In increasing optimal methotrexate dose might be a better traditional DMARD strategy in RA treatments: a randomized case-control trial of Hakka people in southern China

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Background: The optimal methotrexate (MTX) dose is defined as 0.3mg/kg/week or ≥20mg/week in 6 months. [1] Considering average weight of Chinese, [2] the optimal MTX should be >15mg/w. However, not more than 30% in 25191 RA cases ever had MTX treatment in CREDIT (Chinese Registry of Rheumatoid arthritis). [3] The biggest concern is side effects of MTX. Our study is to investigate whether increasing MTX would get better results accompanied with more side effects to Chinese people.

Objectives: Hakka people have the purest genes of the majority people-Han in China. It is planned to recruit 160 RA patients in Meizhou, where is a gathering place of Hakka people.

Methods: The RA volunteers had no relief with 10mg/w oral dose of MTX with/without other 1-2 inadequate dose of DMARDs for at least 3 months. They were randomly divided into 1:1 groups. The experimental group would be treated with original DMARDs and incremental MTX (gradually increased to the optimal oral dose (0.3mg/kg/w) in the first 12 weeks and folic acid (the dose adjusted on patient’s condition). While the control group would be treated with original MTX dose (10mg/w) but incremental original DMARDs (gradually increased to the maximum dose in the first 12 weeks). The two groups would keep the treatment at 12th week last to the 36th week, and the efficacies and safety indexes would be evaluated during the whole study.

Results: 1)We planned to recruit 160 RA patients in our study. 46 Hakka RA patients were enrolled in the study so far. 2 of 46 finished the 24th week visit and 24 finished the 36th week visit. The average age was 54.2±9.3 years old, the average age weight is 59.1±11.1kg, and the female to male ratio is 41:5.
2)The average Folic acid dose is 14.4±9.5mg/w in the experimental group at the 1st 12 weeks and folic acid (the dose adjusted on patient’s condition) 15mg/w in the experimental group at the 6 months.
3)The morning stiffness time, PGA, PhGA, HAQ, DAS28 were better in experimental group after 12 weeks though slightly worse during 0-12 weeks. 100%(12) in experimental group after 12 weeks.
4)Only 1 case (5.9,1/23) had adverse event while 6 cases (26%,6/23) occurred adverse events. All events were mild level. 1 case (4.2%,1/23) in control group withdrew from the study because the disease was getting worse during 0-24 weeks.

Conclusion: Hakka patients in China might have better outcomes due to increasing MTX to the 0.3mg/kg/wose than increasing the other DMARDs. Therefore, We recommended the Hakka Chinese patients choose MTX as first increment of DMARD. The appropriate dose of Folic acid plus with the optimal dose of MTX in our study is higher than previous studies (such as 13.0±4.8mg/w reported by Gaujoux-Viala, 2018[1]). We recommended Chinese patients take 15mg/w folic acid to prevent MTX side effects in view of lower folic acid level in Chinese population.[3]