ORAL MERONIDAZOLE VERSUS PASTEURIZED YOGHURT IN THE TREATMENT OF BACTERIAL VAGINOSIS

Thesis

Submitted for partial fulfillment of the Master Degree in *Obstetrics and Gynecology*

By

Nahla Gamal Helmi Sherif M.B., B.Ch, 2004, Ain Shams University Resident in Nacer City Inssurance Hospital

Under Supervision of **Prof. Dr. Alaa Eldin Hamed Elfeky**

Professor of Obstetrics and Gynecology Faculty of Medicine - Ain Shams University

Prof.Dr. Fekria Ahmed Salama

Professor of Obstetrics and Gynecology Faculty of Medicine - Ain Shams University

Dr. Ahmed Adel Tharwat

Lecturer of Obstetrics and Gynecology Faculty of Medicine - Ain Shams University

> Faculty of Medicine Ain Shams University 2011

المقارنة بين استخدام الزبادى المبستر واستخدام عقار الميتر ونيدازول في علاج الإلتهاب المهبلى البكتيرى

رسالة

توطئة للحصول على درجة الماجستير في أمراض النساء والتوليد

مقدمة من الطبيبة / نهله جمال حلمى شريف بكالوريوس الطب والجراحة 2004 طبيب مقيم بمستشفى مدينة نصر للتأمين الصحى

تحت إشراف أ.د/ علاء الدين حامد الفقى أستاذ أمراض النساء والتوليد كلية الطب - جامعة عين شمس

أ.د/ فكريه أحمد سلامه

أستاذ أمراض النساء والتوليد كلية الطب - جامعة عين شمس

د/ أحمد عادل ثروت

مدرس أمراض النساء والتوليد كلية الطب - جامعة عين شمس

كلية الطب جامعة عين شمس 2011

SUMMARY

This study will be single blinded randomized clinically interventional trial which will be held upon 60 ladies complaining from bacterial vaginosis who are attending the outpatient gynecologic clinic at Ain Shams University Maternity Hospital. This study was conducted to evaluate the efficacy and patient compliance of oral metronidazole versus oral pasteurized yoghurt in the treatment of BV among non pregnant women during their child bearing period.

Diagnosis of BV was based on Amsel's criteria, defined as the presence of three out of the following four criteria:

- 1. Full history will be taken; a homogenous and grayish non inflammatory discharge that adheres to the vaginal walls and symptom of vulvovaginitis as itching and dysparenia.
- 2. Microscopic examination with the presence of clue cells.
- 3. PH of vaginal fluid >4,5
- 4. Whiff test is positive.

(Amsel et al., 1988)

Those who fulfilled the inclusion criteria (N=60) were randomly divided into two equal groups after an informed consent, full medical history taking and medical examination, each group included 30 participant.





First, I would like to express my greatest gratitude and thanks to "ALLAH" how gives me strength and help me to accomplish this work.

I would like to extend my feeling of deep respect, gratefulness to Prof. Dr. Alaa Eldin Hamed Elfeky, Professor of Obstetrics and Gynecology, Faculty of Medicine - Ain Shams University for his generous assistance, kind supervision, constructive criticism, expertise, continuous unlimited support. I am greatly thankful for his valuable advice, continuous encouragement, indispensable guidance and great effect he has devoted in his supervision of this work.

My profound gratitude and respect to Prof.Dr. Fekria Ahmed Salama, Professor of Obstetrics and Gynecology, Faculty of Medicine - Ain Shams University, for the great help and support she provided me during supervision of this work. Her inspiring enthusiasm made it possible and with out her assistance that has made the easiest out of the most difficult, I would not have been able to start and reach the production of this work indeed, I am very privileged and honored to have her as my supervisor.

Last but not least, my deepest thanks and gratitude to Dr. Ahmed Adel Tharwat, Lecturer of Obstetrics and Gynecology, Faculty of Medicine - Ain Shams University, for help and support and kind supervision, his continuous advice help to bring this work to life.

