Role of Rabeprazole on Chest Discomfort of Uncertain Origin
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(Received November, 2012)                 (Accepted April, 2013)

Abstract:
Chest discomfort is a common challenge to clinicians; conditions vary from benign to life threatening. The differential diagnosis includes and overlaps cardiovascular, respiratory, gastrointestinal, neuromusculoskeletal & psychiatric problems, all requiring careful history and thorough investigations. However, a significant number of cases remain undiagnosed despite meticulous investigations and thus require empirical therapy (Fagring et al, 2005; Thomas, 2012). The present study was aimed to find the effect of one of the Proton-pump inhibitors (PPIs; Rabeprazole) on patients having non-traumatic, non severe chest discomfort, diagnosis of which could not be confirmed. Forty eight eligible patients were divided into 2 groups: PPI group and placebo group. Before and after 4 weeks of therapy, they were studied with visual analog scale for pain and its frequency, duration and intensity. Rabeprazole treated patients responded much better than the placebo group. Seventy five percent were pain free or had appreciable relief in pain intensity after 4 weeks. In contrast to Rabeprazole group, in placebo group none became pain free; 45 % had marginal relief while 55 % derived no benefit. Proton-pump inhibitors are of value in the treatment of non specific chest discomfort.

Key Words: Rabeprazole, Nonspecific Chest discomfort.

Introduction:
Chest discomfort is one of the most common reasons for people to seek healthcare advice (Cayley, 2005). In most cases of clinical presentation, a thorough history taking followed by meticulous physical examination is a must. In patients with non-traumatic chest discomfort, most clinicians appear to rely on a process of ‘pattern recognition’ for most of the time. In this diagnostic approach patients are fitted to ‘prototypes’ of disease that are developed and held in the clinician’s mind, and which are subject to modification in the light of clinical examination, subsequent laboratory investigations and further development (Pottle, 2005; Ryan et al, 2002). These include:

1. Pain on exertion: indicates cardiovascular pathology, especially when their primary symptom is gripping chest discomfort (Pope et al, 2000).
2. Presence of indigestion: indicates gastrointestinal pathology and in most cases the differences between cardiac and esophageal pain can be discerned clinically, although this is problematic in 20% of instances (Bennett, 2001).
3. Presence of sharp pain and chest wall tenderness: which is often more characteristic of pulmonary conditions and musculoskeletal pain.
4. Pain confined to particular area or dermatome: may be a sign of post or evolving herpetic neuralgia (Dubinsky et al, 2004).
5. Associated emotional distress: may indicate functional basis (Bass & Mayou, 2002).

In some cases symptoms tend to overlap. These cases require a plethora of tests. Some of the investigation modalities that have to be employed to reach to any conclusion are Routine Electro Cardiograph (ECG), stress ECG and ECHO cardiology for any cardiac cause; Barium meal and pH manometry for gastrointestinal cause; chest X-ray and Computerized Tomography (CT) for lung pathology and musculoskeletal problem; psychological evaluation if there is a hint of depression in family. However, in a significant number of cases the cause does not become obvious despite careful history and meticulous examination.

The present study was confined to these non severe chest discomfort cases, cause of which was uncertain.
Material & Methods:

Selection of patients:

The study was performed at a tertiary care hospital in Kanpur from May 2011 to Sept 2012. After approval of institute’s ethics committee, an informed consent was discussed, approved and signed by all volunteers. All these participants were between 18 to 45 years of age, non alcoholic, non smoker and were otherwise healthy but with complain of non traumatic non severe chest discomfort. These cases were intensively scrutinized and allocated to respective clinical department depending on the cause ascertained. Those in which diagnosis was uncertain, were taken up for this study. A total of 62 such cases were included for the present study.

Participants thus selected were randomly assigned to take either 40 mg of Rabeprazole or a similar looking inert tablet daily.

Patients were asked for symptoms and were helped to grade the frequency, duration and particularly the intensity using the characteristics (Table I, Fig. I).

Faces rating scale (FRS):

Participants who had difficulty using the numbers on the visual/numerical rating scale were assisted with the use of the six facial expressions suggesting various pain intensities. They were asked to choose the face that best described how they felt. Here the far left face indicates ‘No hurt’ and the far right face indicates ‘Hurts worst’. Number corresponding to the face chosen was documented.

These participants were asked to report after 1 & 4 weeks and were tested again on the same scale.

The data thus obtained was evaluated by using the statistical Package for Social Science (IBM SPSS v. 20). A Wilcoxon Signed ranks test was used to analyze the percentage change.

