OBESITY AND RELATED DERMATOSES

Essay

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By

Haiam Mohamed Abdallah Mahmoud

(M.B, B.Ch.)

Supervised by

Prof. Khaled Hassan El-Hoshy
Professor of Dermatology
Faculty of Medicine
Cairo University

Dr. Dina M. Kadry Ismail
Lecturer of Dermatology
Faculty of Medicine
Cairo University

Dr. Iman Mohammad Amin
Lecturer of Dermatology
Faculty of Medicine,
Cairo University

Faculty of Medicine
Cairo University
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ABSTRACT

Modern studies of obesity strongly indicate that it is a multifactorial problem. The effect of obesity on skin has received minimal attention, inspite of the profound impact of obesity on clinical dermatology.

Obesity is related to a number of significant changes in skin physiology, including effects on skin barrier function, sebaceous glands and sebum production, sweat glands, lymphatics, collagen structure and function, wound healing, microcirculation and macrocirculation, and subcutaneous fat.

Obesity is implicated in a wide spectrum of dermatological diseases, including acanthosis nigricans, acrochordons (skin tags), keratosis pilaris, hyperandrogenism and hirsutism, striae distensae, adiposis dolorosa and fat redistribution, lymphedema, chronic venous insufficiency, plantar hyperkeratosis, cellulitis, skin infections, hidradenitis suppurativa, psoriasis, insulin resistance syndrome, and tophaceous gout.

Key Words

Obesity

Dermatoses

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LIST OF ABBREVIATIONS

ACTH…….……..Adrenocorticotrophic Hormone

BMI ……..…..…..Body Mass Index

CHD …….....Coronary Heart Disease

CHF …….....Congestive Heart Failure

CRP…….…..C-Reactive Protein

CVD ……...…….....Cardiovuscular Disease

DM.....Diabetes mellitus

FFA ……..Free Fatty Acids

GLUT ……..Glucose Transporter

HDL…….....High Denisty Lipoprotein

HIV …….….Human Immunodeficiency Virus

HPA …….....Hypothalamic- Pituitary- Adrenal axis

HS …….....Hidradenitis Suppurativa

ICAM …….....Intracellular Adhesion Molecule

IGF……..….Insulin like Growth Factor

IL-1 ……...…...Interleukin-1

IRS ……...Insulin Receptor Substrate

MC….……...Melanocortin peptides

MCP …….Monocyte Chemotactic Protein

MSH …….Melanocyte Stimulating Hormone

NO …….....Nitric Oxide

Ob ……....Obesity gene

PAI …….....Plasminogen Activator Inhibitor

PCO …….Polycystic Ovary Syndrome

POMC …….Pro-Opiomelanocortin

PVD……..Peripheral Vascular Disease

PVN …….Para Ventricular Nucleus

PWS…….Prader-Willi Syndrome

SHBG .....Sex Hormone Binding Globulin

TEWL ……..…...Transepidermal Water Loss

TNF …….Tumor Necrosis Factor

VCAM ……....Vascular Cell Adhesion Molecule

VLCD …….....Very Low Calorie Diets

WHO ……...World Health Organization

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INTRODUCTION

Obesity, in simple terms, may be defined as a state of imbalance between calories ingested versus calories expended which would lead to excessive or abnormal fat accumulation. Body Mass Index (BMI) is a measure of weight correlated for height and has been the most accepted parameter for defining overweight ***(Goodman and Strauss, 2008).***

Obesity has been thought to be simply related to an imbalance between energy intake and expenditure. However, more recently research has suggested that genetic, physiological, environmental, psychological, social and economic factors also play a significant role in the etiology of obesity ***(Bray, 2004).***

There is a well recognized relationship between mortality and weight. Obesity is also known to be directly related to increased risk of many diseases. However the effect of obesity on skin has received minimal attention, although the profound impact of obesity on clinical dermatology ***(Pender and Pories, 2005).***

AIM OF WORK

The aim of this study is to review the skin disorders among obese patients & highlight them for dermatologists.

OBESITY

Obesity, highly and increasingly prevalent, is now considered a pandemic. As in 2005, more than 400 million adults worldwide were diagnosed as obese and this number is expected to rise to more than 700 million by the year 2015 ***(WHO, 2009).*** This situation is more than a mere crisis, since obesity is causally associated with several chronic diseases, most notably type 2 diabetes mellitus (DM) and cardiovascular disease (CVD). Additionally, obesity can promote the development of nonalcoholic fatty liver disease, gall bladder disease, skin diseases, hypertension, osteoarthritis, sleep apnea, and some cancers like breast cancer and cancer colon ***(Bray, 2004).*** Given the burgeoning population of obese individuals with their increased risk for cardiometabolic and other obesity-related diseases, it is clear that more effective intervention to prevent or treat obesity must become a priority if health outcomes for these individuals are to be improved ***(Aronne et al., 2009).***

Why Obesity Qualifies As A Disease

According to ***Dorland's Illustrated Medical Dictionary,*** a disease is " any deviation from or interruption of the normal structure or function of any part, organ, or system (or combination thereof) of the body that is manifested by a characteristic set of symptoms and signs and whose etiology, pathology, and prognosis may be known or unknown." Using this definition as a framework, obesity meets all of the criteria for a medical disease, including a known etiology, recognized signs and symptoms, and a range of structural and functional changes that culminate in pathologic consequences ***(Aronne et al., 2009).***

Aetiology Of Obesity:

