

Oral N-Acetyl cysteine versus rectal indomethacin for prevention of post ERCP pancreatitis: A Multicenter Multinational Randomized Controlled Trial

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Abstract

Introduction: Acute pancreatitis as most important complication of ERCP, reported to occur in 2–10% of patients undergoing ERCP overall and up to 40% in high-risk patients. Rectal Indomethacin is accepted as an effective modality in the prevention of post-ERCP pancreatitis (PEP) based on a multicenter RCT but there is conflicting data from other studies. The efficacy of

oral or IV N-acetyl cysteine (NAC) in the prevention of PEP is unclear based on studies with discrepant results. so this multicenter multinational RCT designed to evaluate and compare efficacy of suppository indomethacin and NAC for prevention of PEP.

Method: During a 6 month period, all of the patients who met standard indications for ERCP in 7 referral centers of 4 countries were randomly assigned to four groups to receive either 1200 mg oral NAC in 150cc water (group A), indomethacin suppository 100mg (group B), 1200 mg oral NAC in 150cc water plus indomethacin suppository 100mg (group C) or 250cc water as placebo (group D) one hour before ERCP. The primary outcomes were the rate and severity of any PEP among participants. The study registered as IRCT20201222049798N1.

Results: a total of 432 patients included (average age 57.3 y, range 16 to 99, 41.4% male) during the study period. The participants were originally citizens of 6 countries and about 60.87% of the study population were of Caucasian descent. The most common indication for ERCP was Choledocholithiasis (66.89%). The patients were randomly allocated to receive either NAC (group A, 84 case), rectal indomethacin (group B, 138 cases), NAC + rectal indomethacin (group C, 115 cases) or placebo (group D, 95 cases). The rate of bleeding and perforation after procedures was 3.94% and 2.54% respectively.

The rate of post ERCP pancreatitis (PEP) in groups A (NAC), B (indomethacin) and C (NAC + indomethacin) in comparison with D (placebo) were 10.7%, 17.4%, 7.8% vs. 20% (P = 0.0[^], 0.614 & 0.01 respectively). The NNT for NAC, indomethacin and NAC + indomethacin were 11, 38 and 8 respectively. 65.5% of the PEP cases were mild with average duration of hospital stay 4.5 days (range 1 to 14 days). The rate of abdominal pain after ERCP in groups A, B, C in comparison with D (placebo) were 28.6%, 33.3%, 19.1% vs. 27.4% (P = 0.85, 0.33 & 0.15 respectively). Average duration of hospital stay after ERCP in groups A, B, C in comparison with D were 3.6 days, 2.6 days, 2.8 days vs. 3.7 days (P= 0.396, 0.010 & 0.012 respectively).

Conclusion: Oral NAC is more effective than rectal indomethacin when compared to placebo for prevention of PEP and the combination of NAC and Indomethacin had the lowest incidence of PEP and may have synergistic effect in prevention of PEP.