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Paracetamol: A Boon to Medicine; A Dangerous Foe- Safe dosing of the Drug

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Original Article
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ABSTRACT

Paracetamol (Acetaminophen) is the most commonly used drug in the world, with a long record of use in acute and chronic pain. In recent years, the use of paracetamol has been questioned and controversial in some conditions like arthritis, back pain, spondylitis, Paget's disease, bone and joint diseases, temporomandibular disorders, and in tumours and carcinomas. Over the same period, the adverse effects of paracetamol have increased, especially in patients with systemic disorders. The present review article summarises the history, indications, adverse effects, and also its uses in dentistry apart from medical use.

Keywords: Acetaminophen Paracetamol, Over Counter Drug, PO–Orally, PR- Systemic Administration.

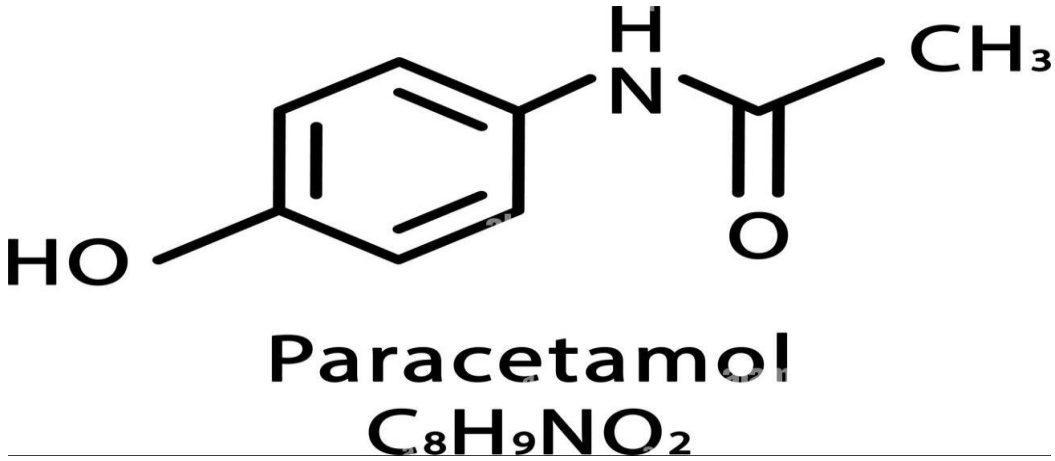
Introduction

Paracetamol (Acetaminophen, N-acetyl-p-aminophenol), is the most widely used over-the-counter analgesic and antipyretic drug. It was synthesized by Joseph Von Mering in 1893, by reacting p-nitrophenol with tin and glacial acetic acid. In the 1880s, paracetamol, and phenacetin, were found to have antipyretic and later, analgesic activity. Initially, Phenacetin gained more popularity than paracetamol, however, because of serious side effects, its clinical use declined and paracetamol was marketed in 1893.[1]

Acetanilide, phenacetin, and acetaminophen are mil analgesics and antipyretics and are important along with aspirin in non-prescription drugs.[2]

C8H9NO2

Number of Carbon, hydrogen and oxygen molecules in a 500mg paracetamol tablet.



Chemical structure of Acetaminophen

Mechanism of action

Paracetamol is a weak inhibitor of the synthesis of prostaglandins (Pgs). However, in vivo, effects are similar to cyclooxygenase– 2 (COX-2) inhibitors. It suppresses swelling and inflammation in rats and mice but does not do so in rheumatoid arthritis. The action of paracetamol is unclear but could be related to the production of reactive metabolites by the peroxidase function of COX-2, which could deplete glutathione, a co-factor of enzymes such as PGE synthase.[3]

Uses of Paracetamol

Paracetamol in adults is used for the management of various types of acute painful conditions that include headache[4], musculoskeletal pain[5], period pain6, osteoarthritic pain7, back pain8, dental pain9 and also for postoperative pain.[10,11]

Paracetamol is widely used analgesic and antipyretic. It is an active readily available substance in a series of readily available over-the-counter (OTC) medications. During pregnancy, paracetamol is considered safe and effective when taken at the recommended dosage.[12]

