

ACUTE PAIN SECTION

Original Research Article

A Risk-Benefit Assessment of Paracetamol (Acetaminophen) Combined with Caffeine

Hazel Palmer, BSc, MSc,* Garry Graham, MSc, PhD,[†] Kenneth Williams, BSc, PhD,[†] and Richard Day, AM, MB BS, MD, FRACP[†]

*Scius Solutions Pty Ltd, Mosman, New South Wales;

[†]Department of Clinical Pharmacology & Toxicology, St Vincent's Hospital, Sydney, New South Wales, Australia

Reprint requests to: Hazel Palmer, BSc, MSc, Scius Solutions Pty Ltd, Suite 9, Level 1357 Military Road, Mosman, NSW 2088, Australia. Tel: 61 29904 1077; Fax: 61 29904 1322; E-mail: hazel@scius.com.au

Abstract

Objective. To determine the risk: benefit of paracetamol combined with caffeine in the short-term management of acute pain conditions.

Design. Database searches were conducted to identify double-blind trials comparing paracetamol/caffeine with paracetamol alone (benefit analysis) and any data pertaining to hepatotoxicity of paracetamol when combined with caffeine (risk analysis).

Interventions. Paracetamol/caffeine (1,000 mg/130 mg) vs paracetamol (1,000 mg) alone.

Outcome Measures. Assessment of benefit has been derived by meta-analysis. Information on the pain condition and number of patients studied, dosing regimen, study design and analgesic outcome measures (total pain relief scores) was extracted and dichotomous outcomes were obtained by calculating the number of patients in each treatment group who achieved at least 50% of the maximum total pain relief score. Assessment of risk has been made by appraisal of the literature.

Results. Eight studies from four papers provided sufficient quantitative data for satisfactory meta-analysis. The relative benefit (of achieving at least 50% pain relief) of paracetamol/caffeine vs paracetamol

alone was 1.12 (95% Confidence Interval 1.05–1.19) across a number of acute pain states (dysmenorrhoea, headache, post-partum pain, and dental pain). Review of the effects of the combination of paracetamol and caffeine on the liver revealed no compelling data to suggest a clinically meaningful increase in hepatotoxicity with use of paracetamol/caffeine combinations.

Conclusions. Paracetamol/caffeine (1,000 mg/130 mg) is effective and safe for use in acute management of pain. The hepatotoxicity of overdoses of paracetamol results from its oxidative metabolism, caffeine does not produce any increase in oxidative metabolism of therapeutic concentrations of paracetamol.

Key Words. Paracetamol; Caffeine; Efficacy; Hepatotoxicity

Introduction

Paracetamol (acetaminophen) is one of the most widely used analgesics. Its mechanism of action has been unclear, but recent work indicates that its primary effect is inhibition of prostaglandin synthesis [1,2]. This inhibition leads to secondary mechanisms of inducing analgesia, most importantly to reinforce descending serotonergic pathways [3].

Paracetamol, in doses up to 1,000 mg, is used as both an over-the-counter (OTC) and a prescription analgesic, where it is the initial analgesic of choice for most mild to moderate acute [4] and chronic [5–8] pain states. In a meta-analysis of 51 studies involving 5,762 patients comparing single doses of paracetamol (1,000 mg) with placebo for post-operative pain, the number needed to treat (NNT) for at least 50% pain relief over 4 to 6 hours was 3.6 (95% confidence interval [CI] 3.4 to 4.0) [9]. Direct comparative studies between paracetamol and a number of OTC and prescription nonsteroidal anti-inflammatory drugs (NSAIDs) showed equivalent analgesic outcome in major surgery (5/6 trials), minor orthopedic surgery (3/3 trials), gynecological surgery (1/3 trials), ear, nose and throat surgery (5/6 trials), and dental surgery (7/15 trials) [10].

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