The use of paracetamol in clinical consultations: are current prescribing practices safe?

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Chronic pain is a very common ailment. An early local survey of 1051 adults revealed that 113 (10.8%) had chronic pain lasting >3 months within the previous year.[1] Of these individuals, 30.1% had attempted self-treatment with analgesics.[1] Female gender (odds ratio [OR]=1.5) and advanced age (≥60 years) [OR=2.2] were independent risk factors for chronic pain.[1] Another local study assessed the prevalence of pain in older people attending a geriatric outpatient specialist clinic at a regional hospital.[2] Among 749 participants, 461 (61.5%) had experienced pain in the previous 2 weeks.[2] Over half (51.3%) of the individuals with pain had taken analgesics.[2]

Paracetamol is an effective and easily accessible first-choice analgesic. It is available alone as a non-prescription medication or in combination with other medications.[3] This drug is considered safe when the daily dose does not exceed 4 g in adults. It is usually preferred over non-steroidal anti-inflammatory drugs, which are associated with renal, gastrointestinal, and cardiovascular side-effects, especially in older people with multiple co-morbidities.[4] Paracetamol is one of the most commonly prescribed analgesics worldwide.[5]

Paracetamol reduces the production of pro-inflammatory prostaglandins and thromboxanes by inhibiting the enzyme cyclooxygenase,[6] which is considered a key mechanism for inducing analgesia. It is extensively metabolised by hepatic glucuronidation and sulphation (85%-90%). The remaining drug is either oxidised by cytochrome P450 isoenzymes to form a toxic metabolite, N-acetyl-p-benzoquinone-imine (5%-10%), or excreted unchanged in urine (5%). N-acetyl-p-benzoquinone-imine is further neutralised by glutathione and excreted in urine. In cases of paracetamol overdose, the accumulation of N-acetyl-p-benzoquinone-imine may lead to acute liver failure. Additionally, paracetamol toxicity is more common in patients with chronic liver diseases or malnutrition. Pharmacokinetic studies have indicated that paracetamol absorption is not altered in older people compared with younger individuals. Nonetheless, both the volume of distribution and clearance of paracetamol metabolites decline with age, especially in frail older people.[7] Thus, older people also have a greater risk of paracetamol-induced hepatotoxicity.

In this issue of the *Hong Kong Medical Journal*, Tsang et al[8] present a territory-wide study of paracetamol-induced hepatotoxicity based on data from 3873 cases of drug-induced poisoning. After the exclusion of ineligible patients, 76 cases were included in the analysis. The findings showed that age >80 years, low body weight (<50 kg), prolonged exposure (>2 days), daily dose >3 g, and malnutrition (documented insufficient energy intake for >1 week) were risk factors for death or acute liver failure.[8] Among these risk factors, prolonged paracetamol use (OR=16.9), older age (OR=7.2), and higher paracetamol dosage (OR=7.2) displayed the strongest effects.[8] The findings are consistent with the STOPP/START criteria (Screening Tool of Older Persons' Prescriptions and Screening Tool to Alert to Right Treatment), which recommend that the daily dose of paracetamol should not exceed 3 g in older people (aged ≥65 years) with malnutrition (body mass index ≤18 kg/m^2) or chronic liver diseases[9] due to the risk of hepatotoxicity. Furthermore, Tsang et al[8] reported other remarkable findings. First, the majority (60.5%) of paracetamol users had pain or fever. Second, over one-third (34.2%) of paracetamol overdose cases were related to cognitive impairment. However, the study had limitations of retrospective design and a modest number of included patients.[8]

Hong Kong is a rapidly ageing society. Cognitive impairment affects one in 10 people aged ≥70 years and one in three people aged ≥85 years.[10,11] Many older people attend multiple medical appointments in public healthcare clinics. Concomitant care in both private and public clinics is also common. Furthermore, they have easy access to paracetamol or paracetamol-containing combination products from community pharmacies. Thus, these individuals

have a risk of paracetamol overdose through the use of multiple sources.[12] Family physicians and community pharmacists play important roles in ensuring medication reconciliation for frail older people with multiple co-morbidities and medical appointments.

In summary, Tsang et al's study offers a timely reminder of the need for cautious use of paracetamol when treating frail older people.[8] Future prospective studies involving a broader population may help enhance the generalisability of these findings.

Author contributions

Both authors contributed equally to the development of the manuscript. Both authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

Both authors have declared no conflicts of interest.

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