Conditions where Paracetamol is less effective or ineffective

Paracetamol does not speed recovery from acute back pain, severe migraine, neural pain, arthritis, or severe bacterial viral or fungal infections. It is ineffective in carcinoma or high-grade fever in case of AIDS infection.[13]

Disadvantages of Acetaminophen

Paracetamol i.e. Acetaminophen, has many disadvantages also. It lacks an anti-inflammatory effect. It is used as a single drug. The analgesic effect of paracetamol is very less and also very much less as compared to other non-steroidal anti-inflammatory drugs. It proves toxic if taken in over dosages, causes serious damage to the liver and kidney, and may also lead to death if not taken in the recommended dosage. It can even cause blood disorders and also severe bleeding. Paracetamol is no or less effective for different levels of prostaglandins. It isn't very effective in the treatment of dysmenorrhoea. In some cases, it can lead to anaphylactic shock. For the treatment of fever, it is the first recommended drug, as it is a good antipyretic medicine.[14]

Contraindications of Paracetamol

Paracetamol is contraindicated in patients who are allergic to it. It is highly not suitable for persons having blood disorders, and liver or kidney disorders. Patients addicted to alcohol should not take this medicine as it may prove toxic to the liver.

Dose reduction of paracetamol is done in patients having kidney stones.[15]

Other side effects include loss of appetite, stomach pain skin rash, dark tarry stools, severe itching in the skin, dark urine, or even jaundice.[16]

Adverse reactions of acetylsalicylate drugs include gastric upset, heartburn, nausea, vomiting, anorexia, and GIT bleeding. Adverse reactions of acetaminophen usually occur with chronic use or when the recommended dosages are exceeded, and are otherwise uncommon.[17]

Paracetamol recommended dose

Immediate-release: Regular strength: 325-650 mg PO/PR q4hr; not to exceed 3250 mg/day; under supervision of a healthcare professional, daily doses of up to 4 g/day may be used.

Extra Strength: 1000 mg PO q6-8hr; not to exceed 3000 mg/day; under the supervision of a healthcare professional, daily doses of up to 4 g/day may be used.

Extended-release: 2 capsules (1300 mg) PO q8hr; not to exceed 3.9 g/day.

Maximum dose: Acetaminophen-containing products: Not to exceed a cumulative dose of 3.25 g/day of acetaminophen; under the supervision of a healthcare professional, daily doses of up to 4 g/day may be used.[18]

In children under 10 years, paracetamol is given in the form of suspension or syrup, according to the body weight of baby or the child.

Paracetamol Poisoning

Acetylcysteine an, antidote (also known as N-acetylcysteine) prevents the hepatic injury, primarily by restoring hepatic glutathione. It is thought to provide cysteine for glutathione synthesis and possibly to form an adduct directly with the toxic metabolite of acetaminophen and N-acetyl-p-benzoquinoneimine and to thus prevent its covalent bonding to the hepatic proteins. In addition, in patients with acetaminophen-induced liver failure, acetylcysteine improves hemodynamic and oxygen use, it increases the clearance of indocyanine green (a measure of hepatic clearance) and decreases cerebral edema.

A. Initial infusion: An initial dose of 150mg/kg of N-acetylcysteine diluted in 200mL of 5% glucose and infused over 15 to 60 minutes.

B. Second infusion: The initial infusion is followed by a continuous infusion of 50mg/kg of N-acetylcysteine in 500 mL of 5% glucose over the next 4 hours.

C. Third infusion: The second infusion is followed by a continuous infusion of 100mg/kg of N-acetylcysteine in 1000 mL of 5% glucose over the next 16 hours.

The most commonly reported adverse effects of intravenous acetylcysteine are anaphylactoid reactions, including rash, pruritus, angioedema, bronchospasm, tachycardia, and hypotension. The most severe adverse effects occur with the erroneous dosing of intravenous acetylcysteine in children. These effects include cerebral edema and hyponatraemia (due to its administration in 5% dextrose). There are rare reports of deaths which were caused due to anaphylactic reactions.[19]

Conclusion

Overall, acetaminophen is a boon to medicine, a true friend, sometimes a dangerous foe. As every drug has tremendous advantages and several disadvantages, acetaminophen is not an exception. Although it is an over-the-counter medication, its dosing should be in safe recommendations as prescribed by registered medical practitioners otherwise its overdose might lead to several serious complications.

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