Is there a link between gastro-esophageal reflux disease and sinus tachycardia? Fallujah General Hospital-Iraq-2012

Faisal K Al-Assaf, Ahmed Babaker, Mustafa K Elnimeiri, Hamid K Al-Janabi

Dr. Faisal K Al-Assaf: Gastroenterologist-Fallujah General Hospital-Fallujah-Iraq
Dr. Ahmed Babaker: Internist Cardiologist-Associate Professor of Medicine-Faculty of Medicine and Health Sciences-Elneelain University-Khartoum-Sudan
Dr. Mustafa K Elnimeiri: Associate Professor of Preventive Medicine and Epidemiology-Faculty of Medicine and Health Sciences-Elneelain University-Khartoum-Sudan
Dr. Hamid K Al-Janabi: Professor of Cardiology. Chief of Cardiology unit-College of Medicine-University of Baghdad-Iraq

ABSTRACT
Introduction: Whenever Gastro-esophageal reflux provokes symptoms or complications it is called gastro-esophageal reflux disease (GERD). The association between gastro-esophageal reflux disease (GERD) and cardiac dysrhythmias is still conjectural in spite of studies that had been conducted. The overall objective of the study is to explore this relationship and to test the efficacy of proton pump inhibitors on GERD related tachycardia. Materials and methods: The study was conducted at Fallujah general hospital – gastroenterology and hepatology unit, in Fallujah City which is located 60 km to the west of Baghdad (Iraq). Gastroscopy and 24 hours ECG Holter monitoring were performed for 120 study subjects (67 males and 53 females, the age of study subjects ranged between a minimum of 16 years to a maximum of 70 years old. The mean age was 34 ±11 years). The study subjects were included for complaining of symptoms of (GERD) after exclusion all relevant risk factors that can influence the heart rate. A second 24 hours Holter study two month followed treatment "as outpatients" by proton pump inhibitors (PPI), and a third Holter study one month after withholding of treatment had been performed. Results: An impressive reduction in frequency count of sinus tachycardia were noticed in 58.3% of study subjects, furthermore, significant recurrence of sinus tachycardia was observed in 75% of patients, one month after discontinuing treatment. Conclusion: Sinus tachycardia can be triggered by GERD, Proton Pump Inhibitor had a significant influence on amelioration of the GERD related sinus tachycardia.

Keywords: Sinus tachycardia, Gastro-esophageal reflux disease, proton pump inhibitors

INTRODUCTION

Gastro-esophageal reflux represents the retrograde flow of gastric contents into the esophagus. It occurs even in healthy individuals and is regarded as "physiologic" as long it does not induce esophageal mucosal abnormalities or symptoms. Whenever Gastro-esophageal reflux provokes symptoms or complications it is called gastro-esophageal reflux disease (GERD).

© 2013 Al Neelain Medical Journal vol.3No. 8 ISSN 1858-627
During the last decades, extra esophageal manifestations of GERD are well known. Is the presence of gastro-esophageal reflux diseases associated with increase the risk of sinus tachycardia? Do proton pump inhibitors decrease the risk of this tachyarrhythmia?

Scarcity of previous conducted studies suggested a potential association between tachycardia and gastro-esophageal reflux diseases.

In the last decades, there has been renewed interest in the functional relationship between the gastrointestinal tract "the esophagus in particular" and the cardiovascular system. Among the reasons for this increased interest is the evidence of a particular subset of dysrrhythmic patients with negative cardiologic examination and symptoms of (GERD). There is clinical evidence showing the role of the esophagus in triggering cardiac dysrhythmias. As there are cases of sinus tachycardia with obscure reasons in spite of all sophisticated diagnostic tests, so this study is expected to contribute to finding one of these reasons.

The overall objective of the study is to explore this relationship and to test the efficacy of proton pump inhibitors on GERD related tachycardia.

MATERIAL AND METHODS

This study is a hospital-based clinical trial prospective study. The study was conducted at Fallujah general hospital – gastroenterology and hepatology unit, in Fallujah City which is located 60 km to the west of Baghdad (Iraq).

A sample of 120 study subjects complaining of esophageal reflux for 2-3 times per week for three month and more, who consulted the gastroenterology unit at Fallujah General Hospital during the period between May 2010 -- May 2012, were enrolled in the study. All characteristics information that can lead to or as a sequence of GERD were considered in the inclusion criteria.

