Celecoxib - StatPearls - NCBI Bookshelf

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Continuing Education Activity

This activity is designed to equip healthcare professionals with the latest evidence and guidelines for safely and effectively utilizing celecoxib, a widely used nonsteroidal anti-inflammatory drug (NSAID) with diverse indications in pain management and disease prevention. Participants will be given the latest information contributing to the comprehensive understanding of celecoxib, covering its mechanism of action, pharmacokinetics, pharmacodynamics, metabolism, and elimination. The program will also explore crucial aspects such as dosing, monitoring, and potential interactions with other drugs and foods.

Furthermore, this activity will address the adverse event profile of celecoxib, including common and severe effects such as gastrointestinal ulcers, bleeding, renal impairment, cardiovascular events, and hypersensitivity reactions. Practical insights will be provided on adjusting celecoxib doses based on patient characteristics and renal function tests. Specific indications for celecoxib in conditions like osteoarthritis, rheumatoid arthritis, acute pain in adult women, primary dysmenorrhea, and familial adenomatous polyposis will be thoroughly discussed, enabling participants to make informed decisions in various clinical scenarios. By completing this program, healthcare professionals will enhance their knowledge, skills, and confidence in prescribing and discussing celecoxib, ultimately improving patient outcomes and promoting safer medication practices in their clinical practice.

Objectives:

- Identify appropriate clinical scenarios where celecoxib can be beneficial, considering its mechanism of action and indications.
- Screen patients for contraindications or risk factors that may impact the safe use of celecoxib.
- Assess patient response to celecoxib therapy, which includes monitoring pain relief, adverse events, and any necessary dose adjustments, allowing clinicians to tailor treatment and optimize outcomes.
- Develop communication with patients about the benefits, risks, and potential adverse effects of celecoxib to enable informed consent and shared decision-making, empowering patients to participate in their treatment actively.

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Indications

Celecoxib is a selective (COX-2) non-steroidal anti-inflammatory drug (NSAID) that received a patent in 1993.

FDA-Approved Indications

- Osteoarthritis
- Rheumatoid arthritis
- Ankylosing spondylitis
- Dysmenorrhea
- Acute pain
- Acute migraine (oral solution formulation only)

Off-Label Uses

- Gout [2][3]
- Familial adenomatous polyposis (to lower the risk of colorectal adenomas) [4]

The drug is also being used increasingly in hospital protocols as part of a multimodal perioperative pain management regimen, frequently given pre-operatively along with adjunct pain medications, including acetaminophen or pregabalin.

Mechanism of Action

Celecoxib is chemically designated 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl] benzenesulfonamide and is a diaryl-substituted pyrazole. The mechanism of celecoxib's action is due to the selective inhibition of cyclooxygenase-2 (COX-2), responsible for prostaglandin synthesis, an integral part of the pain and inflammation pathway. This pharmacologic activity gives celecoxib its analgesic, anti-inflammatory, and antipyretic effects. Celecoxib also weakly inhibits COX-1, affecting platelet function less than aspirin.

Celecoxib also has anticancer properties discussed below and exerts its anticancer properties by binding cadherin-11 (CDH11), which likely plays a significant role in the malignant progression of cancerous cells.

Pharmacokinetics

Absorption:

Celecoxib undergoes rapid absorption in the GI tract, with peak plasma levels achieved within 3 hours of a single dose.

Distribution:

The steady-state volume of distribution of celecoxib is about 429 L, suggestive of broad distribution into various tissues.

Metabolism:

Celecoxib is extensively metabolized through cytochrome P450 2C9 (CYP2C9) and may interact with other medications that are substrates of CYP2C9.[9]

Elimination:

Celecoxib has a half-life of 11.2 hours. The drug is primarily eliminated via hepatic metabolism, with a small amount of the drug unchanged in the feces. When taken orally, about 57% of the dose is excreted in the feces and 27% in the urine as metabolites.