LIST OF CONTENTS

Title	Page No.
Introduction	0
Aim of the Work	34
Review of Literature	
Microbial Ecology in The Lower Gen	ital Tract in Females. 35
Bacterial Vaginosis	43
Management of Bacterial Vaginosis	77
Common Complementary and Alternative	ative Therapies 87
Recurrence	97
Patients and Methods	100
Results	105
Discussion	111
Summary	117
Conclusion And Recommendations	121
References	122
Arabic Summary	<u> </u>

LIST OF TABLES

Tab. No.	Title	Page No.
Table (1):	Classification of bacteria in the hu	uman vagina 37
Table (2):	Standardized scoring method for stained smears for the diagnosis of	
Table (3):	Comparison between ages in both	groups105
Table (4):	Comparison between contraception	on in both groups 105
Table (5):	Comparison of discharge between test	
Table (6):	Comparison of vaginal pH betwee t test	
Table (7):	Comparison of whiff test between test	
Table (8):	Comparison of clue cells between test	
Table (9):	Comparison of cure rates between Chi ² test	

LIST OF FIGURES

Fig. No.	Title	Page No.	
Figure (1):	Comparison between the two gro		
Figure (2):	Comparison of vaginal pH between	en the two groups.107	
Figure (3):	Comparison between the two gr	1 0	
Figure (4):	Comparison between the two gro		
Figure (5):	Comparison between the two gro		

LIST OF ABBREVIATIONS

Abbrev.	Meaning
AIDS	Acquired Immune Deficiency Syndrome
b.	Bacteroid
BLSs	Bacteriocin Like Substances
\mathbf{BV}	Bacterial Vaginosis
C. albicans	Candida albicans
CDC	Center of disease control
CIN	Cervical intraepithelial neoplasia
Cfu	Colony forming unit
DNA	Deoxyribonucleic acid
E. coli	Escherichia coli
FAO	Food and Agriculture Organization of the United Nations
FDA	Food and Drug Administration
FOS	Fructo-oligosaccharides
G. vaginalis	Gardnerella vaginalis
GIT	Gastrointestinal Tract
GLC	Gas Liquid Chromatography
H2O2	Hydrogen peroxide
HDL	High Density Lipoproteins
HIV	Human Immune Deficiency Virus
HPF	High power field
Hsp	Heat-shock protein
IgA	Immunoglobulin A
IUD	Intra Uterine Device
IVF	Intermediate vaginal flora
КОН	Potassium hydroxide
L.	Lactobacillus
M. curtisii	Mobiluncus curtisii
M. Mulieri	Mobiluncus Mulieri
M. hominis	Mycoplasma hominis
PAP	Proline amino peptidase
PAMPs	Pathogen associated molecular patterns
Pap smear	Papanicolaou smear
P. bivia	Prevotella bivia
PCR	Polymerase chain reaction
PID	Pelvic inflammatory disease

LIST OF ABBREVIATIONS

Abbrev.	Meaning
PROM	Premature rupture of the membranes
RCT	Randomized control study
RVVC	Recurrent vulvovaginal candidiasis
spp.	Species
T. vaginalis	Trichomonas vaginalis
UTI	Urinary tract infection
U. urealyticum	Ureaplasma urealyticum
VECs	Vaginal epithelial cells
VVC	Vulvo-vaginal candidiasis
WBCs	White blood cells
WHO	World Health Organization

ORAL MITRONIDAZOL VERSUS PASTEURIZED YOGHURT IN THE TREATMENT OF BACTERIAL VAGINOSIS

Protocol of Thesis

Submitted for partial fulfillment of the Master Degree in *Obstetrics and Gynecology*

By

Nahla Gamal Helmi Sherif
M.B., B.Ch, 2004, Ain Shams University
Resident in Nacer City Inssurance Hospital

Under Supervision of

Prof. Dr. Alaa Eldin Hamed Elfeky Professor of Obstetrics and Gynecology Faculty of Medicine - Ain Shams University

Prof.Dr. Fekria Ahmed Salama

Professor of Obstetrics and Gynecology Faculty of Medicine - Ain Shams University

Dr. Ahmed Adel Tharwat

Lecturer of Obstetrics and Gynecology Faculty of Medicine - Ain Shams University

> Faculty of Medicine Ain Shams University 2009

INTRODUCTION

Bacterial vaginosis is a condition characterized by alteration of the vaginal ecology, in which the normal flora is dominated by lactobacilli and replaced by a mixed bacterial flora which includes Gardnerella vaginanlis and other anaerobes (*Tabrizi et al.*, 2006).

