Mid Luteal Serum Progesterone Evaluation in Patients with Recurrent Vulvovaginal Candidiasis

Thesis

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تقدير نسبة هرمون البروجيسترون بالدم في منتصف الطور الأصفري (الإفرازي) في المريضات المصابات بالتهابات الكانديدا الفرجية المهبلية المتكررة

رسالة

توطئة للحصول على درجة الماجستير

في أمراض النساء والتوليد

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Ahmed M. Abd-Elmalek

List of Abbreviations

CMI	Cell mediated immunity
COC	Combined oral contraceptive pills
DHEA	Dehydro-epiandenosterone
E2	Estradiol
EC	Epithelial cells
FSH	Follicular stimulating hormone
hCG	Human chorionic gonadotropins
HIV	Human immunodeficiency virus
IFN	Interferon
IL-4	Interleukin-4
KOH	Potassium hydroxide
LH	Luteinizing hormone
LPD	Luteal phase defect
MBL	Mannose binding lectin
MCP-1	Macrophage chemotactic protein 1
PBMC	Peripheral blood mononuclear cells
P levels	Progesterone levels
PID	Pelvic inflammatory disease
PMNs	Polymorphonuclear leucocytes
RVVC	Recurrent vulvovaginal candidiasis
STD	Sexually transmitted disease
VVC	Vulvovaginal candidiasis
WBCs	White blood cells

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Introduction

Vulvovaginal candidiasis (VVC) is a mucosal infection caused by *Candida* species ***(Sobel, 2002)***. *Candida albicans*, a dimorphic commensal organism of the genital and gastrointestinal tracts, is the causative agent of VVC in approximately 85 to 90% of patients with positive vaginal fungal cultures, the remainder of the cases are due to non-*C. albicans Candida* species, the most common of which are *C. glabrata* and *C. tropicalis* (***Spacek J. et al., 2005***).

An estimated 75% of all women will experience an episode of *Candida* vaginitis in their lifetime ***(Sobel, 1988)***. In fact, vaginitis is among the most common clinical problems in women of childbearing age. In the United States alone, approximately 13 million cases of VVC occur annually, accounting for 10 million gynecologic office visits ***(Kent, 1991)***. Of the women diagnosed with an episode of sporadic VVC, a significant percentage will experience subsequent recurrent episodes of acute VVC.

The condition of recurrent VVC (RVVC) is defined as three or more episodes per annum (***Ringdahl EN. , 2000***).

Sporadic VVC or RVVC can be classified as primary or secondary depending upon established underlying causes ***(Sobel, 1996)***. Secondary sporadic VVC refers to those infrequent vaginal infections precipitated by pregnancy or by exogenous factors such as antibiotics or wearing of tight undergarments ***(Fidel and Jack, 1996)***. Secondary recurrent vaginal candidal infections commonly occur as a result of uncontrolled diabetes mellitus, immuno-suppressive therapy, hormone replacement therapy, and possibly AIDS. Primary sporadic VVC and RVVC are idiopathic with no known causes ***(Zhang et al., 2000)***.

Unfortunately, the cause of this disease is concealed in most women, and the etiopathogenesis of RVVC remains to be determined ***(Fidel, 2004)***. The development of an attack depends on a number of factors but, generally, both the immunity represented by the local defense mechanisms of the vaginal compartment and the actual hormonal status are possible candidates for a principal role in the pathogenesis ***(Fidel, 2004)***.

The walls of vagina, especially during reproductive years, are lined with the pavement of epithelial cells rich in glycogen. Such conditions constitute a potentially favourable environment for the growth of pathogens ***(Segal et al., 1984)***. The state of the vaginal mucosa reflects female hormonal status in different lifetime stages. Specific histological changes in the vaginal epithelium correlate mainly with the level of estrogens ***(Kinsman and Collard, 1986)***. "Luteal phase defect" is due to decrease production of progesterone from corpus luteum or early degeneration of corpus luteum or due to inability of the endometrium to respond adequately to a normal hormonal stimulus ***(Malcolm and Cumming 2003)***.

Vaginal colonization of Candida species requires adherence to the vaginal epithelial cells, with both estrogens and progesterone promoting the adherence of C. albicans to the genital mucosa ***(Kalo and Segal 1988)***. On the other hand, it is believed that progesterone has an antiproliferative and exfoliative effect on the epithelial cells, mainly between the 23rd and 28th day of the cycle, coinciding with the blood progestin peak ***(Glazener et al., 1985)***.

Progesterone is excreted as a pregnanediol glucuronide in urine. They are used for the demonstration of ovulatory (biphasic) cycles, the monitoring of infertility treatment, and for the determination of ovulation ***(Blackwell et al., 1998)***. The production of progesterone may be assessed by direct midluteal-phase sampling from the serum or by repeated determination of urine pregnanediol glucuronide during the luteal phase ***(Malcolm and Cumming 2003)***.

Aim of the work

The aim of the study is to evaluate if there is a relation between mibd luteal serum progesterone level and recurrent vulvo-vaginal candidiasis in order to investigate a possible role of the altered hormonal status in case of luteal phase defect in the pathogenesis of recurrent vulvo-vaginal candidiasis.

Physiology and Microbiology of The Vagina

The vagina is a fibromuscular canal that extends from the vulva to the uterus, it has many functions, the excretory canal of the uterus through which uterine secretion and menstrual flow escape, the female organ of copulation, and a part of the birth canal ***(Cunningham et al., 1994)***.

Its walls consist of a mucosal layer lined by stratified squamous epithelium, a layer of smooth muscle and an outer advential layer, in the relaxed state the vaginal wall collapses to obliterate the lumen and the vaginal epithelium is thrown up into folds, the dense lamina propria contains many elastic fibers, has a rich plexus of vein and is devoid of glands ***(Burkitt et al., 1993)***.

The vaginal desquamative tissue is made up of vaginal epithelial cells that are responsive to varying amounts of estrogen and progesterone. Superficial cells, the predominant cell type in women of reproductive age, predominate when estrogen stimulation is present. Intermediate cells predominate during the luteal phase

because of progestogenic stimulation. Parabasal cells predominale in the absence of either hormone, a condition that may be in post menopausal women who are not reeiving hormonal replacement therapy ***(Soper, 1996)***.

During the menstrual cycle, the epithelium undergoes cyclical changes which include slight keratinisation of the superficial cells. Thoughout the cycle, the superficial cells produce glycogen which is anaerobically metabolized by vaginal commensal bacteria to form lactic acid which inhibits the growth of pathogenic microorganisms ***(Burkitt et al., 1993)***.

Normal Vaginal Discharge And Flora:

In reproductive aged women, normal vaginal discharge consists of 1 to 4 mL fluid (per 24 hours), which is white or transparent, thick, and mostly odorless. This physiologic discharge is formed by mucoid endocervical secretions in combination with sloughing epithelial cells, normal bacteria, and vaginal transudate. The discharge may become more noticeable at times, as an example during pregnancy, use of estrogen-progestin contraceptives, or at midmenstrual cycle close to the time of ovulation. It can be somewhat malodorous and accompanied by irritative