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ORAL ANTICOAGULANTS VS. HEPARIN IN THE MANAGEMENT OF EARLY RECURRENT PREGNANCY LOSS DUE TO ANTIPHOSPHOLIPID SYNDROME

A thesis
Submitted for Partial Fulfillment of the Master Degree in Obstetrics and Gynecology

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مقارنة تأثير مضادات التجلط التي تعطى عن طريق الفم بالهيبارين في علاج الإجهاض المبكر المتكرر الناتج عن متلازمة مضادات الفوسفوليبيدات

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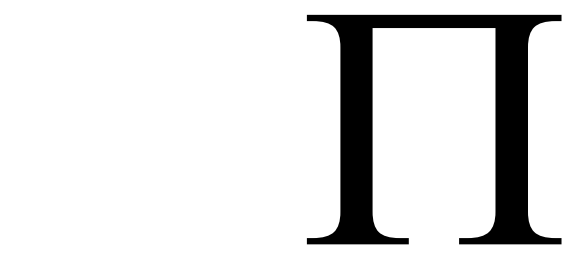

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من علق {٢} إقرأ وربك الأكرم {٣} الذى
علم بالقلم {٤} علم الإنسان ما لم يعلم {٥}

سورة العلق الآيات ١- ٥

Introduction

INTRODUCTION

Habitual abortion or recurrent pregnancy loss (RPL) is the occurrence of repeated pregnancies that end in miscarriage of the fetus, usually before 20 weeks of gestation. RPL affects about 0.34% of women who conceive ***(Christiansen et al., 2005).***

Habitual abortion (recurrent pregnancy loss or recurrent miscarriage) is the occurrence of 3 consecutive spontaneous miscarriages (spontaneous abortions). The majority (85%) of women who have had two miscarriages will conceive and carry normally afterwards, so statistically the occurrence of three abortions at 0. 34% is regarded as "habitual" ***(Moffett et al., 2004).***

There are various causes for habitual abortions, and some are treatable. Some couples never have a cause identified, often after extensive investigations. These causes include the following:

Anatomical conditions, Uterine conditions, Cervical conditions, Chromosomal disorders, Translocations, Aneuploidy, Endocrine disorders, Thrombophilia, Immune factors, Antiphospholipid syndromes, Increased uterine NK cells, Parental HLA sharing, Ovarian factors, Reduced ovarian reserve, Luteal phase defects, Lifestyle factors and Infection ***(RCOG. 2002).***

The thrombotic defects associated with fetal wastage are quite common and are due to thrombosis of early placental vessels. Peak fetal loss occurs in the first trimester, but loss also occurs in the second and third trimesters. The thrombotic hemostasis defects associated with recurrent fetal loss include lupus anticoagulants and anticardiolipin antibodies (these 2 comprise the antiphospholipid syndromes associated with recurrent fetal loss), factor XII deficiency, dysfibrinogenemias associated with thrombosis, protein C deficiency, antithrombin deficiency, heparin cofactor II deficiency, and fibrinolytic defects (plasminogen deficiency, tissue plasminogen activator deficiency, and elevated plasminogen activator inhibitor type 1) ***(Gris et al.,1993)***.

Heparin is used as an injectable anticoagulant. It is also used to form an inner anticoagulant surface on various experimental and medical devices such as test tubes and renal dialysis machines ***(Linhar et al., 1991)***. Heparin acts as an anticoagulant, preventing the formation of clots and extension of existing clots within the blood. While heparin does not break down clots that have already formed. It allows the body's natural clot lysis mechanisms to work normally to break down clots that have already formed ***(Mulloy et al.,1993)***.

In the past decade there has been widespread implementation of oral anticoagulation (warfarin) in preference to antiplatelet treatment (aspirin, indoprofen) ***(Whitlon et al.,1978)***.

Anticoagulants are given to people to stop thrombosis (blood clotting inappropriately in the blood vessels). This is useful in primary and secondary prevention of deep vein thrombosis, pulmonary embolism, myocardial infarctions and strokes in those who are predisposed ***(Austin et al., 1999).***

The most important Oral Anticoagulants are Warfarin (Coumadin), Acenocoumarol, phenprocoumon and Phenindione ***(Whitlon et al., 1978)***.The oral anticoagulants can be divided into two groups, the 4-hydroxycoumarins and the indandiones. The most common of these include brodifacoum, difenacoum, and chlorphacinone. ***(Hoffman et al., 2001)***.

Warfarin crosses the placenta and has been associated with an increased incidence of spontaneous abortion, prematurity, and stillbirth. Warfarin embryopathy occurs in 4% to 10% of patients. The risk may be dose-related and appears to be highest if exposure occurs during the 6^{th} to 12th weeks of gestation ***(Austin et al., 1999)***.

Another type of anticoagulant is the direct thrombin inhibitors .Current members of this class include argatroban, lepirudin, and bivalirudin. An oral direct thrombin inhibitor, ximelagatran (Exanta) may replace warfarin for some indications ***(Holbrook et al., 2005)***.

Aim of the Work

AIM OF THE WORK

- To assess safety and efficiency of oral anticoagulants in treating cases of recurrent miscarriage due to antiphospholipid syndrome.
- To compare pregnancy outcome between heparin and oral anticoagulants groups.

Contents

List of Tables

Continued

List of Figures

List of Abbreviations

ACOG	Amirican College of Obstetricians & Gynecologists
ANP	Atrial Natriuretic Peptide
BMI	Body mass index
CVD	Cerebrovascular disease
DBP	Diastolic blood pressure
DIC	Disseminated intravascular coagulopathy
EFF	Efficacy
EGF	Endothelial growth factor
FP	False positive
GA	gestational age
GH	gestational hypertension
HCG	Human Chorionic Gonadotrophin
HELLP	A syndrome of Haemolysis, Elevated liver enzymes and Low platelet count
HIF	Hypoxia inducible factor
HO	Homo oxygenase
Ht	Height
IL	Interleukin
IRR	Incidence rate ratio
IUGR	Intrauterine growth restriction
N	Number
P	Probability of error

Continued