**Dyspepsia: Test and treat for *H pylori* or start PPIs?**

**Start empiric PPIs.** In patients with undifferentiated dyspepsia symptoms (epigastric pain with or without heartburn but without a specific diagnosis), empiric acid suppression (omeprazole 20 mg daily for 1 month) and testing for and treating *Helicobacter pylori* infection had similar results.

The percentage of patients who were symptom free at 1 year was similar between the 2 groups. Increased costs of testing were offset by decreased costs in subsequent testing and procedures.


**Level of evidence**

1b: Individual randomized controlled trials (with narrow confidence interval)

Is it reflux? Peptic ulcer? So-called functional dyspepsia? The trend in primary care is toward empiric treatment to control symptoms, and away from a strict diagnosis in patients who have no alarm symptoms such as hematemesis.

This study enrolled 699 adults with general symptoms of epigastric pain, heartburn, or both, lasting for at least 4 weeks but without alarm symptoms. Using concealed allocation, the patients were randomly assigned to 1 of 2 intervention groups.

The test-and-treat group was tested for *H pylori* using the urea breath test; 29% had positive results and were treated with eradication therapy and 1 month of acid suppression with a low-dose proton pump inhibitor (omeprazole 20 mg daily). Patients with negative test results were treated only with acid suppression.

Patients in the empiric treatment group did not undergo testing but received the same dose and duration of acid suppression.

Using intent-to-treat analysis, the cost, percent of patients who were symptom free at the end of 12 months, and quality of life were compared. Final results were expressed as quality-adjusted life years. Data were available for 76% of patients.

**Similar quality of life at 1 year**

No difference was noted between the test-and-treat group and the empiric acid suppression group, in number of patients with symptoms at 1 year, quality of life, or costs. The increased initial cost of *H pylori* testing was offset by decreases in costs incurred by other imaging.

**STUDY DETAILS**

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Oral or IV steroids for inpatient COPD?

**Oral steroids** are as effective as intravenous (IV) steroids for nonsevere exacerbations of chronic obstructive pulmonary disease (COPD). Because oral steroids are cheaper and less invasive, they are preferred.


**Level of evidence**

1b: Individual randomized controlled trials (with narrow confidence interval)

Although the oral bioavailability of corticosteroids is excellent, many physicians persist in using IV steroids for patients with exacerbations of COPD.

In this study, 210 hospitalized adults older than 40 years with COPD and at least 24 hours of exacerbation were randomized to receive 5 days of oral or IV prednisolone (60 mg daily) followed by a tapering oral dose. Patients with a severe exacerbation (pH <7.26 or PaCO₂ >9.3 kPa) were excluded. Allocation was concealed and patients were randomized using a “minimization protocol” that balances groups for key variables such as age, sex, smoking history, and supplemental oxygen use.

The primary outcome was treatment failure, defined as death, admission to the intensive care unit, readmission, or the need to intensify treatment. Groups were balanced at the start of the study, and analysis was by intent to treat; withdrawals and exclusions were uncommon and similar between groups.

No difference was noted between groups in the primary outcome either early (ie, within 2 weeks), late (ie, after 2 weeks), or overall. The treatment failure rate was relatively high in both groups, usually because of the need to intensify treatment.

**STUDY DETAILS**

- **Design**: Randomized controlled trial (double-blinded)
- **Funding**: Unknown/not stated
- **Setting**: Inpatient (any location)

Do risks of hormone therapy persist after discontinuation?

No. This analysis of continued health outcomes 3 years after stopping hormone replacement therapy (HRT) in the active treatment group of the Women’s Health Initiative (WHI) no longer detected a significantly increased risk of cardiovascular events or invasive breast cancer compared with the control group during the postintervention phase. The initial benefit of HRT for reducing fracture risk was also no longer observed after stopping therapy. All-cause mortality risk continued to be not significantly different between the 2 groups, but the overall “global index of risk versus benefit” remained higher among women who received active hormone treatment.