Results:

Out 62 cases enrolled for the present study, only 48 participants completed the study; 28 in the Rabeprazole group and 20 the in placebo group. After a week of therapy these participants were again put to visual analog scale; 7.2% became pain free in Rabeprazole group; 21.4% had some relief while rest 71.4% had no relief in pain intensity. Compared to this in placebo group none became pain free, 25% had some relief, rest 75% had no relief. All these participants were counselled to continue their “medication” for another 3 weeks.

After a total of 4 weeks of therapy, study results were much more encouraging. Rabeprazole treated patients responded much better than the placebo group. Five patients became absolutely pain free (17.86%), 8 patients were almost pain free (28.57%).
Table II: Change in Chest discomfort parameters during treatment in Rabeprazole and placebo groups.

<table>
<thead>
<tr>
<th>Change in Chest discomfort</th>
<th>Rabeprazole (n=28)</th>
<th>Placebo (n=20)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>At baseline</td>
<td>After 4 weeks</td>
</tr>
<tr>
<td>Frequency</td>
<td>7.00±1.3</td>
<td>4.57±2.8</td>
</tr>
<tr>
<td>Duration</td>
<td>4.93±1.2</td>
<td>3.86±2.2</td>
</tr>
<tr>
<td>Intensity</td>
<td>3.89±1.3</td>
<td>2.25±1.7</td>
</tr>
</tbody>
</table>

Other eight had appreciable relief in pain intensity (28.57%), 7 patients however did not had any benefit (25%). Compared to this, in placebo group none became absolutely pain free (0 %), 6 (30%) reported that they are much better, 3 (15%) had some relief while 11 patients (55%) had no improvement or complained of worsening of symptoms (Fig. II & Table II).

Discussion:
Chest discomfort is a symptom most commonly associated with heart disease, but it may also be present in many different disease processes (Fass & Navarro-Rodriguez, 2008). Objective findings from the physical examination of the cardiovascular and peripheral vascular systems along with results of investigations support or refute each differential diagnosis for a patient who presents with chest discomfort. No system is exempt from evaluation outside of the context of the full examination (Seidel et al, 2003). It is true to say that the majority of the diagnosis is based on the patient’s history and the clinical examination. The chief aim for a clinician is to rule out any serious life threatening malady and there, the role of investigation cannot be underestimated. How can one rule out “Cardiac Syndrome X” (Crea & Lanza, 2004) without a stress ECG or an aneurysm without CT thorax (Klompas, 2002)? However, even in most optimum setting the diagnosis remain uncertain in some of the cases, more so if the chest discomfort is sub acute. These cases tax the resourcefulness of treating clinician as they do not have the remotest idea how to approach these patients. They usually follow the strategy of ROAST (rule out all serious things). Reassurances that there is nothing serious, anxiolytics, sedatives, antacids and psychotherapy (Esler & Bock, 2004) are usually offered. Randomized trial data indicate that cognitive therapy and group interventions lead to decrease in symptoms for such patients. Easier said than done.
One of the trials took 12 months to produce a positive outcome in only 48% of cases (van Peski-Oosterbaan et al, 1999). Compared to this the present study showed a positive outcome in 75% of cases and that too in just one month. Most of other trials are not clear about the length of therapy and percentage of positive outcomes.

Proton-pump inhibitors (PPIs) are the class of drugs which inactivates H+/K+ ATPase (proton pump) in gastric parietal cells which is the final pathway of acid production in stomach. They are very routinely prescribed and has very satisfactory safety profile. In certain condition, they also promote release of abundant quantity of pituitary mediated β-endorphin, a powerful nociceptive and an endogenous opioid (Jarmukli et al, 1999). Omeprazole was reported to be 100 times more effective than placebo in release of β-endorphin, thus having a potent antinociceptive property (Budzyński et al, 2010). Similar results were observed with Rabeprazole (Dickman et al, 2005) and Lansoprazole (Bautista et al, 2004). It is suggested that both, these mechanism of action produced amelioration of symptoms in the present study either individually or synergistically as some of the patients might be suffering from transient acid reflux phenomenon even if not proved by suitable investigations. The present study clearly demonstrates that in these baffling cases of chest discomfort a fair trial with Rabeprazole is warranted.

**Conclusion:**

The result of this study clearly proves the superiority of Rabeprazole (40 mg OD) over placebo in management and treatment of nonspecific non acute chest discomfort due to its gastric acid suppressive and β-endorphin release property and a course of PPI in these cases is suggested.

**References:**

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Source of Support: Nil.
Conflict of Interest: None declared.