Congenital and acquired cardiac diseases, patients on drugs influencing the heart beat, metabolic and degenerative diseases affecting cardiac events, endocrine related cardiac diseases, alcohol and drugs abusers, all those were excluded from the study.

A thorough physical examination and investigations for identifying any signs of cardiac, metabolic and endocrinial, diseases that might influence the cardiac conduction were performed for all patients. Basic ECG, (1st) 24hrs ECG monitoring and gastroscopy had been conducted for all enrolled patients to the study. Proton pump inhibitors (PPIs) in a form of Rabeprazole 20 mg twice daily for two month were prescribed. Followed that a second 24 hrs ECG monitoring was performed.

An ethical clearance was obtained from the institutional review Board at Elneelain University. As well an ethical clearance was obtained from the authority/Institutional Review Board at Fallujah Hospital. An informed consent was obtained from each patient before enrollment in the study after through explanation of the study objectives, procedures, anticipated benefits and potential hazards of the study and the discomfort it may entail.

Data of all patients were collected via a case record formula which transfer to Microsoft access and excel, then SPSS system was used for analysis. In addition univariate analysis was conducted to
calculate the proportions, percentages and frequencies. Then bivariate analysis was conducted through cross tabulations and using the Chi Square for testing of statistical significance. Paired T-test, Wilcoxon Signed Rank test were used.

RESULTS

The results presented in this study were based on the analysis of 120 patients with a diagnosis of esophageal reflux disease. The age of study subjects ranged between a minimum of 16 years to a maximum of 70 years old. The mean age was 34 ±11 years (SD). Males constituted 67 patients (55.8%) of the sample, with a male to female ratio of 1.25.

As shown in table 1, the highest proportion of study subjects (89.2%) had no obvious abnormality on ECG trace. Tachycardia was the commonest abnormality found in 6.7% of the sample. Partial / complete RBBB, atrial fibrillation and ventricular ectopics were interpreted in 4.1% only of the subjects.

Table 1: The basic ECG finding among the study subjects

<table>
<thead>
<tr>
<th>ECG findings</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>No obvious abnormality</td>
<td>107</td>
<td>89.2</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>8</td>
<td>6.7</td>
</tr>
<tr>
<td>Partial / complete RBBB</td>
<td>3</td>
<td>2.5</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Ventricular ectopics</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Total</td>
<td>120</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Gastroscopy showed at least one sign of GERD histological changes which constituted around (78.8%) of the study subjects. 21.2% of the study subjects had normal esophageal mucosa.

Effect of treatment on sinus tachycardia

Holter monitor was used to count the attacks of (sinus tachycardia) during 24 hours period. A baseline record was carried out before starting treatment. A second Holter record was conducted in 72 study subjects two months after treatment to show the effect of treatment on frequency of (sinus tachycardia). Treatment was stopped after the second Holter for another month and then a third Holter recording was conducted for 12 subjects only to show the effect of stopping treatment on reversing the changes observed in frequency of sinus tachycardia attacks.

As shown in table 2, at baseline the count of tachycardia incidents ranged between none to 433 per 24 hours with a median frequency of 49. Treatment for two months was associated with changes in frequency compared to its pre-treatment level ranging between a maximum reduction of 421 to maximum increase in frequency of 250. Treatment was assumed to be the cause behind a statistically significant median reduction in frequency of tachycardia.
incidents of 20 per 24 hours. Stopping treatment on the other hand was associated with a statistically significant median increase in frequency by 27 per 24 hours compared to the after treatment level, figure 1 and 11.

As shown in table 3, the magnitude of changes in frequency of tachycardia incidents in response to treatment or stopping treatment was compared to its starting value and then multiplied by 100 to present the results as a percentage of the starting level. A change of <20% increase or <20% reduction was considered as trivial and labeled as “No obvious change” since it probably reflects random variation in frequency of atrial ectopics. A reduction that is higher than the “no obvious change level” but less than 50% of its baseline level was considered as an “Obvious reduction”, while a reduction that is ≥ 50% was considered as an “impressive reduction”. On the other side a positive change (increase) in frequency of atrial ectopics that surpassed the “no obvious change” cut-off value of 20% was labeled as “Obvious increase”. The positive side of the change was left ungraded (obvious versus impressive) since any noticeable amount of increase in frequency of ectopics is considered as failure of treatment effect.

