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**Rectal diclofenac versus indomethacin for prevention of post-ERCP pancreatitis (DIPPP)**

**Rectal diclofenac versus indomethacin for prevention of post-ERCP pancreatitis (DIPPP): a multicentre, double-blind, randomised, controlled trial. *Gut* 2025; 74(7): 1094-1102. doi: 10.1136/gutjnl-2024-334466.**

Post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis (PEP) is a common complication, occurring in up to 10% of patients, with higher risks in certain subgroups. Nonsteroidal anti-inflammatory drugs (NSAIDs) like diclofenac and indomethacin are recommended for prophylaxis, but their comparative efficacy remains unclear. A multicentre, double-blind, randomised controlled trial (DIPPP, NCT03947861) across nine Chinese tertiary centres compared 100 mg rectal diclofenac versus 100 mg rectal indomethacin for preventing post-ERCP pancreatitis (PEP). The study enrolled 1204 patients (aged 18–90) with native papilla undergoing ERCP, randomised 1:1 to receive either drug before the procedure. The primary outcome was the incidence of PEP, with secondary outcomes including other ERCP-related complications.

The trial was terminated early for futility following a scheduled interim analysis. Baseline characteristics were balanced. PEP occurred in 8.8% (53/600) of the diclofenac group and 6.1% (37/604) of the indomethacin group (relative risk 1.44, 95% CI 0.96–2.16, p=0.074), showing no significant difference. In high-risk patients (e.g., sphincter of Oddi dysfunction, prior PEP, difficult cannulation, multiple pancreatic duct injections), PEP rates were 14.2% (35/247) vs. 9.8% (26/266) for diclofenac vs. indomethacin (p=0.124); low-risk rates were 5.1% (18/353) vs. 3.3% (11/338) for diclofenac vs. indomethacin (p=0.227). Other complications, like bleeding and infection, were similar. Subgroup analyses showed consistent results across sex, age, procedural difficulty, and pancreatic duct instrumentation.

These findings confirm that both NSAIDs are equally effective for prophylaxis, supporting their interchangeable use in clinical practice to reduce PEP risk, particularly in high-risk patients, while highlighting the value of interim analyses for trial efficiency.