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Letter to the Editor**Paracetamol for osteoarthritis; is there a need for revision of guidelines?**

Sir,

Paracetamol (PCT) is the most commonly prescribed drug for pain of osteoarthritis (OA).¹ Its advantage over non-steroidal anti-inflammatory drugs (NSAIDs) in terms of better gastrointestinal and renal safety had made this choice obvious especially in the elderly; a few years ago. Considering the current treatment guidelines (American College of Rheumatology,² National Institute for Health and Care Excellence³ and European League against Rheumatism) which uphold PCT as the first choice drug for OA, a few studies have questioned the aforesaid advantage of PCT against its modest efficacy in patients with OA.⁴⁻⁶ Thus, a study was planned to evaluate the efficacy of PCT in patients with OA with respect to its impact on pain, clinician's global evaluation of symptomatic improvement and quality-of-life (QOL) as primary efficacy parameters. The study was conducted in the outpatient department of orthopedics in a tertiary care hospital over duration of 1-month after approval by Ethics Committee. Treatment naïve patients of knee OA (with pain rated as >4 on numeric rating scale (NRS) at baseline) were enrolled into the study after taking a well-informed written consent. All patients were given PCT 500 mg twice a day for 4 weeks. Primary efficacy parameter was improvement of pain score on NRS. A questionnaire, specially predesigned and pretested to assess different aspects of QOL like day to day physical activity, general health, vitality, and daily work accomplishment with a maximum score of 20 was used to assess the effect of therapy on QOL at the end of 4 weeks as compared to baseline. Clinical assessment of symptomatic improvement by investigator for all symptoms like pain, stiffness, number of joints involved, swelling, joint instability, interference with squatting as compared to baseline was done on a predesigned symptom score chart. A total of 15 patients (6 males and 9 females, ranging from 42 to 70 years of age and body mass index ranging from 18.93 to 32.88) with knee OA were included in the study. The mean NRS score was 7.2±2.2 at baseline and reduced to 7.1±2.3 at the end of the study (p=0.5457). The QOL score increased from 10±1.9 to 11±2 (p=0.0967). Difference in both these parameters was not statistically significant. Clinical assessment of symptomatic improvement showed that all symptoms on symptom score chart persisted despite therapy but there was improvement in joint stiffness and pain following therapy as compared to baseline in eight patients while seven of them showed

no improvement at all. None of the patients complained of any adverse reactions to PCT. There was no significant improvement in pain score, clinical symptom score or QOL indices in patients with OA treated by low doses of PCT suggesting a poor efficacy profile at these doses. Higher doses of PCT used in other studies are reported to be toxic, and recommendations for dose reductions have been made.⁴⁻⁶ This has led to poor patient satisfaction and a considerable drop-out of patients and clinicians deviating from guidelines. However, findings of this study have to be interpreted in the light of its limited sample size. But the findings of this study are in concordance with a new draft of NICE guidelines released in 2012, which said that efficacy of PCT in OA was questionable. But due to lack of primary studies evaluating the efficacy of PCT in OA, the older version has been retained. This small study although only hypothesis generating comes up with an addition to primary data on efficacy of PCT in OA and some brief suggestions to improve patient satisfaction. Despite poor patients' satisfaction, complete substitution of PCT by an alternative could be a very drastic step at this juncture since, this could lead to overuse of more toxic NSAIDs and opioids as the first line drugs. This leaves us with the option of retraining the status of PCT with some modification like using add-ons such as topical NSAIDs, opioids like codeine and/or tramadol. Using a step-down approach (utilizing multiple drugs and doses as per initial clinical requirement and slowly reducing the number of drugs and their doses) rather than the currently recommended titrated dose approach may be more appropriate. The reason for this discretion being, pain control once achieved is easy to maintain. Some studies have shown increased gastrointestinal bleeding with a combination of PCT with NSAIDs,⁵ and thus this combination may be reserved for patients with severe pain. For most patients, however, a pharmacological multidimensional approach utilizing drugs with different mechanisms of action and safer routes of administration may have more to give than unidimensional approach that is followed today. However, as of today, despite a need for guideline revision, more studies evaluating efficacy and safety of pharmacological step-up and step-down approaches will have to be conducted before attempting at guideline revision.

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