A comparetive Study on the Effectiveness of *Nigella sativa*, methotrexate and their combination in the treatment of moderate to severe psoriasis.

A thesis

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Abstract

Background

Psoriasis is a common, chronic, relapsing, distressing skin disease with no unique curative systemic or topical treatment that affects 2-3% of the world's population. Many drug regimens are available to reduce the severity of symptoms and lessen their impact on the patient's quality of life. Methotrexate and cyclosporine the principal drugs for psoriasis are expensive and frequently associated with significant systemic toxicity which requires close and careful monitoring of patients. *Nigella sativa* (Black Cumin), a medicinal plant which has antioxidant, anti-proliferative and anti-angiogenesis properties, and has been shown in one study effective in mild to moderate psoriasis.

Objectives

This study was designed to investigate the effectiveness and safety of *Nigella sativa* in moderate to severe psoriasis as monotherapy and in combination with methotrexate and to evaluate the anti oxidant effect of *Nigella sativa*, methotrexate and their combination.

Methods

This study is an open-label, therapeutic, outpatient-based study that enrolled 60 patients with moderate to severe psoriasis (PASI score greater than ten) attending the Department of Dermatology and Venereology in Al-Sadder Teaching Hospital in Basrah during the period November 2011 to December 2012. were enrolled in this an open-label, therapeutic, outpatient-based study.

The patients were randomly divided into three groups. Patients in group 1(20 patients) were treated with *Nigella sativa* as 20% w/w ointment twice daily and capsules 500mg three times daily. Group 2(20 patients) were treated with MTX tablets15mg weekly and patients in group 3(20 patients) were treated with the combination of MTX tablets15mg weekly and *Nigella sativa* ointment 20%w/w twice daily and capsules 500mgthree times daily. The patients were then assessed clinically using PASI scoring system at baseline visit and every 2 weeks for a total of 12 weeks and also by laboratory measures through assessment of oxidative stress (by measurement of malondialdehyde (MDA) level before and after 12 weeks of treatment), liver enzymes (ALT and AST) and complete blood counts every four weeks. Clinical assessment was confirmed by photographic viewing of patients every two weeks and during the follow up period for 12 weeks. Patients satisfaction and side effects were also evaluated.

Results

Eighty one patients, 45 men and 36 women were enrolled in this study. Out of these 81 patients, twenty one defaulted from the study (nine of them due to loss of follow-up, seven defaulted after achieving a good response four weeks of treatment, six women unexpectedly became pregnant during the study, and seven patients due to other severe illnesses). Out of the remaining sixty patients; there were 37 (61.67 %) males, mean of age (43.9$\pm$17.87) years and 23(38.33 %) were females with a mean age of (35.04$\pm$13.29) years. For patients on *Nigella sativa* (G1) a good response was achieved four weeks after starting treatment in 60% of patients, with a relapse rate of 33.33% observed 4 weeks after cessation of treatment. Patients treated with MTX tablets (G2) a good response was noticed four weeks after starting treatment in 80% of

patients, and the disease relapsed in 56.25% of patients four weeks after cessation of treatment.

In G3 (combination), a good response was achieved in 90% of patients which appeared early after 2 weeks, with a relapse rate of (27.77%).

There was a direct and significant correlation between percent reduction of PASI score and percent reduction of MDA in G1with a correlation coefficient of ($r=0.457$) and a p-value<0.001. Patients in G3 demonstrated even better correlation between percent reduction of PASI score and percent reduction of MDA with a correlation coefficient of ($r=0.653$) and p-value <0.0001. Whereas there was a significant direct correlation between percent reduction of PASI score and percent elevation in MDA in G2 with a correlation coefficient ($r= 0.543$) and $p<0.0001$. There were no significant changes in liver enzymes (ALT and AST) and complete blood counts, after treatment with *Nigella sativa*, MTX and the combination in comparison to pretreatment values.

Nigella sativa was well tolerated with no side effects reported from their use while patients on MTX tablets reported gastric upset of various severity. A striking observation was reported by all patients that gastric upset caused by MTX did not appear when capsules of *Nigella sativa* and MTX was given in combination.

Conclusion

Topical and oral treatment with *Nigella sativa* (Black Cumin) was found to be relatively safe and effective in the treatment of moderate and severe psoriasis. The combination of *Nigella sativa* and methotrexate have additive effect. *Nigella sativa* alone and with MTX was found to induce longer remission and less relapse rate. *Nigella sativa* ameliorated gastric upset caused by MTX. Hepatotoxicity reactions were not reported in any patient

treated with *Nigella sativa* alone or with MTX during the period of the study. *Nigella sativa* reduced the oxidative stress measured by MDA, whereas MTX increase it.