Paracetamol still persona grata or game over in Rheumatology? Comment on article by Machado et al.

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Paracetamol, a grade I analgesic is recommended as the first line therapy in osteoarthritis (1-3). Despite reports of its limited efficacy in this disease (4,5), rheumatologists continue to urge general practitioners on the importance of prescribing paracetamol in first intention, this, in compliance with present guidelines (6). Discussions on the efficacy and safety of paracetamol have resurfaced in the year 2015 (7,8).

A systematic review with meta-analysis by Machado et al. showed that in the short term, paracetamol is not effective in reducing pain intensity, disability and the improvement of the quality of life of patients with low back pain. For knee and hip osteoarthritis, though paracetamol provides a significant reduction of pain intensity and disability in the short term, this efficacy is not clinically apparent (7). Machado et al. also raised some issues as concerns the safety of paracetamol. Indeed, patients taking paracetamol (3 000 mg to 3 900 mg) are more likely to have abnormal results of liver function tests in the short term. However, the relevance of these liver abnormalities remains unclear (7) thereby warranting a long-term evaluation of the consequences of this disturbance of liver function tests so as to provide answers to this question. The long term safety of paracetamol has been questioned in several reports (1,4,8), particularly in a recent systematic review conducted by Roberts et al (8). Despite methodological limitations, this review enhances the blaze by showing that paracetamol is associated with cardiovascular, gastrointestinal, and renal adverse events. Moreover, paracetamol might increase mortality (8). Association with non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen has also been shown to increase the risk of mild gastrointestinal bleeding (9).

Therefore, the apparent unfavorable benefit to risk ratio of paracetamol raises a key issue: should we change our paradigm for the management of osteoarthritis and recommend as first line therapy grade II analgesics and/or NSAIDs? (10,11).

So far we have been blinded by a double game on paracetamol: its double name (acetaminophen and paracetamol) and its double AA+ (good efficacy and good tolerance). Today it seems to make room to a double CC− status (poor efficacy and poor safety). Notwithstanding, the benefit to risk ratio of any drug should also be evaluated owing to its duration in the armamentarium of prescription. Indeed, acetaminophen when prescribed at high dose on the long term, might be risky for the cardiovascular system but also for the gastrointestinal tract (9). However, we lack data on the safety profile of paracetamol when given on a short period of time. We should therefore think on this question and know what is most effective and safe in a disease such as osteoarthritis which has a limited available therapeutic arsenal. Consequently, excluding
paracetamol as first line analgesic in such a situation may open the door for grade II analgesics and/or NSAIDs which have severe associated side effects, especially in osteoarthritis patients who often have multiple comorbidities (9-11).

The answer might be that in a disease like osteoarthritis it is time to consider not only the effect size of one drug but the additional effect of several non-pharmacological and pharmacological therapies among which paracetamol. Meanwhile, the approach would be to use the lowest dose of paracetamol for the shortest duration.
References


