Paracetamol and pain: the kiloton problem

R Andrew Moore,1 Nicholas Moore2

As a unit, the kiloton is most often linked to the explosive yield of nuclear weapons in tons of TNT (trinitrotoluene, an explosive). For drugs, we are more comfortable with milligrams, a unit one million million times smaller. With paracetamol, at a population level, the kiloton unit may be more appropriate: in Europe, paracetamol sales range from under 200 tons in Greece and Portugal to 6300 tons in the UK and 10 000 tons in France.1 On a per capita basis the range is 4–5 tons per million to 30–50 tons per million. These figures relate to the total population exposure, including over-the-counter (OTC) sales, though prescribing of paracetamol is not negligible. In the UK in 2014, 42 million paracetamol-containing medicines were prescribed at a cost of £191 million, and 200 million packs sold OTC.3

Paracetamol was discovered in the 1950s, and the general view that it is effective and safe has led to such widespread use. Yet there has been considerable uncertainty over how it works. Only recently has it been generally accepted that it inhibits COX-1 and COX-2 isoenzymes, and is in fact a weak nonsteroidal anti-inflammatory drug (NSAID).5

The last few years have seen paracetamol and other commonly used drugs subjected to greater scrutiny, particularly the sharp focus of evidence-based medicine; 2015 and 2016 have seen pivotal new evidence. The picture is not quite as rosy as has been assumed. The future for treating pain lies in new formulations of NSAIDs. For chronic pain we have evidence of absence of any clinically useful effect of paracetamol, either alone or in combination, and at doses of up to 4000 mg daily. There may of course be circumstances where paracetamol might be useful, in paediatric pain, for treating patent ductus arteriosus, or for intransitory use during surgery.

Balanced against this at-best-modest analgesic efficacy we have considerable evidence of harm, including all the concerns that also affect NSAIDs, but with liver failure and (possibly) renal failure added. These are dose-related; more risk of harm at higher doses.

If paracetamol were an important and little-used drug, none of this might amount to much. But it is a drug whose use is measured in thousands of tons, has little or no effect in many conditions and has significant adverse events. Maybe it is time to consider the evidence again and think about the possibility of change.

Patients with pain regard only large reductions in that pain to be relevant, and large reductions in pain are accompanied by major improvements in associated symptoms, including quality of life, function and work, and lower costs to health services.18–20 We know that only a minority of patients have adequate pain relief on any particular drug.21 We know that the majority of people with chronic pain still have moderate or severe pain while on treatment, indicating that treatment to be inadequate.22 We know that switching to another medicine in that situation results in major benefits for many.23

The future for treating pain lies in new thinking about how we deal with analgesic failure, rather than remorselessly continuing to use kilotons of a drug that we know will fail and may do harm.

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