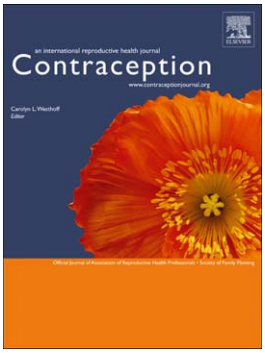

Clarification of contraceptive drug pharmacokinetics in obesity

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Commentary

Clarification of contraceptive drug pharmacokinetics in obesity

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Abstract

Related to concerns about the role of obesity in the efficacy of contraceptive drugs, a review of the literature was carried out in regard to the pharmacokinetics of ethinyl estradiol and various progestins given by various routes of administration. Most studies show that obese women exhibit modestly lower plasma concentrations of these drugs (circa 30%) when given the same doses as normal weight women. While the mechanism is uncertain, precedence in the literature suggests that this is due to body weight-related differences in metabolism rates. Confusing in some of the literature is that a few studies have reported erroneously calculated pharmacokinetic parameters after multiple-dosing of oral contraceptives. A demonstration of appropriate pharmacokinetic methodology is provided.

Key Words: Obesity, contraceptives, body weight, ethinyl estradiol, levonorgestrel, pharmacokinetics.

Introduction

There has been concern expressed about the effectiveness of contraceptive drugs in obese women. Over one-third of American women over 20 years old are clinically obese, having a Body Mass Index (BMI) greater than 30 kg/m^2 [1]. A recent assessment of Oral Contraceptive (OC) clinical trials by the FDA indicated that obesity may increase the risk of unintended pregnancy pointing out that future studies should assess pharmacodynamics and compliance as contributing factors [2]. Of course, measurement of drug exposure (pharmacokinetics) will be needed in such studies as well. On the other hand, a survey by McNicholas et al [3] in 2013 concluded that, "overweight and obese females do not appear to be at increased risk for contraceptive failure when using the contraceptive pill, patch, or vaginal ring". Owing to these issues and uncertainties, there has been increased attention paid to the pharmacokinetics (PK) of contraceptive drugs in obese women. The purpose of this communication is to provide a review of recent PK studies of contraceptive drugs in obesity and to point out some misunderstandings in the interpretation of PK data from some of these studies.

Physiological Changes in Obesity

Obesity is generally a complicating factor in physiology and in the pharmacokinetics and pharmacodynamics (PK/PD) of drugs and hormones. The increase in body weight, besides adding to the mass of excess adipose tissue, produces variable changes in renal, hepatic, endocrine, and other organ