**Level of evidence**

1b: Individual randomized controlled trials (with narrow confidence interval)

The WHI randomized 16,608 postmenopausal women with an intact
NSAIDs, Aspirin, and Warfarin—Serotonin release by platelets plays an important role in hemostasis. Epidemiologic studies of case-control and cohort design have demonstrated an association between use of psychoactive drugs that interfere with serotonin-reuptake and the occurrence of upper gastrointestinal bleeding. These studies have shown that concurrent use of an NSAID or aspirin may potentiate this risk of bleeding. Alteration anticoagulant effects, including increased bleeding, have been reported when SSRIs and SNRIs are coadministered with aspirin. Heparin and warfarin therapy should be carefully monitored when aspirin is initiated or discontinued. Ethanol—A clinical study has shown that desensitization does not improve the incidence of mental or motor skills caused by ethanol. However, as with all CYP inhibitors, Pristiq should be advised to avoid alcohol consumption while taking Pristiq. Potential for Other Drugs to Affect Desensitization—Intestinal—Pristiq is a substrate for CYP3A4 in a minor pathway for the metabolism of many drugs. Concurrent use of Pristiq with potent inhibitors of CYP3A4 may result in higher concentrations of Pristiq, and in increased adverse drug reactions. Based on in vitro data, drugs that inhibit CYP isozymes 1A2, 1A2, 2D6, 2C9, 2C19, and 3A4 may result in increased metabolism of these CYP isozymes. Potential for Desensitization to Other Drugs—Drug metabolism by CYP2D6, eg, warfarin, has been shown to affect the pharmacokinetics of drugs that are metabolized by these CYP isozymes. P-glycoprotein Transporter—In vitro, desensitization is not a substrate or an inhibitor for the P-glycoprotein transporter. The pharmacokinetics of Pristiq are unlikely to be affected by drugs that inhibit the P-glycoprotein transporter, and desensitization is not likely to affect the pharmacokinetics of drugs that are substrates for the P-glycoprotein transporter. Electrococcal Therapy—The clinical data establishing the risks and benefits of electrococcal therapy with Pristiq is treatment USE IN SPECIFIC POPULATIONS: Pregnancy—Pristiq should be avoided to notify their physician if they become pregnant or intend to become pregnant during therapy. Teratogenic effects—Pregnancy Category C. There are no adequate and well-controlled studies of Pristiq in pregnant women. Neonates—Pristiq should not be used during pregnancy only if the potential benefits justify the potential risks. Non-teratogenic effects: Neonates exposed to SSRIs (Serotonin and Noradrenergic Reuptake Inhibitors), or SNRIs (Selective Serotonin Reuptake Inhibitors), late in the third trimester have developed complications requiring prolonged hospitalization, respiratory support, and tube feeding. Such complications can arise immediately upon delivery. Reported clinical findings have included respiratory distress, cyanosis, apnea, anuric, increased transbilirubinemia, increased bleeding time, prolonged bleeding time, shock, vomit, hypothermia, hyperpyrexia, hyperglycemia, tremor, jitteriness, irritability, and constipation. These features are consistent with either a direct toxic effect of SSRIs and SNRIs or, possibly, a drug discontinuation syndrome. It should be noted that, in some cases, the clinical picture is consistent with serotonin syndrome (see Warnings and Precautions (5.12)). When treating a pregnant woman with Pristiq during the third trimester, the physician should consider the potential risks and benefits of treatment (see US Drug Administration (2.2)). Labor and Delivery—The effect of Pristiq on labor and delivery in pregnant women is unknown. Pristiq should be used during labor and delivery only if the potential benefits justify the potential risks. Nursing Mothers—It has been shown that Pristiq is excreted in human milk. Because of the potential for serious adverse reactions in nursing infants from Pristiq, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. If the decision is made to discontinue the drug, the infant should be monitored for adequate infant feeding and growth. The importance of breastfeeding should be considered when nursing infants from Pristiq. Pristiq should not be used by breastfeeding women if the expected benefits outweigh any possible risk. Pediatric Use—Safety and effectiveness in pediatric populations have not been established (see Warnings and Precautions (5.12)). Anyone considering the use of Pristiq in a child or adolescent must balance the potential risks with the clinical need. Geriatric Use—The clinical pharmacology of Pristiq is excerted in elderly patients. Pristiq is not expected to affect the activity of CYP2C19, CYP3A4, and other CYP enzymes. CYP2C19 is a major metabolizer of prazosin, QRS prolongation, and adverse effects of rifampicin. Pristiq and desensitization therefore, may result in decreased clearance of desensitization should be considered when determining dose (see US Drug Administration (2.2) and Clinical Pharmacology (12.7) for the full prescribing information). Renal Impairment—In subjects with renal impairment the clearance of Pristiq was decreased. In subjects with severe renal impairment (CRCL ≤ 30 mL/min) and end-stage renal disease, elimination half-life were significantly prolonged, increasing exposures to Pristiq metabolites. Desesatization therapy should be used in those patients (see US Drug Administration (2.2)) and Clinical Pharmacology (12.7). In the full prescribing information). Hepatic Impairment—The mean L1, changed from approximately 10% to 20% of those with mild hepatic impairment to approximately 10% to 15% in those with moderate and severe hepatic impairment, respectively. No adjustment in starting dosage is necessary for patients with hepatic impairment.

