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THE USE OF PARACETAMOL IN MODERN CLINICAL PRACTICE: FROM GENERAL MEDICINE TO SURGERY

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1. Introduction: Paracetamol (acetaminophen) remains one of the most widely used analgesic and antipyretic medications globally. Its excellent safety profile when used at therapeutic doses and its versatility make it a first-line agent for managing mild to moderate pain and fever across diverse patient populations, including children, the elderly, and postoperative patients. Unlike non-steroidal anti-inflammatory drugs (NSAIDs), paracetamol exhibits minimal anti-inflammatory activity but also lacks significant gastrointestinal toxicity and does not affect platelet aggregation, expanding its utility in clinical scenarios where NSAIDs are contraindicated.

2. Mechanism of Action:

The precise mechanism of paracetamol's action, long a subject of debate, is now primarily attributed to its central activity within the nervous system.

- Central Cyclooxygenase Inhibition: Paracetamol is believed to selectively inhibit a variant of the cyclooxygenase (COX) enzyme, often referred to as COX-3 in the central nervous system, though this classification is nuanced. This inhibition reduces the synthesis of prostaglandins in the brain, which are key mediators of pain and fever.
- Serotonergic and Cannabinoid Systems: Emerging evidence suggests that paracetamol's metabolite, AM404, enhances the activity of the serotonergic descending inhibitory pain pathways and may also interact with the endocannabinoid system, contributing to its analgesic effect.
- Minimal Peripheral Effect: Its weak inhibition of peripheral COX enzymes explains its lack of significant anti-inflammatory action and its favorable gastrointestinal and renal side-effect profile compared to NSAIDs.

3. Broad Spectrum of Clinical Applications

Paracetamol's utility spans numerous medical fields:

- General Medicine and Pediatrics: First-line treatment for febrile conditions (e.g., viral infections) and non-specific pain (headache, myalgia, dental pain).

- Surgical Practice (Multimodal Analgesia): This is a critical application. Paracetamol is a foundational component of multimodal analgesia regimens, which aim to control pain through multiple mechanisms, thereby reducing the reliance on opioids.
- Obstetrics: Considered safe for use during pregnancy and breastfeeding for pain and fever management.
- Chronic Pain Conditions: Used for osteoarthritis and chronic low back pain, often in combination with other analgesics.

4. Paracetamol in Surgical Practice: Reducing the Opioid Burden

The role of paracetamol in surgery is paramount and represents a modern standard of care.

- Preemptive and Postoperative Analgesia: Administered preoperatively or intraoperatively (often intravenously), it can reduce acute postoperative pain and the subsequent development of chronic postsurgical pain.
- Opioid-Sparing Effect: By providing effective baseline analgesia, paracetamol significantly reduces the total dose of opioids required postoperatively. This leads to a marked decrease in opioid-related adverse effects, such as nausea, vomiting, sedation, respiratory depression, and ileus.
- Enhanced Recovery After Surgery (ERAS): As a key element of ERAS protocols, paracetamol facilitates earlier mobilization, shorter hospital stays, and improved patient satisfaction.

5. Safety Profile and the Critical Importance of Dosing

While exceptionally safe at recommended doses, paracetamol has a narrow therapeutic window.

- Hepatotoxicity: Overdose, whether intentional or unintentional (through cumulative dosing), can cause severe, sometimes fatal, liver necrosis due to the saturation of glucuronidation and sulfation pathways and the subsequent accumulation of a toxic metabolite, N-acetyl-p-benzoquinone imine (NAPQI).
- Risk Mitigation: Adherence to maximum daily doses (4 grams for adults, often lower for the elderly or those with liver impairment) is crucial. The availability of a specific antidote, N-acetylcysteine, has improved outcomes in cases of overdose.

6. Conclusion and Clinical Implications

Paracetamol is an indispensable and versatile drug in the modern therapeutic arsenal. Its efficacy in treating pain and fever, combined with its favorable safety profile in appropriate doses, ensures its continued status as a first-line analgesic. In surgical practice, its integration into multimodal analgesia protocols is a cornerstone of enhanced recovery, effectively minimizing opioid consumption and its associated complications. Ongoing education on its correct dosing and awareness of its potential hepatotoxicity are essential for maximizing its benefits and ensuring patient safety across all clinical settings.

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РЕНАЛЬНА ДЕНЕРВАЦІЯ ПРИ РЕЗИСТЕНТНІЙ АРТЕРІАЛЬНІЙ ГІПЕРТЕНЗІЇ

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Актуальність. У XXI столітті незважаючи на значний прогрес у медикаментозному лікуванні гіпертензії, у приблизно 10 % пацієнтів артеріальний тиск залишається неконтрольованим на фоні комбінації понад 3 антигіпертензивних засобі – такий стан, визначають як резистентна артеріальна гіпертензія. Активність симпатичної нервової системи, особливо ниркових симпатичних шляхів, відіграє ключову роль у патогенезі даного стану: підтриманні підвищеного тонусу, активації реніну, затримці натрію та вазоконстрикції. Саме через це, ми у нашому дослідженні розглянемо один з інвазивних методів лікування резистентної артеріальної гіпертензії, що полягає у селективному пригнічєнні симпатичної активності ниркових нервових сплетінь. Ренальна денервація за допомогою радіочастотної абляції еферентних