****

**Parecoxib sequential with imrecoxib for occurrence and remission of severe acute pancreatitis**

Huang L, Feng Z, Yang W, et al. Parecoxib sequential with imrecoxib for occurrence and remission of severe acute pancreatitis: a multicentre, double-blind, randomised, placebo-controlled trial. Gut 2025;74(9): 1467-1475. doi: 10.1136/gutjnl-2024-334038.

This large multicentre randomised controlled trial looked at whether cyclooxygenase-2 inhibitors (COX-2Is) can change the course of acute pancreatitis. Severe acute pancreatitis (SAP) remains a very serious condition, with mortality rates of 20–40%, mainly driven by persistent organ failure and infected necrosis. Presently, management is supportive, with no proven drug that alters outcomes.

In this study, 348 patients with predicted SAP were randomised to receive either sequential COX-2 inhibition (intravenous parecoxib for three days, followed by oral imrecoxib for 30 days) or placebo, on top of standard care. The main outcome was duration of organ failure. Results were striking: patients in the COX-2I group had shorter organ failure (median 4 vs. 7 days) and fewer developed SAP (62% vs. 78%). Respiratory failure was the most common problem, and its duration, as well as need for mechanical ventilation, were both significantly reduced in the treatment arm.

Importantly, COX-2Is were also linked to fewer local complications (pseudocysts, necrotic infection), lower systemic inflammatory markers, shorter hospital stays, and reduced 30-day mortality (3.4% vs. 8.6%). Treatment costs were also lower. The regimen was well tolerated, with only a small number of gastrointestinal bleeds, not clearly drug related. Patients enrolled earlier (within 48 hours of symptom onset) seemed to benefit most, but even later treatment shortened organ failure duration.

In conclusion this trial offers high-quality evidence that COX-2 inhibition could be the first disease-modifying treatment for SAP. If confirmed in further studies, it has the potential to change routine practice by improving survival and reducing complications.