ovariectomy + Fish oil group**
OVX-FX	**Ovariectomy + Flaxseed oil group**
P450aro	**Aromatase enzyme**
P450scc	**Cholesterol side-chain cleavage enzyme**
PDGF	**Platelet-derived growth factor**
PG	**Prostaglandins**
PGE2	**Prostaglandin E2**
PGI	**Prostacyclins**
PI3K	**Phosphatidyl inositol 3 kinase**
PLCγ	**Phospholipase Cγ**
PPARγ	**Peroxisome proliferator-activated receptor-γ**
PTH	**Parathyroid hormone**
PTHrP	**Parathyroid hormone-related protein**
PUFA	**Polyunsaturated fatty acid**
RANK	**Receptor Activator of Nuclear Factor kappa B**

RANKL	**Receptor activator of nuclear factor kappa B ligand**
RBC	**Red blood cell**
RGD	**Arginyl-glycyl-aspartic acid sequence**
ROS	**Reactive oxygen species**
RUNX2	**Runt-related transcription factor 2**
SFA	**Saturated fatty acid**
Spry1	**Sprouty Homolog 1**
TGF-β	**Transforming growth factor beta**
TNF-α	**Tumor necrosis factor alpha**
TRAF	**TNF receptor-associated factor**
TREM	**Triggering receptor expressed in myeloid cells**
TX	**Thromboxanes**
VEGF	**Vascular endothelial growth factor**
Wnt	**Wingless-related integration site**