Medical Prevention of Post-ERCP Pancreatitis

Byung Moo Yoo, M.D., Ph.D.
Dept. of Gastroenterology, Ajou University School of Medicine, Suwon, Korea

Pancreatitis is the most common complication of endoscopic retrograde cholangiopancreatography (ERCP)\textsuperscript{1,2}, with a reported incidence ranging from 1.8\% to 7.2\% in most prospective series\textsuperscript{3,4}. Numerous attempts have been made to identify a pharmacological agent that could be used to reduce the incidence and severity of PEP. An ideal agent should be highly effective in reducing PEP, safe for the patient, well tolerated, relatively affordable, and not require a prolonged administration time.\textsuperscript{5}

Rectally administered nonsteroidal anti-inflammatory drugs

Many studies were reported about rectal indomethacin or diclofenac.\textsuperscript{6-9} A meta-analysis of these RCTs, involving 912 patients, demonstrated a robust 64\% reduction in PEP associated with rectal NSAIDs (relative risk, 0.36; 95\% confidence interval, 0.22-0.60) and no increase in associated adverse events.\textsuperscript{10} Rectal NSAIDs (100 mg diclofenac or indomethacin immediately before or after ERCP) can be recommended for patients undergoing high-risk ERCP. Controversy remains regarding the role of NSAIDs in low-risk cases. The European Society of Gastrointestinal Endoscopy recommends rectal indomethacin or diclofenac for almost all patients undergoing ERCP as a grade A recommendation.\textsuperscript{11} Rectally administered indomethacin and diclofenac are appropriate for clinical use at a dose of 100 mg immediately before or after ERCP in high-risk cases; strong consideration should be given to their use in low-risk cases.

Nitroglycerin

Nitroglycerin is a smooth muscle relaxant that may lower sphincter of Oddi (SO) pressure and increase pancreatic parenchymal blood flow.\textsuperscript{12} Few studies have been performed for the prevention of PEP. However, there are conflicting results.\textsuperscript{13-19} A recent small comparative effectiveness RCT demonstrated that the combination of sublingual nitroglycerin plus rectal indomethacin was more effective than indomethacin alone in a study sample that largely did not receive a pancreatic stent.\textsuperscript{20} The use of sublingual nitrates may be considered in patients with NSAID allergy or as an adjunct to NSAIDs in high-risk patients who do not/cannot receive a prophylactic pancreatic stent.\textsuperscript{21}
Somatostatin

Somatostatin is a potent inhibitor of pancreatic exocrine function and may therefore prevent or mitigate the pathophysiological processes that lead to pancreatic inflammation. Benefit has been demonstrated more consistently with bolus administration (3 of 5 published studies positive) than with infusion (3 of 8 published studies positive). An RCT of somatostatin in combination with diclofenac demonstrated benefit. Because of these inconclusive but promising results, a confirmatory RCT of bolus somatostatin (the most practical and likely cost-effective approach) is necessary.

Nafamostat

Nafamostat mesylate is a low-molecular weight protease inhibitor that inhibits trypsin, a proteolytic enzyme considered to play an initial role in the pathogenesis of pancreatitis. Nafamostat has a half-life that is 20 times longer and a potency 10-100 times greater than gabexate mesylate. A recent meta-analysis demonstrated approximately 60% benefit associated with nafamostat (relative risk, 0.41; 95% confidence interval, 0.28-0.59).26 Major concerns related to the use of nafamostat are its high cost, need for a prolonged intravenous infusion (7-25 hours), and apparent absence of benefit in high-risk cases.21

In summary, only rectal NSAIDs can be recommended for pharmacologic PEP prophylaxis in clinical practice. Interested investigators should consider the findings of this systematic review when selecting agents and dosing regimens for future RCTs of PEP pharmacoprevention. A systematic and evidence-based approach to study selection as well as a commitment to conducting high-quality clinical trials may improve our research success in this traditionally disappointing area.

References