OVERDOSAGE: Human Experience with Overdosage—There is limited clinical experience with desensitization in humans. In postmarketing studies, no cases of fatal acute overdosage of desensitization were reported. The adverse reactions reported within 5 days of an overdose - 1000 mg that were possibly related to Pristiq included vomiting, diarrhea, anorexia, nausea, vomiting, dry mouth, paresthesia, and tachycardia. Desensitization (Pristiq) is the major active metabolite of venlafaxine. Overdose experience reported with venlafaxine (the parent drug of Pristiq) is presented below the detailed information can be found in the Overdosage in the Overdosage section of the venlafaxine package insert. In postmarketing experience, overdose with venlafaxine (the parent drug of Pristiq) has occurred predominantly in combination with alcohol and/or other drugs. In overdose events in which venlafaxine is involved, changes in level of consciousness (ranging from somnolence to coma), mydriasis, seizures, and vomiting, Electrolyte imbalances (e.g., prolongation of QT interval, bundle branch block, QRS prolongation, sinus and ventricular tachycardia, bradyarrhythmia, hypotension, miosis, muscle rigidity, convulsion, agitation, and hyperexia, and exchange transposition are unlikely to be of benefit. No specific antidotes for desensitization are known. In managing an overdose, consultation with a possible multiple drug involvement. The physician should consider contacting a poison center for additional information on the treatment of overdosage. Telephone numbers for certified poison control centers are listed in the Physicians Desk Reference®.

The Journal of FAMILY PRACTICE


This brief summary is based on Pristiq Prescribing Information W10029C001, revised February 2008.

uterus, ages 50 to 79 years, to receive either conjugated equine estrogen (CEE) plus progesterin (Prem-Pro) or matched placebo (concealed allocation assignment). The original trial was stopped after 5.6 years because of concern about an increased risk of invasive breast cancer and cardiovascular events in the intervention group. These investigators reported the continued health outcomes for 95% (n=15730) of these women 3 years after the intervention was stopped. As in the original trial, individuals masked to treatment group assignment continued to report outcomes, and analysis was by intent to treat.

The initial significantly increased risk of cardiovascular events and invasive breast cancer among women assigned to the CEE/progesterin group was no longer observed during the postintervention phase. The benefit of a reduced risk of fracture with hormonal therapy was also no longer observed after the intervention. The “global index of risk versus benefit” remained essentially unchanged, maintaining a nominally significant 12% increase for women in the active treatment group. All-cause mortality rates remained similar in the active and placebo treatment groups.

STUDY DETAILS

Design Randomized controlled trial (double-blinded)

Funding Foundation

Allocation Concealed

Setting Population-based