

## **Risks of taking paracetamol long-term may have been underestimated by clinicians**

*Experts call for review of paracetamol's effectiveness and tolerability for certain conditions*

Doctors may have underestimated the risks for patients who take paracetamol long-term, suggests research published online in the journal **Annals of the Rheumatic Diseases** (doi 10.1136/annrheumdis-2014-206914).

There should also be a systematic review carried out to ensure the effectiveness of the commonly taken drug and how it is tolerated for certain conditions.

Paracetamol is the most widely used over-the-counter and prescription analgesic worldwide and is recommended as first-line pharmacological therapy by a variety of international guidelines for a multitude of acute and chronic painful conditions. It is also generally considered to be safer than other commonly used analgesics such as non-steroidal anti-inflammatory drugs (NSAIDs) or opiates.

However, the analgesic benefit of paracetamol has recently been questioned in the management of acute lower back pain and the chronic painful condition of osteoarthritis and a recent estimate of the true risks of paracetamol at standard analgesic doses has not been available.

A UK team of researchers, led by Professor Philip Conaghan of the Leeds Institute of Rheumatic and Musculoskeletal Medicine, set out to conduct a systematic review of existing studies that had assessed the association between chronic use of paracetamol and major adverse events in the general adult population.

They identified eight suitable studies to analyse. Of two studies that showed mortality, one found a dose–response and reported there had been an increased relative rate of mortality from 0.95 to 1.63 for increasing standard doses of paracetamol when comparing patients who had been prescribed paracetamol with those who had not.

Of four studies reporting cardiovascular adverse events, all showed a dose–response with one study reporting an increased risk ratio of all cardiovascular adverse events from 1.19 to 1.68.

One study reporting gastrointestinal adverse events reported a dose–response with a higher relative rate of events or bleeds from 1.11 to 1.49.

Finally, of four studies reporting renal adverse events, three reported a dose–response with one reporting a more likely decrease in estimated glomerular filtration rate – a test used to check how well the kidneys are working – from 1.40 to 2.19.

The authors said that although the eight observational studies were likely to have biases related to those people who needed long-term paracetamol (often people who already had multiple medical problems requiring other analgesics and medications), their findings demonstrated a consistent dose–response relationship between paracetamol at standard analgesic doses and adverse events typical of those often observed with non-steroidal anti-inflammatory drugs.

This included a dose–related relationship between paracetamol and increasing incidence of mortality, cardiovascular, gastrointestinal and renal adverse events, though the overall risks of these problems remained small.

They acknowledged that with every prescribing decision, there was a calculation of risk versus benefit or a trade-off of efficacy versus tolerability.

However, when analgesic benefit was uncertain, as had been suggested in previous studies of paracetamol in the treatment of osteoarthritis joint pain and acute low back pain, it was necessary for clinicians to take more careful consideration before recommending or prescribing it for long-term use.

The authors concluded: "Based upon the data presented above, we believe the true risk of paracetamol prescription to be higher than that currently perceived in the clinical community. Given its high usage and availability as an over-the-counter analgesic, a systematic review of paracetamol's efficacy and tolerability in individual conditions is warranted.