

Hysteroscopy in the Evaluation of Postmenopausal Bleeding

Thesis

Submitted for partial fulfillment of master degree
in Obstetrics and Gynecology

By

Mona Mosa Dikary

M.B.B.Ch (2011)

*Faculty of Medicine Sirt University
Resident of Obstetrics and Gynecology
Ibn Sina Hospital (Sirt), Libya*

Supervised by

Dr. Noha Hamed Rabei

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

Dr. Ahmed Mohamed AbdelHameed

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

**Faculty of Medicine
Ain Shams University
2018**




Acknowledgments

*First and forever, thanks to **Allah**, Almighty for giving me the strength and faith to complete my thesis and for everything else.*

*Words fail to express my sincere gratitude to **Dr.Noha Hamed Rabei**, Professor of Obstetrics and Gynecology, Faculty of Medicine - Ain Shams University, under her supervision, I am deeply grateful for her professional advice, guidance and support.*

*My deep gratitude to **Dr. Ahmed Mohamed AbdelHameed**, Lecturer of Obstetrics and Gynecology Faculty of Medicine - Ain Shams University for his invaluable efforts and tireless guidance in every step of this work,*

I can't forget to thank all members of the Early Cancer detection Units for their cooperation and help during the whole work,

*Last but not least, I would like to thank all my **family**, especially my **parents** and my **sister**, for their kind care, help and encouragement..  **Mona Mosa Dikary***

List of Contents

<i>Subject</i>	<i>Page No.</i>
List of Abbreviations.....	i
List of Tables.....	iii
List of Figures	iv
Protocol.....	v
Introduction	1
Aim of the Work.....	4
Review of Literature	
Postmenopause	5
Endometrial sampling.....	35
Hysteroscopy	44
Patients and Methods.....	63
Results.....	70
Discussion	88
Summary	94
Conclusions	97
Recommendations	98
References	99
Arabic Summary	—

List of Abbreviations

<i>Abbrev.</i>	<i>Full-term</i>
ACOG	: American College of Obstetricians and Gynecologists
AUB	: Abnormal uterine bleeding
BAK	: Bias-adjusted kappa
CO₂	: Carbon dioxide
COCs	: Combined oral contraceptive
D&C	: Dilatation and curettage
DVT	: Deep venous thrombosis
EEC	: Endometrial echo-complex
FIGO	: International Federation of Gynecology and Obstetrics
FSH	: Follicle stimulating hormone
HRT	: Hormonal replacement therapy
HT	: Hormonal therapy
ISGYP	: International Society of Gynecological Pathologists
ITP	: Immune thrombocytopenic purpur
IUDs	: Intrauterine Devices
IV	: Intravenous
KTP	: Potassium-Titanyl-Phosphate
LH	: Lutenizing hormone
MHT	: Menopausal hormone therapy
MPA	: Medroxy progesterone acetate
NAMS	: North American Menopause Society
Nd YAG	: Neodymium: Yltrium -Aluminium Garnet laser
NIH	: National Institute of Health

NPV	: Negative predictive values
OD	: Outer diameter
PABAK	: Prevalence-adjusted bias-adjusted kappa
PMB	: Postmenopausal bleeding
PPV	: Positive predictive values
RPL	: Recurrent pregnancy loss
RR	: Relative risk
SCSH	: Saline contrast sonohysterography
SD	: Standard deviation
SSRI	: Selective serotonin reuptake inhibitors
STRAW	: Stages of Reproductive Aging Workshop
TVUS	: Transvaginal ultrasound
WHIMS	: Women Health Initiative Memory Study
WHO	: World health organization

List of Tables

<i>Table No.</i>	<i>Title</i>	<i>Page No.</i>
Table (1):	Causes of postmenopausal bleeding.....	10
Table (2):	Descriptive statistics for the whole study population regard as general characteristics	70
Table (3):	Descriptive statistics for the whole study population regard as past history.....	71
Table (4):	Descriptive statistics for the whole study population regard as obstetric history	71
Table (5):	Descriptive statistics for the whole study population regard as menstrual history	71
Table (6):	Hysteroscopic findings in the study population.....	72
Table (7):	Histopathological findings in the study population.....	73
Table (8):	Accuracy of hysteroscopy for diagnosis of endometrial atrophy.....	74
Table (9):	Accuracy of hysteroscopy for diagnosis of endometrial hypertrophy	76
Table (10):	Accuracy of hysteroscopy for diagnosis of endometrial polyp.....	78
Table (11):	Accuracy of hysteroscopy for diagnosis of subendometrial myoma	80
Table (12):	Accuracy of hysteroscopy for diagnosis of subendometrial hyperplasia	82