Administration

Dosage Forms and Strengths

Celecoxib is a medication taken orally and is available in capsule form in 50, 100, 200, and 400 mg doses. In rare cases, celecoxib can also be added to customized compounds for topical administration with or without iontophoresis or other topical delivery mechanisms. Celecoxib also comes in an oral solution of 120 mg/4.8 mL (25 mg/mL).

Adult Dosing

Osteoarthritis: 200 mg orally daily or 100 mg twice daily.

Rheumatoid Arthritis: 100 to 200 mg orally twice daily, using the lowest effective dose.[10]

Ankylosing Spondylitis: 200 mg by mouth daily. Dosing can increase to 400 mg. Always use the lowest effective dose for the shortest possible treatment duration. Prescribers should consider discontinuing the drug if there is no response at the highest dose after 6 weeks.

Dysmenorrhea: 200 mg by mouth twice daily. Dosing can increase to 400 mg. Always use the lowest effective dose for the shortest possible treatment duration. Prescribers should consider discontinuing the drug if there is no response at the highest dose after 6 weeks.

Acute Pain: 200 mg orally twice daily; patients can start with 400 mg for a single dose on day 1 of therapy, with an additional 200 mg on the first day if necessary.

Acute migraine: (Oral solution only) 120 mg orally, with or without food.[11]

All doses should be given with food if GI upset occurs. In patients who are poor CYP2C9 metabolizers, consider starting at 50% of the lowest dose.

Special Patient Populations

Hepatic impairment: Avoid use in hepatic insufficiency if the patient is Child-Pugh Class C. For Child-Pugh Class B, decrease the dose by 50%.

Renal impairment: CrCl >60 requires no adjustment. CrCl of 30 to 60 is undefined. Avoid use in renal impairment of creatinine clearance is less than 30 mL/s.

Pregnant women: Clinicians should weigh the risks vs benefits if the patient is under 30 weeks gestation, especially from 20 to 29 weeks gestation; limit dose and duration; and consider amniotic fluid monitoring if the drug is used for more than 48 hours. Avoid using celecoxib after 30 weeks of gestation.

Breastfeeding women: Celecoxib can be used while breastfeeding; human data shows no known risk of infant harm.

Pediatric patients: Juvenile idiopathic arthritis (age 2 and older):

- 10 to 25 kg: 50 mg orally twice daily; use the lowest effective dose for the shortest duration possible.
- >25 kg: 100 mg twice daily; use the lowest effective dose for the shortest duration possible.

Older patients:

Appropriate studies to date have shown no specific problems that would limit the use of celecoxib in older patients. However, this population is more prone to renal, hepatic, and GI issues, so monitor for renal and hepatic impairment and signs of GI bleeding.

Adverse Effects

Celecoxib is a generally safe and well-tolerated agent; its risks are similar to most other NSAIDs. Common adverse events include dyspepsia, diarrhea, abdominal pain, nausea, vomiting, and elevated AST/ALT or BUN.

Severe adverse reactions to celecoxib include GI bleeding or perforation/ulcer, MI, stroke, and thromboembolism. In addition to these, celecoxib may cause new or worsening hypertension, fluid retention in patients with congestive heart failure, renal toxicity, liver toxicity, anaphylactic reactions, and skin changes ranging from a non-severe rash to Stevens-Johnson syndrome.

Contraindications

Due to its cardiovascular risk, celecoxib is contraindicated for the treatment of perioperative pain in the setting of coronary artery bypass graft (CABG) surgery.

Celecoxib also contains a sulfonamide group and is contraindicated in patients who have demonstrated severe allergic reactions to drugs with a sulfonamide group (eg, sulfamethoxazole). Studies have shown that allergies to sulfonamide antimicrobials are a risk factor for allergic reactions to the sulfonamide chemical group. A history of penicillin allergy is at least as strong a risk factor for an allergic reaction. Thus, providers should understand that this phenomenon is likely not solely due to the cross-reactivity of sulfonamide-containing antimicrobials and non-antimicrobials and that certain patients have an increased propensity to celecoxib allergy if allergic to any antimicrobial drug.

