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[Intervention Review]

Proton pump inhibitors for functional dyspepsia

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ABSTRACT

Background

Functional dyspepsia (FD or non-ulcer dyspepsia) is defined as continuous or frequently recurring epigastric pain or discomfort for which no organic cause can be found. Acid suppressive therapy, including proton pump inhibitors (PPIs), has been proposed as a therapeutic option in FD, but its efficacy remains controversial. While PPIs are generally considered safe and well tolerated, they have been associated with adverse events, especially in the long term. For this reason, decisions on whether to initiate or continue PPI therapy should be made based on an appropriate clinical indication. Therefore, we conducted a systematic review to evaluate whether PPI therapy provides symptomatic relief in FD.

Objectives

To determine the efficacy of proton pump inhibitors in the improvement of global symptoms of dyspepsia and quality of life compared to placebo, H₂ receptor antagonists or prokinetics, in people with functional dyspepsia.

Search methods

We searched in the following electronic databases: the Cochrane Library (to May 2017), MEDLINE (OvidSP; to May 2017), Embase (OvidSP; to May 2017), and SIGLE grey literature (up to May 2017) and clinical trial registries; we handsearched abstracts from conferences up to May 2017. We screened non-systematic reviews, systematic reviews and guidelines to identify any additional trials. We contacted trialists to obtain missing information.

Selection criteria

All randomized controlled trials (RCTs) comparing any PPI with placebo, H₂ receptor antagonists (H₂RAs) or prokinetics for the treatment of FD of at least two weeks' duration. Participants were adults (aged 16 years or greater) with an adequate diagnosis of FD (any validated criteria such as Rome I, II, III or Lancet Working Group).

Data collection and analysis

Two review authors independently assessed eligibility and trial quality, and extracted data. We collected data on dyspeptic symptoms, quality of life and number of overall adverse events. Specific adverse events were beyond the scope of this review.

Main results

We identified 25 RCTs from 27 papers (with 8453 participants) studying the effect of PPIs versus placebo, H₂RAs or prokinetics for improvement of global symptoms of dyspepsia and quality of life in people with FD. Low-dose PPIs had similar efficacy as standard-dose PPIs, therefore we combined these subgroups for the analysis. PPI was more effective than placebo at relieving overall dyspepsia symptoms in people with FD (risk ratio (RR) 0.88, 95% confidence interval (CI) 0.82 to 0.94; participants = 6172; studies = 18; number needed to treat

for an additional beneficial outcome (NNTB) 11; moderate quality evidence). PPIs may have little or no effect compared with H2RAs (RR 0.88, 95% CI 0.74 to 1.04; participants = 740; studies = 2; low quality evidence), and may be slightly more effective than prokinetics (RR 0.89, 95% CI 0.81 to 0.99; participants = 1033; studies = 5; NNTB 16; low quality evidence) at relieving overall dyspepsia symptoms in people with FD. PPIs plus prokinetics have probably little or no effect compared with PPIs alone at relieving overall dyspepsia symptoms (RR 0.85, 95% CI 0.68 to 1.08; participants = 407; studies = 2; moderate quality evidence).

There was no difference when subgrouped by *Helicobacter pylori* status, country of origin, or presence of reflux or Rome III subtypes. There were no differences in the number of adverse events observed between PPIs and any of the other treatments. There were fewer adverse events in the combination of PPI plus prokinetics compared to prokinetics alone (RR 0.60, 95% CI 0.39 to 0.93; participants = 407; studies = 2; moderate quality evidence).

Authors' conclusions

There is evidence that PPIs are effective for the treatment of FD, independent of the dose and duration of treatment compared with placebo. PPIs may be slightly more effective than prokinetics for the treatment of FD; however, the evidence is scarce. The trials evaluating PPIs versus prokinetics are difficult to interpret as they are at risk of bias. Although the effect of these drugs seems to be small, the drugs are well tolerated.

PLAIN LANGUAGE SUMMARY

Proton pump inhibitors for functional dyspepsia

Review question

How effective are medicines that suppress stomach acid for the treatment of indigestion in adults with no other major disease?

Background

Acid suppression is a possible treatment for functional dyspepsia (indigestion), which is recurring pain over the stomach, bloating, burping or the feeling of being full. Several medicines are used to treat functional dyspepsia; proton pump inhibitors (PPIs) and H2 receptor antagonists (H2RAs) reduce stomach acid, and prokinetics accelerate stomach emptying. There is no clear evidence that one medicine is more effective than another. Although these are considered safe, a few people have side effects. The most common side effects are headache, tummy (abdominal) pain, bloating, diarrhoea and feeling sick (nausea). Long-term use of PPIs has been associated with infectious diarrhoea (inflammation of the stomach and small intestine), bone fracture and bacterial overgrowth. Therefore, we need to know whether these medications are effective and safe for people with indigestion.

Search date

We searched medical databases for clinical trials in which treatment was allocated by chance (called randomized controlled trials) in adults with functional dyspepsia up to May 2017. We included results from 25 studies from 27 publications. We found two studies awaiting further details and no other ongoing studies.

Study characteristics

We included 25 studies (with 8453 participants). There were six studies (2304 participants) comparing low-dose PPIs versus standard-dose PPIs (the dose used in clinical practice); 18 studies (6172 participants) comparing PPIs with placebo (pretend treatment); two studies (740 participants) comparing PPIs with H2RAs; five studies (1033 participants) comparing PPIs with prokinetics and two studies (407 participants) comparing PPIs plus prokinetics versus prokinetics alone.

The duration of the treatment lasted at least two weeks. Seven studies reported treatment for two weeks, 12 studies reported treatment for four weeks and five studies reported more than six weeks of treatment. The treatment period was unclear in one study.

Study funding sources

Seventeen of the 25 studies were sponsored or funded by a pharmaceutical company and two by an institution grant. There was no information on funding in eight studies.

Key results

Our review showed that PPIs are more effective than placebo, and are probably slightly more effective than prokinetics for the treatment of functional dyspepsia. Low-dose and standard-dose PPIs were similarly effective on the relief of indigestion, so we combined the results of the two doses of PPI. PPI was more effective than placebo, with 31% of the PPI group reporting no or minimal symptoms compared with 26% of the placebo group. The effect of PPI was probably slightly more effective than H2RAs; however, the two studies involved in the analysis were so different that it may have influenced the results. There was no difference in the number of reported side effects when comparing PPIs, H2RAs and prokinetics.

Quality of the evidence

The studies evaluating the effect of PPIs compared to placebo or PPIs combined with prokinetics versus prokinetics were in general of good quality. However, the studies that compared PPIs versus H2RAs and prokinetics had serious quality issues.