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Coffee for the relief of symptoms of methotrexate intolerance among patients with rheumatoid arthritis

Patients with rheumatoid arthritis (RA) and some of the other systemic autoimmune rheumatic diseases are commonly prescribed methotrexate (MTX) at the dose of ≤ 25-30 mg/week. Depending upon the patient's condition and the dosage prescribed, some patients need oral tablets while the others are prescribed subcutaneous injections. It is a highly effective drug for the treatment of RA and is considered the 'anchor drug' for its treatment. Unfortunately, despite being such an effective drug for RA, it has an annoying problem of intolerance often leading to its discontinuation. The word 'intolerance' means different symptoms in different patients that may be categorised as *gastrointestinal (GI), behavioural* and *non-specific symptoms as follows:* 1. The GI symptoms include nausea, bloating, discomfort, pain, heaviness, acidity, epigastric distress, belching, loose motions, abdominal cramps, constipation; 2. Behavioural symptoms including anticipatory symptoms include anxiety, depression, aversion to its name, sight, thought; aversion to food, unpleasant taste and odours, insomnia, giddiness, headaches, difficulty in concentrating, 3. Non-specific symptoms include loss of appetite, weakness and fatigue, the whole body feeling hot, burning in the chest etc. The LD-MTX intolerance-related symptoms often make it difficult for the patient to continue taking it with consequent loss of disease control. To overcome LD-MTX intolerance, different methods have been tried in different patients with variable results. Anti-emetics, antacids or shifting from oral to subcutaneous route of administration are the commonest tricks tried in patients with variable results. Joel Kraemer, a leading rheumatologist in Albany, NY, USA, during a talk at the 2014 annual meeting of the American College of Rheumatology suggested the use of 'a few extra cups of coffee' to ward off these adverse effects. Based upon his suggestion, the effect of the addition of coffee in the treatment regimen for offsetting LD-MTX intolerance systematically studied. The coffee schedule advised was as follows: 2 strong cups of coffee early in the morning on the day of the week on which the LD-MTX dose was scheduled. This was repeated in the late evening 1 hour before the dose of MTX (which was usually advised to be taken with dinner). A 3rd dose of 2-cups of strong coffee was repeated the next morning. This schedule was repeated every week synchronised with the weekly dose of LD-MTX. If the intolerance symptoms disappeared completely over time, the patient was advised to discontinued coffee unless the patient liked coffee and preferred to continue taking it.

In the present study of a total of 855 patients with RA being treated with LD-MTX, 542 (63.4%) patients had some degree of LD-MTX intolerance. Among them, 422 (77.8%; 49.3% of the total patients) had 'minimal' intolerance not requiring any intervention. The remaining 120 (22.1%) of the 542 (14% of the total 855) patients had 'moderate' to 'severe' LD-MTX intolerance. Among 120 patients with moderate to severe LD-MTX intolerance, 55% had complete relief of symptoms with the above schedule of coffee intake. Such patients were able to continue taking the advised dose of MTX; 13.3% had partial improvement and were able to continue taking MTX but only with anti-emetics; 7.5% were minimally better but were somehow managing; 10% were complete coffee failure without any relief; 14.2% did not like coffee or did not want to take it**.**

In conclusion the study showed that if given in the above mentioned schedule, coffee relieved the symptoms of MTX intolerance in 56% and gave partial relief in another 13% of the patients. The patients and their

caregivers would find this work of interest in helping their patients offset the problem of LD-MTX intolerance increasing the rate of compliance to this drug for satisfactory disease control.

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Publication

Methotrexate intolerance in the treatment of rheumatoid arthritis (RA): effect of adding caffeine to the management regimen.
Malaviya AN
Clin Rheumatol. 2017 Feb