As shown in table 3, after 2 months of treatment 58.3% of the study subjects showed an impressive reduction in frequency of tachycardia attacks, while only 25% showed an obvious increase in frequency. Reversal of the overall beneficial treatment effect observed in 3 fifths with impressive reduction was shown after one month of stopping treatment. Three quarters (75%) of the 12 subjects that were followed with a third recording of Holter after stopping treatment showed an obvious increase in frequency of tachycardia compared to the after treatment value, figure 3.

**Table 2: Changes in count of tachycardia attacks (measured by holter monitor) in response to treatment and after stopping treatment**

<table>
<thead>
<tr>
<th>Tachycardia attacks</th>
<th>Baseline holter</th>
<th>second holter</th>
<th>Changes after treatment</th>
<th>Third holter</th>
<th>Changes after stopping treatment compared to second holter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range</td>
<td>(0 to 433)</td>
<td>(0 to 322)</td>
<td>(-421 to 250)</td>
<td>(1to334)</td>
<td>(-8 to 252)</td>
</tr>
<tr>
<td>Median</td>
<td>49</td>
<td>12</td>
<td>-20</td>
<td>41</td>
<td>27</td>
</tr>
<tr>
<td>Inter-quartile range</td>
<td>(8 to 115)</td>
<td>(2.5to67.5)</td>
<td>(-93.5 to 2)</td>
<td>(6.5to123)</td>
<td>(5.5 to 105.5)</td>
</tr>
<tr>
<td>N</td>
<td>82</td>
<td>72</td>
<td>72</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>P (Wilcoxon Signed Rank test) of median</td>
<td>0.001</td>
<td>0.008</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Figure 1: The median (with inter-quartile range) count of tachycardia incidents at baseline, after treatment and after discontinuing treatment.
Figure 2: The median (with inter-quartile range) of changes in count of tachycardia attacks after treatment (compared to baseline) and after discontinuation of treatment (compared to after treatment).

Table 3: Quantification of changes in tachycardia after treatment and stopping treatment

<table>
<thead>
<tr>
<th>Changes in tachycardia</th>
<th>Percent change after treatment compared to baseline</th>
<th>Percent change after stopping treatment compared to treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impressive reduction (-100 to -50%)</td>
<td>N=42, %58.3</td>
<td>N=0, %0.0</td>
</tr>
<tr>
<td>Obvious reduction (-49.9 to -20%)</td>
<td>N=2, %2.8</td>
<td>N=0, %0.0</td>
</tr>
<tr>
<td>No obvious change (-19.9 to +19.9%)</td>
<td>N=10, %13.9</td>
<td>N=3, %25.0</td>
</tr>
<tr>
<td>Obvious increase (&gt;=+20%)</td>
<td>N=18, %25.0</td>
<td>N=9, %75.0</td>
</tr>
<tr>
<td>Total</td>
<td>N=72, %100.0</td>
<td>N=12, %100.0</td>
</tr>
</tbody>
</table>
Figure 3: The percentage change in Tachycardia after treatment compared to baseline and after stopping treatment compared to treated.

Gender had a statistically significant association with the count of tachycardia incidents as the median count of tachycardia attacks was significantly lower (15) among males compared to females (62), table 4. While the difference in severity of symptoms showed no significant correlation with count of tachycardia.
Table 4: The median count of tachycardia attacks (measured by holter monitor at pretreatment baseline) by severity of symptoms and gender.

<table>
<thead>
<tr>
<th>Selected explanatory variables</th>
<th>Tachycardia-Baseline holter</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median</td>
</tr>
<tr>
<td>Severity of symptoms</td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>52</td>
</tr>
<tr>
<td>Moderate</td>
<td>28</td>
</tr>
<tr>
<td>Severe</td>
<td>81</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>62</td>
</tr>
<tr>
<td>Male</td>
<td>15</td>
</tr>
</tbody>
</table>

DISCUSSION

This study shows in selected patients with GERD, clear evidence of: i. correlation between sinus tachycardia and GERD. ii. Statistically significant reduction in frequency count of sinus tachycardia after two month treatment by PPI given for associated GERD. iii. Significant recurrence of sinus tachycardia count after hold of PPI for one month.

