

Natural Approach to Coexisting Non-alcoholic Fatty Liver Disease and Polycystic Ovarian Syndrome

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Abstract

Polycystic Ovarian Syndrome (PCOS) is a common reproductive and metabolic disorder. It is considered the ovarian manifestation of metabolic syndrome and is a common cause for an ovulatory infertility. PCOS commonly coexists with other metabolic manifestations such as Non-alcoholic Fatty Liver Disease (NAFLD) which leads to therapeutic challenges especially when infertility is involved. Existing treatment strategies for PCOS have limited success, side effects or are costly giving rise to a curiosity in women to seek alternative therapies such as Chinese Medicine. Chinese medicine formulae with multiple natural ingredients may have beneficial endocrine, cardio metabolic and reproductive effects offering an optimal treatment approach for women with NAFLD, PCOS and infertility.

Keywords: Polycystic ovarian syndrome; Nonalcoholic fatty liver disease; Infertility; Chinese herbal medicine; Clinical trial

Introduction

Polycystic Ovarian Syndrome (PCOS) is a common disorder affecting up to 21% of women of childbearing age [1]. Initially thought to be primarily a reproductive disorder, recent findings suggest that 50–80% of women with PCOS are obese and have insulin resistance, a hallmark of metabolic syndrome [2]. It therefore seems appropriate to consider PCOS as the ovarian manifestation of metabolic syndrome. Similarly, Nonalcoholic Fatty Liver Disease (NAFLD) has been defined as the hepatic manifestation of metabolic syndrome. Clinically, PCOS commonly coexists with NAFLD [3], which further complicates the therapeutic approach, especially when infertility is of concern.

Conventional approaches to PCOS with infertility have been well documented in the literature [4,5], including lifestyle modifications and the use of metformin either alone or in combination with clomiphene, gonadotropins, ovarian drilling or assisted reproductive techniques. However, there are few studies for management of the complex of hyperglycaemia, NAFLD and PCOS with infertility. Alongside this, the combination of NAFLD and PCOS impedes treatment with some of the chemical pharmacotherapies available when there is liver damage and impaired liver function [6]. The clinical features of PCOS associated with NAFLD are heterogeneous and vary in intensity. The treatment for the combination of NAFLD and PCOS with infertility therefore presents a therapeutic challenge. A recent report suggests that women with a diagnosis of NAFLD prior to giving birth have increased risks for adverse pregnancy outcomes, including gestational diabetes, preeclampsia, caesarean section and preterm birth [7]. It is this context along with the increase in prevalence of coexisting PCOS and NAFLD that often gives rise to a curiosity in women to seek alternative therapies, especially for those who are desirous to achieve conception naturally. Over the last ten years, this condition has become one of the most treated disorders in our Chinese medicine clinic with much success.

Chinese medicinal herbs have been used for many years to treat gynaecological disorders according to Traditional Chinese Medicine (TCM) theory. In the last decades, experimental and clinical studies have shown that these herbal ingredients could regulate gonadotropin-releasing hormone to induce ovulation and promote blood flow and microcirculation to the ovaries and uterus to improve their function [8,9]. Zhang et al. have summarized four randomized controlled trials that demonstrated a synergetic effect of CHM on clomiphene for PCOS with subfertility [10]. We have also observed that most patients with PCOS and NAFLD present with a 'blood stasis syndrome' in TCM which is related to hyperlipidaemia and a prethrombotic state.

Therefore, our treatment strategies for PCOS and NAFLD initially focuses on ameliorating hyperlipidaemia and decreasing thrombotic factors by using herbs such as *Radix Salvia miltiorrhizae*, *Fructus Crataegus pinnatifida*, *Fructus Gardenia florida*, *Radix Angelicae sinensis* and *Rhizoma Coptis chinensis*.

Herbal medicines, such as *Fructus Gardenia florida*, *Fructus Lycium barbarum* and *Rhizoma Coptis chinensis*, have also demonstrated a beneficial effect on insulin resistance and glucose intolerance [11–13]. This is particularly relevant when hyperlipidaemia and NAFLD implicates liver damage as the use of drugs such as statins and metformin are subsequently cautioned. Given that NAFLD significantly contributes to adverse outcomes of pregnancy in women with PCOS, *Salvia miltiorrhizae* and *Fructus Gardenia florida* are important ingredients for PCOS women with NAFLD because the active compounds, such as tanshinone IIA and gypenoside, lower serum cholesterol and triglycerides and also prevents ectopic fat deposition in the liver [14]. Oxidative stress plays a role in both liver damage and ovarian dysfunction in NAFLD and PCOS respectively [15]. Naturally occurring compounds in the formulae, such as berberine and polysaccharides, improve clinical outcomes which may be through their antioxidant activity [16,17].

Furthermore, as herbal formulae contain many different ingredients, the effect is often multi-targeted. In my clinical practice it has become evident that treating metabolic manifestations simultaneously achieves results more quickly than simply targeting one aspect, in the way that monotherapies operate. Chinese medicine formulae with multiple natural ingredients is capable of producing beneficial endocrine, cardiometabolic, and reproductive effects offering an optimal treatment approach for women with NAFLD, PCOS and infertility. Additionally herbal medicines have fewer side effects compared to standard drug therapies. Despite these benefits, most studies for PCOS are small, nonrandomized or uncontrolled and there is no clinical study reported

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for CHM treatment for the combination of NAFLD and PCOS with infertility. This case report presents the use of CHM to target multiple abnormalities, firstly focusing on hyperlipidaemia and impaired liver function while inducing menstruation for amenorrhea and subsequently shifting to focus on improving ovarian function and fertility. Although the evidence is limited by one case, successful treatment with CHM for this case highlights the potential of natural therapy to manage coexisting NAFLD and PCOS cohesively whilst promoting fertility.

In summary, co-existing NAFLD and PCOS with infertility presents a therapeutic challenge for both pharmaceutical medication and natural therapy. A uniform treatment for this complex metabolic, endocrinal and reproductive disorder does not exist. To achieve successful conception and reduce adverse outcomes of pregnancy, the best-tailored treatment with CHM should be applied after an accurate evaluation of patients' characteristics. Meanwhile, randomized and controlled multicenter trials should be performed to establish evidence-based CHM therapy for the treatment of NAFLD and PCOS with infertility.

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