ABSTRACT

The Effect Of Potassium Supplement On Pain In Rheumatoid Arthritis (RA)

Key Words: rheumatoid arthritis, pain ,potassium , diet intervention, potassium rich diet, diet supplement.

Objective: The primary purpose of the study was to evaluate the effect of oral diet based K+ intervention to reduce pain in patients suffering from RA; other objectives included benefits on disease activity.

Background: National Health and Nutrition Survey III (USA) data showed a low K+ body status in RA.K+ is critical to ‘pain’[nociceptive processing, K+ ion channel downregulation and related process e.g. oxidant tissue damage and T lymphocytes function(K2P5.1, Kv1.3& KCa3.1) channels and cortisol secretion. A short duration intervention study in Iran with oral K+ supplement showed a significant reduction in pain and disease activity in RA with hypokalemia.

Methods: The current research study was duly approved by the ethics committee and carried out in a rheumatology center. Patients provided a voluntary informed consent that was video recorded (as per ICMR). Comprehensive literature review identified the sparse data on the subject and helped define the research approach for the current study. It also provided some clinical and experimental data to support the putative role of K+ as an adjunct therapy. Next a planned controlled (healthy community) dietary survey and analysis was carried out using indigenously designed diet recall questionnaires in 139 patients suffering from RA .Indian dietary standards and a web based application for data analysis was used ; both as per the Guidelines of
the National Institute of Nutrition, Hyderabad. Another cohort of 99 RA patients were enrolled to complete a cross sectional study to validate an Indian version of RA pain scale (RAPS) which captures physical, functional, cognitive and affective aspects of pain. In the main interventional study, 172 chronic RA patients (ACR 1987 classified, mean age 49.9 years, 89 % women, 74% seropositive RF) with active pain (visual analogue scale > 4 cm) were randomized into an assessor blind, three arm study of 16 week duration as per protocol (registered with CTRI Ref No REF/2015/05/008963). Standardized oral K+ intake was based on K+ rich vegetarian diet in Arm A (3.5-4 gm K+ daily) and an additional food based K+ supplement (mixed with oral rehydration salt, Indian pharmacopeia to boost up K+) in Arm B (7.5-8 gm K+ daily). Arm C was control (routine diet, 2-3 gm K+ daily). Patients continued standard rheumatology care (72% methotrexate, 60% low dose steroid) and monitored analgesic rescue. Standard efficacy/safety measures and diet intake were evaluated every month. Compliance check included urinary K+ assay. The sample size was calculate with an assumption of 10% difference in pain VAS between the high K+ intervention arm and control and a 20% drop out. The study (80% power, significant p <0.05) was analyzed by using SPSS; NS: p, not significant. Arms were well matched for several measures (for mean DAS 28: A=4.9; B=5.5; C=4.9) and withdrawals (A: 8.8%; B: 12.1%; C: 8.8%).

Results: The dietary survey in the pilot study showed that dietary K+ was low (p<0.5) in RA patients and more so in women (p<0.05). It further showed that the rest of the RA diet was well matched with Indian standards of RDA and seemed adequate in proteins, fats, minerals and vitamins.
The Indian version of RAPS was determined to have face and content validity with a fair-good correlation with several measures of disease activity and quality of life; used in main study.

Pain and efficacy measures improved (P<0.05) by intervention; difference was NS by intent to treat analysis (mean change pain VAS: A=-1.3 cm; B=2 cm; C=1.2; p=0.17, ANOVA). But completer analysis showed significant change (p=0.04) in mean pain VAS in Arm B (K+ supplement). B arm showed best response (P<0.05) in proportion patients with at least 50% reduction and minimal clinical important difference in pain VAS on completion from baseline. B arm also showed maximum improvement (NS) in HAQ (Indian validated version) and SF 36 physical score. There was reduction (NS) in in mean DAS 28 score (A:-1.4; B:-1.2; C:-0.9). Only mild adverse events were reported (<8% patients by study arm). Routine laboratory measures of hemogram, metabolic renal hepatic parameters remained normal. None withdrew due to AE. Withdrawal rate was ~10% and mostly due to logistic issues. On completion, B arm demonstrated a maximum serum cortisol (AM) increase. K+ intervention arms showed reduction in systolic BP. Ongoing medication, dietary factors and compliance, disease activity status may confound results. The inverse association (r=-0.22) between dietary K+ and pain VAS was significant (p<0.01), albeit modest. Disease duration, serum K+, allocation to Diet K+ arm and body mass index were significant predictors of pain relief (pain VAS) in a robust logistic regression model.

Conclusion: The diet of RA patients is insufficient in K+ though of adequate match to Indian standards. An Indian version of RAPS was found valid for measuring pain.
This pragmatic study showed a clinically important pain reduction, though modest, over and above that obtained by standard care using dietary K+ augmentation. Other possible benefits were reduced disease activity and improved BP (cardiovascular) status. Overall, this seemed to be a gentle useful adjunct therapy in RA.