Obesity is most commonly caused by excess energy consumption (dietary intake) relative to energy expenditure (energy loss via metabolic and physical activity). However, attributing obesity solely to these factors is an oversimplification, rather the etiology of obesity is highly complex and dynamic, encompassing genetic, physiologic, environmental, psychological, social and economic factors that interact in varying degrees to promote the development of obesity ***(Bray, 2004).***

1-Diet and physical activity

Environmental factors in the presence of a genetic predisposition, lead to fat gain through an increase in food intake and a reduction in physical activity or both ***(Sorensen et al., 1992).*** Diet composition, particularly fat intake, is associated with obesity ***(Maffeis et al., 1996).*** Sedentary behaviour, which promotes a reduction in energy requirements, favours the development and persistence of obesity ***(Moore et al., 1995).*** The impact of sedentary behaviour is so strong that ***Epstein et al., (1995)*** identified the reduction of sedentary activity as one of the three most important targets in the treatment of childhood obesity, together with diet and behavioural modifications. Several studies have shown that sedentary behaviour is associated with overweight in both adults and children ***(Maffeis et al., 1997).***

2-Hormonal factor

Several hormones and neuropeptides may play a role in development of obesity.

a-Insulin

It is an anabolic hormone, not only in regards to muscle, but also to fat. Insulin is known to direct the storage and utilization of energy in the adipocytes ***(Laviola et al., 2005).***

Abdominal obesity is related to insulin resistance and type II diabetes ***(Rorive et al., 2005).*** While increased body weight moderately reduces hepatic and peripheral insulin sensitivity, central obesity causes far greater impairments ***(Pinkney and Kopelman, 2004).***

b-Leptin

It is a cytokine-like polypeptide produced by the adipocytes under the control of obesity (Ob) gene, it controls food intake through the activation of hypothalamic receptors ***(Schwarts et al., 2000).*** Leptin receptors (Ob-R) have been located on tissues, including keratinocyte, fibroblast, endothelial cells, and adipose tissue ***(Margetic et al., 2002).*** Leptin promotes fibroblast proliferation and collagen synthesis. It is also known to promote endothelial growth and angiogenesis ***(Li et al., 2005).***

Leptin is produced proportionately to the adipose mass and thus informs the brain of the fat store level. Once leptin binds to its receptor (Ob-R) in the hypothalamic arcuate nucleus, it induces the synthesis of α-melanocyte stimulating hormone (α-MSH). Subsequently, α-MSH binds to MC4 receptor in the paraventricular nucleus which inhibits the effectors of food intake ***(Schwarts et al., 2000).***

Obese humans do not have a deficiency of leptin, but surprisingly have higher levels of circulating leptin in the body. This would indicate

that leptin deficiency is not a primary cause of obesity, but rather a decreased response to leptin ***(Colin et al., 2005).***

c-Cortisol

It is a glucocorticoid known to have powerful metabolic effects. These include mobilization of fatty acids from stored triglycerides, hepatic gluconeogenesis, and proteolysis. ***Bjorntorp and Rosmond., (2000)*** made it clear that there is an association between hypercortisolemic states and obesity which appears to be related to a hypothalamic dysfunction. Equally important, it seems that the hypothalamic-pituitary-adrenal (HPA) axis works in concert with acute increases in insulin after feeding ***(Dallman et al., 2004).*** This synergistic action could possibly lead to increases in visceral adipose tissue storage. Researchers have found an association between central body fat, perceived stress and elevated Cortisol ***(Bjorntorp and Rosmond, 2000).***

d-Ghrelin

This is a growth hormone secretagogue, which is highly concentrated in the stomach. Gastric ghrelin expression and secretion increases with fasting and hence stimulate feeding and declines in the postprandial state ***(Cummings et al., 2001).*** Surprisingly, reduced plasma ghrelin concentrations have been reported in human obesity ***(Pinkney and Kopelman, 2004).***

e-Norepinephrine

It stimulates and also decreases food intake depending on which type of receptor it interacts with. When it acts on α-1 adrenoreceptors in the paraventricular nucleus (PVN) it decreases food intake. Conversely,

when norepinephrine acts on α-2 adrenoreceptors in the PVN it results in the stimulation of food intake ***(Bray, 2003).***

f-Other biological factors

Serotonin, Interleukin-6 and (TNF-α) have been shown to influence energy intake and possibly contribute to obesity ***(Bray, 2003).***

3-Genetic factors

Knowledge concerning obesity was derived from large-scale linkage analyses in mice that had naturally occurring mutations that led to extreme obesity. These analyses resulted in the detection of disease loci and the identification of candidate genes ***(Ardeli et al., 2002).*** Using such an approach, the majority of mutations in genes underlying murine obesity have now been cloned ***(Barsh et al., 2000).***

Rankinen et al., (2006) detected nearly 200 cases of human obesity associated with a single gene mutation. Furthermore, these mutations all lie in one of 11 genes**.** These cases, which obey Mendelian genetics, are characterized by extremely severe phenotypes that present themselves in childhood and are often associated with additional behavioral, developmental, and endocrinal disorders ***(Farooqi and O`rahilly, 2005).***

Examples of gene products involved in obesity and their associated phenotypes include: *leptin* responsible for satiation and metabolism, *melanocortin* responsible for feeding behaviour, *ghrelin* concerned with appetite stimulation and *neuromedin β* responsible for feeding behaviour and satiety. Of these genes, two gene products are known to have direct effects on skin; leptin and pro-opiomelanocortin (POMC).One possible gene is the obesity (Ob) gene that produces leptin which is a hormone