Its clinical presentation is typical with fishy discharge that is more noticeable after intercourse. The discharge is thin and homogenous. Pruritus and inflammation are usually absent and most patients are symptoms free (*Quan*, 2000).

The diagnostic criteria established by Amsel and his colleagues have proved to be simple and useful in clinical practice. Three of the following four signs are required to establish a diagnosis of bacterial vaginosis:

1. History:

A homogenous and grayish discharge that adheres to the vaginal walls.

2. Microscopic Examination:

The presence of clue cells; are vaginal epithelial cells heavily coated with bacteria.

3. Investigations:

- 1-PH of vaginal fluid >4.5.
- 2-Whiff test positive (fishy odor from vaginal discharge after addition of 10% KOH). (Amsel et al., 1983)

The prevalence of bacterial vaginosis in pregnant women was found to be 15-23%, half of them were asymptomatic (*McCoy et al., 1995*). However, bacterial vaginosis may result in potentially severe complications; increased risk of abortion, premature rupture of membranes, chorioamnionitis and preterm labor (*Klebanoff et al., 2005*).

The prevalence of bacterial vaginosis among non pregnant women was found to be from 5% for women without any symptoms to 25% for those with gynecologic symptom (*Hillier*, 1998). It may result in some morbidities among young women including pelvic inflammatory disease (PID) with long sequel that may end with infertility (*Haggerty et al.*, 2004).

It appears that the loss of vaginal lactobacilli is the major factor in the cascade of changes leading to bacterial vaginosis (*Aroutcheva et al.*, 2001). On the other hand relapses are associated with failure to establish healthy lactobacilli dominated vaginal flora (*Reid and Bruce*, 2003)

Lactobacilli are gram positive, catalase negative, non-sporing rods that dominate vaginal flora (*Ronnqvist et al.*, 2006). Types of lactobacilli found in the vagina flora include Lactobacillus Acidophilus, Fermentum Crispatus (*Reid and Bocking*, 2004). The human vagina is normally lined by multilayered stratified squamous non-keratinized epithelium. The middle and superficial layers contain glycogen, which is set free by the breakdown of superficial cells. Free glycogen is fermented by lactobacilli producing lactic acid and hydrogen peroxide (*Andreu*, 2004). Women with hydrogen peroxide producing strains of lactobacilli have 4% prevalence rate of bacterial vaginosis compared with 32% in women colonized by non-hydrogen peroxide producing strains and 56% in those without Lactobacilli (*Ugwumadu and Hay*, 1999).

The common antimicrobial therapies that are used for the treatment of bacterial vaginosis are metronidazol and clindamicine. Two different antibiotics are recommended. Either can be used with non-pregnant or pregnant women, but the recommended dosages differ (*Darwish et al.*, 2007). Metronidazole is often poorly tolerated due to its side effects; metallic taste, infrequently neurological and/or hematological adverse reactions. In addition, cure rates associated with this treatment are low. There is a high incidence of overgrowth of pathogenic bacteria after treatment (*Reid and Bruce*, 2003).

Although antimicrobial agents are quite effective at providing clinical cure for bacterial infection, urogenital pathogen, but have local side effects including disruption of the protective vaginal flora, which create an increased risk of recurrent infections (*Shennan et al.*, 2006). Antibiotics can cause general adverse effects including palpitations, flushes, nausea, vomiting, diarrhea, abdominal pain, rashes, headache and dizziness (*Reid et al.*, 2004). Such side effects, interfere with the compliance of the drug, with subsequent decrease cure rate, while on the other hand may increase the recurrence rate.

Among the alternative medicines that women commonly use for the treatment of vaginal symptoms is yoghurt. Such alternative medicine is increasingly used among women on the expense of antimicrobial therapies. It has been recorded that 96% are symptomatically relieved by alternative medicine. So it is important for women's healthcare providers to be knowledgeable about such therapies (*Trutnovsky et al.*, 2001).

The administration of these lactobacilli by mouth, intravaginally or both has been shown to be safe, effective, low cost and less side effect to reducing and/or treating vaginal infection and urogenital infection (*Reid*

and Burton, 2002). So it may be more tolerable for the patient to treat bacterial vaginosis with a natural product with fewer side effects (*Reid et al.*, 2004).