Noncardiac Chest Pain-Treatment Approaches

Sami R. Achem, MD, FACP, FACG, AGAF

KEYWORDS

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Noncardiac chest pain (NCCP) is a very common disorder of international proportions. In the United States, nearly 70 million patients (23% of the population) suffer from NCCP.¹ Population-based studies have also reported similar figures in: Australia, 33%;² South China, 21%;³ Argentina, 24%;⁴ and Spain, 8% to 28%.⁵ Patients with NCCP represent a significant economic impact. They account for 2% to 5% of all emergency room evaluations and are one of the most frequent causes of hospital admission in the western world.⁶ A United States household survey of functional gastro-intestinal disorders found that NCCP patients are usually gainfully employed and lose an average of 13 days of work each year.⁵

The pathophysiology of NCCP is complex and poorly understood. Several mechanisms have been identified as possible sources of pain, including gastroesophageal reflux (GER), visceral hyperalgesia, esophageal motility disorders, psychiatric dysfunction, abnormal biomechanical properties of the esophageal wall, sustained esophageal contractions, abnormal cerebral processing of visceral stimulation, and disrupted autonomic activity. 8–11 Treatment of NCCP is challenging due to the heterogeneous nature of this disorder. It is also possible that many patients suffer from more than one condition. Selection of therapy is frequently aimed at the suspected underlying process. The purpose of this article is to provide a focused review of available treatment modalities for this challenging disorder.

GASTROESOPHAGEAL REFLUX

GER is the most common cause of NCCP, and the best studied.¹² The benefits of acid inhibition in NCCP have been demonstrated during short- (1 day–2 weeks) and long-term (6–8 weeks) trials. **Tables 1** and **2**^{13–24} summarize the studies that have examined the impact of acid-inhibitory therapy in NCCP. These trials underscore the favorable effect of acid suppression in NCCP. **Table 1** shows that for long-term therapy, only two studies were double blind and placebo controlled; and one is available only as an abstract. **Table 2** shows that for short-term therapy, five studies were placebo controlled and two studies (available only as an abstract) were not. Overall, sample size is

Mayo College of Medicine, Mayo Clinic, 4500 San Pablo Road, Jacksonville, FL 32224, USA *E-mail address:* achem.sami@mayo.edu

Author, Reference, Year	Number of Cases	Type of Trial	Medication and Dosage	Outcome
Achem et al, ¹³ 1993	12 (Nutcracker and GER)	Open-label	High-dose ranitidine, 150 mg/qid, or omeprazole 20 mg bid for 8 weeks	80% improved
Stahl et al, ¹⁴ 1994	13	Open-label	Ranitidine, 150 mg/qid for 8 weeks	100% improved
Achem et al, ¹⁵ 1997	36	Double-blind, placebo- controlled	Omeprazole, 20 mg/bid for 8 weeks	81% improved on omeprazole, 6% on placebo
Chambers et al, ¹⁶ 1998	23	Open-label	Omeprazole, 40 mg bedtime for 6 weeks	Improvement, but complete resolution in only 30%
Flook et al, ¹⁷ 2007 (abstract only)	599 (Intention to treat)	Double-blind placebo- controlled	Esomeprazole, 40 mg/bid versus placebo for 4 weeks	Post-hoc analysis, esomeprazole improvement was 33.1% versus 24.9% for placebo (P = .035)

small: 12 to 36 subjects for long-term studies (with the exception of Flook's¹⁷ study, an abstract containing 599 subjects) and 17 to 68 subjects in short-term trials.

In contrast to the robust data available comparing medical to surgical therapies for the treatment of typical forms of GER, there is limited information regarding the surgical outcome for extra-esophageal GER, particularly NCCP. Furthermore, there are no randomized surgical trials. Six studies have addressed the effects of anti-reflux surgery on NCCP (Table 3).^{25–30} All are retrospective, uncontrolled studies. The results of these investigations found that between 41% and 100% of these patients obtain symptom relief. Patient selection has not been described, though it is likely to be highly selective. Complications were uncommon, but when they occurred, some were serious. All studies come from academic centers experienced in esophageal surgery, thus it is unknown how these results apply to community centers. Well-designed, prospective, controlled trials are needed to determine the efficacy of anti-reflux surgery in patients with GER related NCCP.

These studies suggest that in approaching patients with NCCP, an initial medical trial of acid suppression provides effective chest pain relief in the majority of the patients. Furthermore, the data from short-term therapeutic trials (**Table 2**) indicate that a brief course of high-dose proton pump inhibitor (PPI) therapy has the potential to serve as both a diagnostic and therapeutic approach to identify patients with GER-related chest pain.

VISCERAL HYPERALGESIA

Patients with NCCP show a heightened sensitivity to a variety of experimental esophageal stimuli such as pharmacologic provocation with cholinergic agonists,

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