Indomethacin and diclofenac in the prevention of post-ERCP pancreatitis: a systematic review and meta-analysis of prospective controlled trials CME

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Background and Aims: Diclofenac and indomethacin are the most studied drugs for preventing post-ERCP pancreatitis (PEP). However, there are no prospective, randomized multicenter trials with a sufficient number of patients for correct evaluation of their efficacy. Our aim was to evaluate all prospective trials published in full text that studied the efficacy of diclofenac or indomethacin and were controlled with placebo or non-treatment for the prevention of PEP in adult patients undergoing ERCP.

Methods: Systematic search of databases (PubMed, Scopus, Web of Science, Cochrane) for relevant studies published from inception to 30 June 2016.

Results: Our meta-analysis of 4741 patients from 17 trials showed that diclofenac or indomethacin significantly decreased the risk ratio (RR) of PEP to 0.60 (95% confidence interval [CI], 0.46-0.78; $P = .0001$), number needed to treat (NNT) was 20, and the reduction of RR of moderate to severe PEP was 0.64 (95% CI, 0.43-0.97; $P = .0339$). The efficacy of indomethacin compared with diclofenac was similar ($P = .98$). The efficacy of indomethacin or diclofenac did not differ according to timing ($P = .99$) or between patients with average-risk and high-risk for PEP ($P = .6923$). The effect of non-rectal administration of indomethacin or diclofenac was not significant ($P = .1507$), but the rectal route was very effective ($P = .0005$) with an NNT of 19. The administration of indomethacin or diclofenac was avoided in patients with renal failure. Substantial adverse events were not detected.

Conclusions: The use of rectally administered diclofenac or indomethacin before or closely after ERCP is inexpensive and safe and is recommended in every patient (without renal failure) undergoing ERCP. (Registration number: CRD42016042726, http://www.crd.york.ac.uk/prospero/.) (Gastrointest Endosc 2017;85:1144-56.)

Abbreviations: CI, confidence interval; NNT, number needed to treat; NSAID, non-steroidal anti-inflammatory drug; PEP, post-ERCP pancreatitis; RCT, randomized controlled trial; RR, risk ratio; ULN, upper limit of normal.

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INTRODUCTION

One of the greatest challenges for endoscopists performing ERCP is to decrease the frequency of post-ERCP pancreatitis (PEP). Since 1978, several basic studies and clinical recommendations have dealt with pharmacologic agents in the prevention of PEP. Diclofenac and indomethacin seem to be the most promising drugs for preventing PEP[1-8]; nevertheless, a comprehensive consensus has not emerged with regard to their efficacy. The results of trials with too few patients[9] differ; therefore a multicenter, carefully planned prospective, randomized, double-blind trial or meta-analysis with a sufficient number of patients can resolve this contradiction. In the absence of such original works, we have collected all prospective trials studying the efficacy of diclofenac or indomethacin for all routes of administration controlled with placebo or

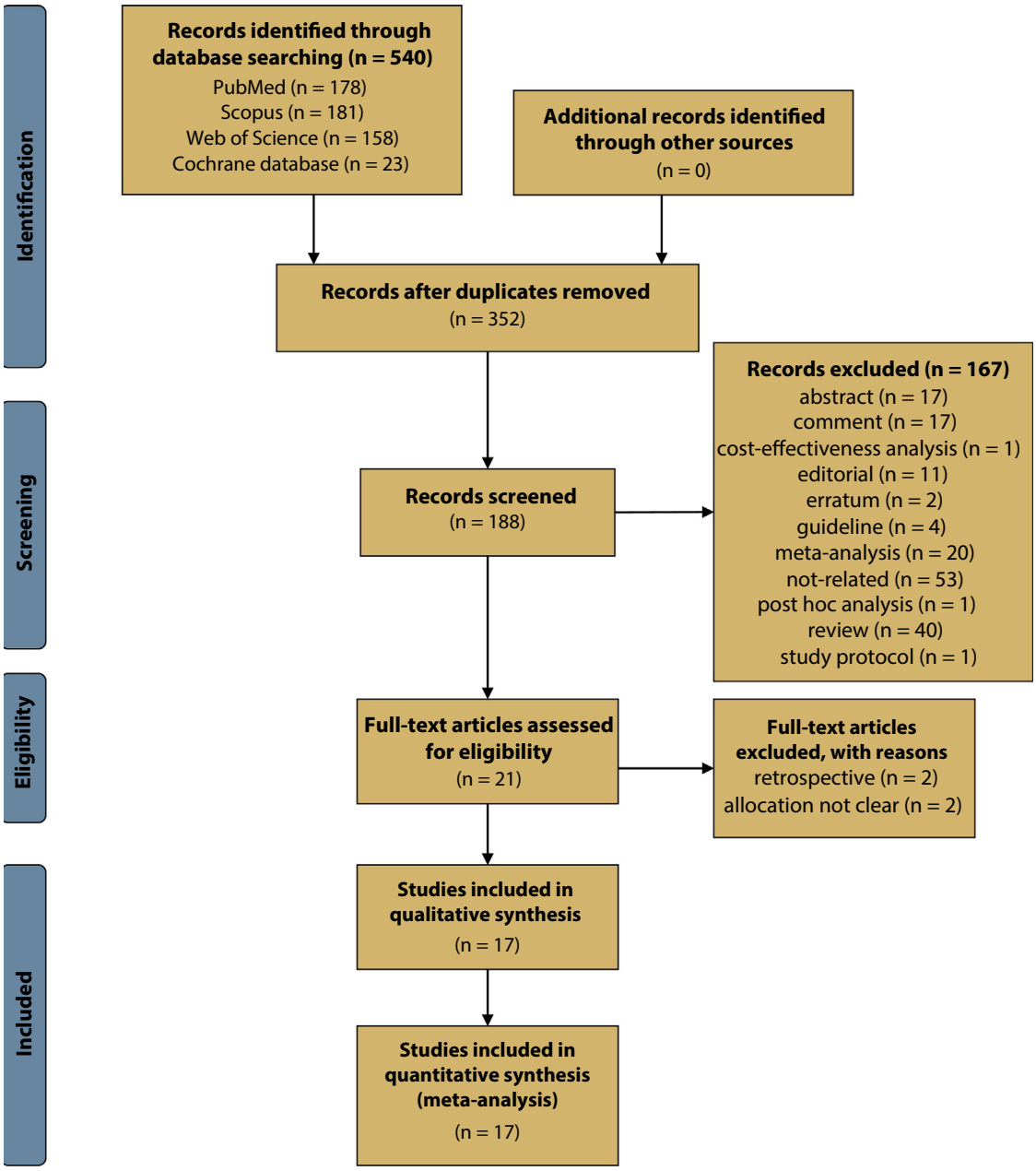

Figure 1. PRISMA flowchart of included and excluded trials.

non-treatment for the prevention of PEP in adult patients undergoing ERCP.

METHODS

Protocol and registration

This study was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[10] The review protocol is registered at the International Prospective Register of Systematic Reviews (PROSPERO), which can be accessed at http://www.crd.york.ac.uk/prospero/ under registration number CRD42016042726.

Eligibility criteria

Studies were included if they were prospective, controlled studies published in full text irrespective of language or publication status.

Information sources and search strategy

The electronic databases PubMed (1990 to 30 June 2016), Scopus (1995 to 30 June 2016), Web of Science (1990 to 30 June 2016), and the Cochrane Central Register of Controlled Trials (1993 to 30 June 2016) were searched, using the free text terms "indomethacin," "diclofenac," "NSAID," and "post ERCP pancreatitis." The full electronic search strategy can be accessed in the