شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم

HANAA ALY

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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

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HANAA ALY

Role of Chromium Versus Metformin supplementations as adjuvant for ovulation induction by clomiphene citrate in infertile patients with polycystic ovary syndrome: Randomized controlled trial

A Thesis

Submitted for partial fulfillment of master degree
in Obstetrics & Gynecology

By

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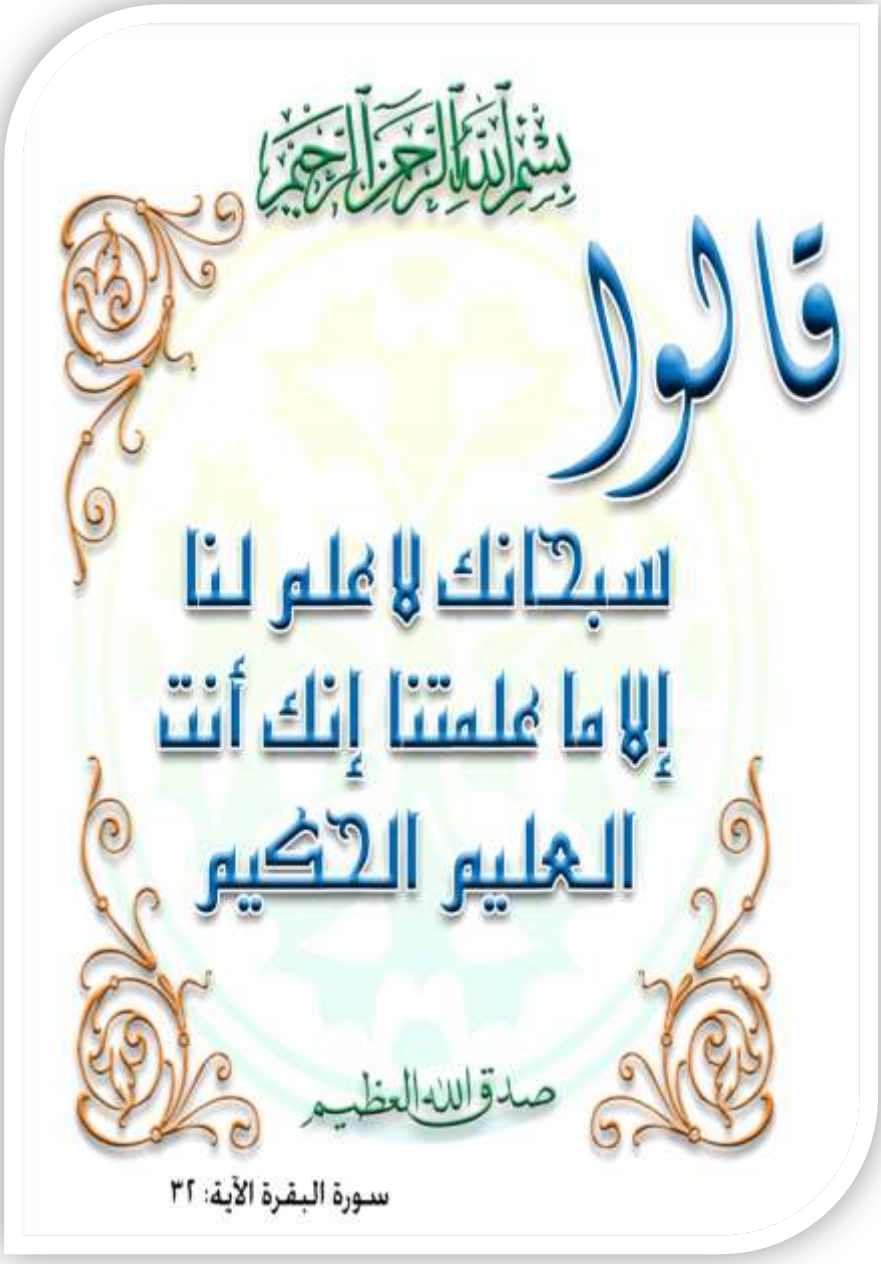
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✍ *Asmaa Gaballah Sayed Hasan*

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List of Abbreviations

Abbr.	Full-term
AE-PCOS	**:** Androgen Excess-PCOS Society
AMH	**:** Anti-Müllerian hormone
AMPK	**:** Adenosine monophosphate-activated protein kinase
BMI	**:** Body mass index
BMP	**:** Bone morphogenetic protein
CYP17	**:** Cytochrome P450c1
DAST	**:** Dexamethasone androgen-suppression test
DENND	**:** Differentially expressed in normal and neoplastic development
DHEA	**:** Dehydroepiandrosterone
DHEAS	**:** DHEA sulfate
DM	**:** Diabetes mellitus
FAH	**:** Functional adrenal hyperandrogenism
FOH	**:** Functional ovarian hyperandrogenism
GDF	**:** Growth differentiation factor
GnRHag	**:** GnRH agonist
GTT	**:** Glucose tolerance test
GWAS	**:** Genome-wide association studies
hCG	**:** Human chorionic gonadotropin
Hippo	**:** Hippopotamus
HOMA-IR	**:** Insulin resistance by homeostatic model assessment
IGT	**:** Impaired glucose tolerance
MNC	**:** Mononuclear cell
NGF	**:** Nerve growth factor

NOM : Normal ovarian morphology
OSA : Obstructive sleep apnea
PCOM : Polycystic ovarian morphology
PCOS : Polycystic ovary syndrome
PCOS-A : Functionally atypical PCOS
PCOS-T : Functionally typical PCOS
POR : Cytochrome P450-oxidoreductase
RD : Reductase
SDAST : Short DAST
SHBG : Sex hormone-binding globulin
SNS : Sympathetic nervous system
VEGF : Vascular endothelial growth factor
V-NOM : Volunteer with NOM
3βHSD2 : 3β-hydroxysteroid dehydrogenase type 2
17OHP : 17-hydroxyprogesterone

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ABSTRACT

Background: One of the most common reproductive endocrine diseases that impact many young women worldwide is polycystic ovary syndrome (PCOS). This hormonal problem affects 4-18% of women of reproductive age exhibiting various symptoms, such as irregular menstruation, hirsutism, infertility and metabolic disorders.