Despite the physiological inter-relationship between the upper gastrointestinal tract and heart is well known for many decades, and the variable reports that had been published during the past decades to highlight a link between GERD and cardiac dysrhythmias; yet, the issue is still under debate as the real mechanism of this relationship is still conjectural.

This study explores the correlation between GERD and tachycardia through follow up of (120) patients who showed an impressive reduction in frequency counts of tachycardia in 58.3% and obvious reduction in 2.8% , two month after treatment by PPI. To date the majority of conducted studies related to this issue, correlates GERD to atrial fibrillation, to my knowledge there is a very limited number of published, prospective clinical trial, study referring to the relationship between GERD and sinus tachycardia.

R.Cuomo et al, concluded, after followed up of 32 patient with GERD and idiopathic cardiac arrhythmia, that 56% of patients showed a significant correlation between heart rate variability and the esophageal pH-metry and 36% of patients without correlation showed a significant improvement or absence of cardiac dysrhythmias.

The medication given, which is one variety of proton pump inhibitors (PPI), for enrolled subjects in the study were assumed to be the causation behind a "statistically significant" reduction in frequency counts of tachycardia.

Diagnosis of GERD by gastroscopy and the used of 24 hours holter monitoring to detect any events of tachycardia, with exclusion of all the risk factors, allowed for
more detailed quantification and comparison of reflux and tachyarrhythmic events. A limited number of authors as, Hirofumi Nakamura, (13) R Cuomo, (12) and Gerson L B (10) referred to the used of 24 hrs ECG monitoring during their inspection the effect of PPI on cardiac dysrhythmias.

Several hypotheses had been proposed to highlight the patho-mechanism of the correlation between GERD and cardiac dysrhythmias, one of these hypothesis reported that the local inflammatory process penetrates the esophageal wall and thus affects the adjacent vagal nerves. Inflammation of peripheral nerves; motor, sensory, and vegetative have been described to affect myelination, discharge rate, and the propagation of stimuli along these fibers. (14) Other "may be" plausible hypothesis is that the propagation of the local inflammatory process through the esophageal wall may cause local pericarditis or atrial myocarditis, although esophagitis tends to be a mucosal and sub-mucosal disease. Atrial myocardial biopsies in patients with lone AF have shown myocarditis in 66% of patients. (15)

Furthermore, Heart rate variability studies with continuous electrocardiogram (ECG) monitoring have shown that stimulation of the esophagus by acid can alter the balance between vagal and sympathetic activity and can trigger dysrhythmias. (12)

Does this result from activation of parasympathetic or sympathetic nervous systems? Parasympathetic stimulation causes bradycardia in most individuals, but triggers atrial tachyarrhythmia in a minority. (16) Haughey B, reported that increase vagal tone that might precipitate the onset of tachycardia has been associated with the postprandial state, cough, nausea, and ingestion of cold food or liquids. (17)

In the majority of admitted subjects to this study (89 %), the basic electrocardiography that had been done on presentation showed no significant abnormality. While the basic 24 holter monitoring revealed, nearly in all patients, at least one of sinus tachycardia in one or more occasions. However this may give evidence that tachycardia associated GERD are paroxysmal in nature in the majority of cases. (13,18)

Atrial arrhythmias may be induced by a mechanical effect on the left atrial wall that is related to the passage of food. (19) This hypothesis may be supported by the fact that the esophagus is in close proximity to the left atrium posterior wall, Cummings et al. reported that the mean distance between the esophagus and left atrium was 4.4 ± 1.2 mm. (20)

Kanjwal Y et al, (21) and Ip JE, (22) reported cases of tachyarrhythmias induced by swallowing.

In conclusion gastro-esophageal reflux disease is a plausible risk factor for tachycardia. An impressive reduction in frequency count of tachycardia has been seen in 58.3%. Clinician must be aware that there are common denominators in between GERD and sinus tachycardia striking the attention to consider a possible correlation between the two diseases.

Physicians need to approach the use of proton pump inhibitors in patients with unexplained sinus tachycardia and symptoms of GERD, as they are less expensive, and have fewer side effects than the conventional anti-arrhythmic drugs.
REFERENCES


13. Hirofumi Nakamura, Gen Nakaji, Hideki shimaz,et al,a case of paroxysmal atrial fibrillation improved after the administration of proton pump inhibitors for