Table (13):	Accuracy of hysteroscopy for diagnosis of endometrial carcinoma	84
Table (14):	Inter-method agreement between hysteroscopy and histopathology for diagnosis of various endometrial and subendometrial lesions	86

List of Figures

<i>Figure No.</i>	<i>Title</i>	<i>Page No.</i>
Figure (1):	Stages of Reproductive Aging Workshop (STRAW).....	6
Figure (2):	Microscopic picture of senile atrophic endometrium	11
Figure (3):	Microscopic picture of endometrioid adenocarcinoma.....	14
Figure (4):	Microscopic picture of endometrial adenoacanthoma	14
Figure (5):	Microscopic picture of uterine papillary serous carcinoma	14
Figure (6):	Microscopic picture of simple hyperplasia....	16
Figure (7):	Microscopic picture of complex hyperplasia.	16
Figure (8):	Investigation of postmenopausal uterine bleeding in women receiving tamoxifen	31
Figure (9):	Karl Storz flexible hysteroscope	46
Figure (10):	Rigid hysteroscopies.....	47
Figure (11):	Submucous myoma	56
Figure (12):	Endometrial polyp	56
Figure (13):	Uterine septum and an endometrial polyp	58
Figure (14):	Telescope with in-out sheath with a side channel 4.5 mm (Storz, Tuttlingen, Germany)	68

Figure (15):	Continuous suction irrigation pump "Endomat".....	68
Figure (16):	Hysteroscopy findings in the study population	72
Figure (17):	Histopathological findings in the study population	73
Figure (18):	Accuracy of hysteroscopy for diagnosis of endometrial atrophy versus histopathology as the gold standard test.....	75
Figure (19):	Accuracy of hysteroscopy for diagnosis of endometrial hypertrophy versus histopathology as the gold standard test.	77
Figure (20):	Accuracy of hysteroscopy for diagnosis of endometrial polyp versus histopathology as the gold standard test.....	79
Figure (21):	Accuracy of hysteroscopy for diagnosis of subendometrial myoma versus histopathology as the gold standard test.....	81
Figure (22):	Accuracy of hysteroscopy for diagnosis of endometrial hyperplasia versus histopathology as the gold standard test.	83
Figure (23):	Accuracy of hysteroscopy for diagnosis of endometrial carcinoma versus histopathology as the gold standard test.	85
Figure (24):	Inter-method agreement between hysteroscopy and histopathology for diagnosis of endometrial and subendometrial lesions.....	87

Introduction

Menopause is permanent cessation of menstruation resulting from loss of ovarian follicular activity. Bleeding that occurs 12 months after the last menstrual period is labeled as postmenopausal bleeding (PMB) (*Indian Menopause Society Guideline, 2010*).

Postmenopausal bleeding is a common gynecologic complain, accounting for up to 69% of postmenopausal women referred to gynecological outpatient clinics (*Tahir et al., 1999*).

Approximately 90% of women with endometrial carcinoma report vaginal bleeding as their only complain (*Giusa-Chiferi et al., 1996*).

Postmenopausal bleeding is a symptom that needs to be investigated thoroughly. At worse, it may signify malignant change, but there are also several less sinister causes (*Elliott et al., 2003*).

Endometrial cancer occurs most commonly after menopause (*Kong et al., 2012*).

In 90% of cases, cancer of the endometrium occurs with postmenopausal bleeding (*Loverro et al., 1999; Elfayomy et al., 2012*).

But just 10-15% of women with postmenopausal bleeding have endometrial carcinoma (*Elfayomy et al., 2012*).

A definitive diagnosis in postmenopausal bleeding is made by histology. Historically endometrial sample have been obtained by dilatation and curettage now days it is more usual to obtain a sample by dilatation and biopsy (*Opmeer et al., 2007*).

Dilatation and curettage (D&C) is a blind procedure; it often results in unrepresentative biopsies with a diagnostic failure that varies from 10 to 25% and false negative rates between 2 and 10%. Prior reports have revealed that in 60% of women submitted to curettage less than half of the uterine cavity was sampled with the curette and that the source of bleeding was frequently not diagnosed (*Sousa et al., 2001*).