Objective: To explore the effect of chromium picolinate compared to the effect of Metformin supplementation with ovulation induction in infertile patients with polycystic ovary syndrome,In particular, its effect on insulin sensitivity, ovarian response and pregnancy rate.

Patients and Methods: This study was conducted as a prospective study, aimed to compare the effect of Chromium and Metformin supplementations on ovulation rate in Polycystic ovary patients undergoing ovulation induction. The present study included 140 women divided into 2 groups each is 70 infertile women diagnosed as polycystic ovary syndrome according to Rotterdam criteria 2017: (oligo-ovulation or anovulation, clinical or biochemical signs of hyperandrogenism, polycystic ovaries on ultrasound).

Results: fasting blood sugar (FBS) and fasting insulin lvel were significantly decreased in metformin group than in Chromium picolinate group after 3 months of treatment (p=0.006) (p=0.026) repectively , Testesterone signifciantly decreased in both groups at follw up as compared to basal level (P-value<0.001, <0.001 respectively with no significant difference between the studied groups regarding testesterone reduction (P-value=0.416) after 3 months of treatment. , the two study groups were not significantly different regarding ovulation and pregnancy rates(P-value 0.157 , 0.550) respectively after 3 months of treatment . The patients who received metformin experienced more side effects compared to those receiving chromium picolinate (p=0.001).

Conclusion: In view of the aforementioned findings, we recommend that metformin could be replaced by chromium picolinate in some PCOS patients, as its better tolerated than metformin due to lower side effects and no significant differences were observed between the two groups regarding ovulation and pregnancy rates.

Keywords: *Chromium picolinate, Metformin, Polycystic ovary Syndrome (PCOS), Clomiphen* citrate**.**

Introduction

One of the most common reproductive endocrine diseases that impact many young women worldwide is polycystic ovary syndrome (PCOS). This hormonal problem affects 4-18% of women of reproductive age exhibiting various symptoms, such as irregular menstruation, hirsutism, infertility and metabolic disorders ***(Moran et al., 2011).***

Anovulation and androgen excess have been considered the hallmark diagnostic criteria of the syndrome. Insulin resistance (IR) has been identified as a significant contributor to the pathogenesis of PCOS ***(Sattar, 2009).***

Nearly 20% of obese women with PCOS have an impaired Glucose Tolerance Test (GTT) or diabetes. Insulin sensitivity is impaired in PCOS and this finding holds in both the presence and absence of obesity. Evidence from in vivo and in vitro studies suggests that insulin has both direct and indirect effects on androgen levels. Moreover, ovaries removed from the women with PCOS exhibited enhanced androstenedione and testosterone release in response to insulin stimulation. Furthermore, it has been shown that acute increment in insulin levels in the women with PCOS induces rises in androgen levels ***(Sedigheh et al., 2013).***

Metformin is an FDA-approved biguanide for the management of type 2 diabetes mellitus (T2DM). Although its mechanism of action remains obscure, metformin was shown to activate adenosine monophosphate-activated protein kinase (AMPK) pathway, inhibiting hepatic production of glucose, reducing oxidation of fatty acids, and increasing peripheral tissue uptake of glucose. Metformin is believed to lower fasting serum insulin levels in insulin-resistant states without inducing hypoglycemia, and helps reduce insulin requirements in insulin-dependent and non-insulin-dependent diabetes ***(Tang et al., 2012).***

Interest in the use of metformin, an insulin-lowering drug, in PCOS increased when it was appreciated that insulin resistance played an important role in the pathophysiology of the disorder. Metformin is typically the first-line treatment for patients with type 2 diabetes; it is not approved for use in prediabetes or PCOS, although it is often prescribed for treatment of these conditions. Early trials in women with PCOS subsequently demonstrated a small benefit for weight reduction, a decrease in serum androgens (without improvement in hirsutism), and restoration of menstrual cycles in approximately 50 percent of women with oligomenorrhea (although not always ovulatory). Early data also suggested that metformin was effective for ovulation induction in anovulatory women with PCOS. As a result, metformin was used "off-label" for a number

of these indications. Although there was widespread enthusiasm for metformin therapy in women with PCOS for a number of years, clinical data do not support the use of metformin for treatment of hirsutism or as first-line treatment for ovulation induction in this population. However, whether metformin has a beneficial long-term effect upon reducing the risk of conversion to diabetes from prediabetes has not been addressed ***(BJOG, 2017).***

The micronutrient chromium, which is gaining popularity as a dietary supplement to improve the actions of insulin under insulin-resistant conditions, merits attention. The potential role of chromium in regulating blood sugar was first indicated in the late 1950s. The 'essentiality' of chromium in human nutrition was suggested when it was found that chromium supplementation reversed glucose intolerance in hospitalized patients receiving long-term total parenteral nutrition ***(Yinah et al., 2010).***

Chromium potentiates the biological action of insulin. A number of studies have found that cr. supplementation can improve insulin sensitivity and blood sugar control in animals and humans with insulin resistance, elevated blood sugar, impaired glucose tolerance and diabetes. Chromium picolinate supplementation significantly lowered fasting insulin and glucose levels ***(Althius et al., 2002).***