Since CYP2C9 metabolizes celecoxib, its use requires caution in patients taking medicines that inhibit CYP2C9, eg, fluconazole, an antifungal drug. As with all NSAIDs, celecoxib should not be taken after 29 weeks of pregnancy because of the risk of patent ductus arteriosus.

Box Warning

Like all NSAIDs, celecoxib carries an FDA box warning for cardiovascular risk, including an increased risk of heart attacks and strokes. As a selective COX-2 inhibitor, celecoxib also faces scrutiny for increased cardiovascular risk due to another selective COX-2 inhibitor, rofecoxib, being withdrawn from production in 2004 due to cardiovascular risk concerns. Extensive reviews have had mixed results regarding whether celecoxib carries non-inferior or increased cardiovascular risk compared to ibuprofen and naproxen.

Like all NSAIDs, celecoxib also carries an additional FDA box warning for gastrointestinal (GI) effects, including bleeding, ulceration, and perforation of the stomach and intestines. This adverse effect makes it particularly dangerous to susceptible populations such as older patients.

Monitoring

Monitoring includes serum creatinine at baseline. In older patients, check for renal or hepatic impairment, CHF, dehydration, or hypovolemia. Prescribers should monitor a patient's blood pressure and renal and liver function and monitor for signs and symptoms of GI bleeding, especially with long-term usage.

Prescribers need to monitor patients for adverse drug reactions due to the risk of celecoxib causing new or worsening hypertension, fluid retention in patients with congestive heart failure, renal toxicity, liver toxicity, anaphylactic reactions, and skin changes ranging from a non-severe rash to more severe reactions including Stevens-Johnson syndrome.

Patients taking medications such as lithium or warfarin should have the concentrations of these drugs monitored more carefully as well due to celecoxib's renal toxicity and inhibition of CYP2C9, respectively. Plasma concentrations of celecoxib are not routinely part of the monitoring to determine therapeutic efficacy.

Toxicity

Unfortunately, no antidote is available for celecoxib overdose. However, celecoxib is a relatively safe medication. There were no reported overdoses of celecoxib during FDA trials, and doses up to 2400 mg per day for 10 days did not result in severe toxicity.

Symptoms of celecoxib overdose would likely be similar to overdoses of other NSAIDs, which include lethargy, drowsiness, nausea, vomiting, and epigastric pain. Activated charcoal may be administered for overdose treatment at the discretion of emergency medical providers if the patient presents within 4 hours of known or suspected ingestion of significant amounts of celecoxib. Due to high plasma protein binding, dialysis, urine alkalinization, or diureses are unlikely to have a significant therapeutic effect on celecoxib overdose.

Enhancing Healthcare Team Outcomes

Significant opportunities are available for improved interprofessional care coordination about celecoxib. In the inpatient setting, celecoxib is increasingly being used as part of pre-operative and post-operative multimodal pain management algorithms. Study results have shown that administering celecoxib peri-operatively for elective procedures such as total hip arthroplasties, total knee arthroplasties, and other procedures demonstrates some success in reducing pain and improving functionality such as early ambulation. The use of non-opioid medications to improve pain and function after surgery is becoming increasingly important due to societal and political pressure to reduce overall opioid analgesic consumption as a response to increasing rates of overdose deaths.

Therefore, all interprofessional healthcare team members, including physicians, advanced practice practitioners, nursing staff, pharmacists, physical and occupational therapists, and other support staff, must coordinate a concerted effort to set patient-specific goals regarding pain and function in the acute care and rehabilitative settings and to reinforce how celecoxib use can help to achieve these goals to the patient. Clinicians and the interprofessional health care team must also maintain constant and open communication while monitoring the patient for improvements in pain and function and for possible adverse effects the patient may be experiencing. This interprofessional approach will yield the best therapeutic results while minimizing the chance of adverse events.

In the outpatient setting, prescribers of celecoxib must also coordinate with pharmacists to prevent and monitor for unsafe drug interactions and with the patient, family members, and caregivers to monitor therapeutic benefits and possible adverse drug effects. When the caregivers function as

a coordinated interprofessional team, patients can obtain maximum benefit from celecoxib with minimal adverse effects.

Review Questions

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