The introduction of intrauterine endoscopy has allowed clinician to evaluate an area of the body that was previously accessible only by the procedure of blind dilation and curettage (D&C). many studies have shown hysteroscopy to be superior to D&C, yet its use has yet to be appreciated adequately (*Al-Kamil, 2001*).

Hysteroscopy is diagnostic gynecological procedure that enable as clinician to visualize the uterine cavity and take endometrial biopsies as required as one of principle investigation of postmenopausal bleeding. Hysteroscopy has integral role in the identification of structure abnormalities of endometrial (*Nice Guideline, 2007*).

It allows direct view of endometrium and biopsies are also possible (*Sousn et al., 2001*).

Hysteroscopy permits and accede macroscopic diagnosis of benign lesion and their removal, allowing (see and treat) approach, but histological samples must always be taken (*Lalchandani et al., 2003*).

It is gold standard to make a histological diagnosis in order to determine the efficacy of hysteroscopy in diagnosing endometrial pathology (*Elfayomy et al., 2012*).

Aim of the Work

Hypothesis:

- In women with postmenopausal bleeding, hysteroscopy may increase the accuracy of diagnosis of the causes of bleeding.

Question:

- In women with postmenopausal bleeding does hysteroscopy improve the accuracy for diagnosis of the cause of the bleeding?

Aim:

- This study aims to assess the accuracy of hysteroscopy use in the diagnosis of the causes of bleeding in women with postmenopausal bleeding.

Postmenopause

Menopause is defined by the World Health Organization as the permanent cessation of menstruation resulting from the loss of ovarian follicular activity (*Gale and Dey, 2009*).

- **Stages of menopause:**

The menopausal transition can span over several years, and often begins with variations in menstrual cycle length in response to rising levels of follicle stimulating hormone (FSH). The mean age of onset of the menopausal transition is 47.5 years and commonly lasts approximately 4 to 5 years (*Nelson, 2004*).

Stages and nomenclature of the menopausal transition were defined by experts in 2001 at the Stages of Reproductive Aging Workshop (STRAW). The group recognized seven stages of the reproductive aging continuum, and acknowledged that most women do not progress precisely through each stage (Fig.1).

STRAW divided the adult female life into three broad phases: reproductive, the menopausal transition, and post-menopause.

	Menarche				FMP (0)					
Stage	-5	-4	-3b	-3a	-2	-1	+1 a	+1b	+1c	+2
Terminology	REPRODUCTIVE				MENOPAUSAL TRANSITION		POSTMENOPAUSE			
	Early	Peak	Late		Early	Late	Early			Late
					Perimenopause					
Duration	variable				variable	1-3 years	2 years (1+1)	3-6 years	Remaining lifespan	
PRINCIPAL CRITERIA										
Menstrual Cycle	Variable to regular	Regular	Regular	Subtle changes in Flow/ Length	Variable Length Persistent ≥7- day difference in length of consecutive cycles	Interval of amenorrhea of >=60 days				
SUPPORTIVE CRITERIA										
Endocrine FSH AMH Inhibin B			Low Low	Variable Low Low	↑ Variable Low Low	↑ >25 IU/L** Low Low	↑ Variable Low Low	Stabilizes Very Low Very Low		
Antral Follicle Count			Low	Low	Low	Low	Very Low	Very Low		
DESCRIPTIVE CHARACTERISTICS										
Symptoms						Vasomotor symptoms Likely	Vasomotor symptoms Most Likely		Increasing symptoms of urogenital atrophy	

* Blood draw on cycle days 2-5 ↑ = elevated
**Approximate expected level based on assays using current international pituitary standard²⁷⁻⁶⁹

Figure (1): Stages of Reproductive Aging Workshop (STRAW)

These three phases included a total of seven stages centered on the FMP, (Stage 0). The reproductive phase was divided into Stages -5, -4, and -3 corresponding to early, peak, and late, respectively. The menopausal transition phase consisted of Stage -2 (early) and Stage -1 (late), and the postmenopause phase contained Stages +1 (early) and +2 (late). Stage -3 was characterized by regular menstrual cycles and increasing levels of FSH. Stage -2 was characterized by variability in menstrual cycle length and increased levels of FSH. Stage -1 was characterized by onset of skipped cycles or amenorrhea of at least 60 days and continued elevation of FSH.