Nonsteriodal Antiinflammatory Drugs As A Risk Factor Of Gastro-Oesophageal Reflux Oesophagitis, And Posterior Laryngitis In Arthritic Patients

Mahmoud A. Saleh M.D*, Khaled H. AbdelMageed**, Kadry M. Elsaied **, And Magdy M Elsharkawy**

*Assist. Prof. of ENT, Elminia University. **Lecturer of Internal Medicine, Ain Shams University.

Abstract:
Non steroidal anti inflammatory drugs (NSAIDs) are known to cause ulcers of the stomach and to a lesser degree, the duodenum. Consumption of NSAIDs has been associated with the infrequent occurrence of ulcers at other locations, such as the jejunum, ileum and colon. Several studies have suggested that consumption of NSAIDS also constitutes a risk factor for the development of erosive oesophagitis, including oesophageal strictures. It is now documented that NSAIDS are associated with gastro-oesophageal reflux disease (GERD). It was found recently that GERD is associated with a variety of laryngeal conditions and symptoms, of which “reflux laryngitis” is the most common. AIM OF THE WORK: is to study the effect of NSAIDs on the development of laryngitis in patients with GERD. PATIENTS AND METHODS: study included 60 patients, 42 males and 18 females aged between 26 – 52 years old (mean 37.9), a detailed history was taken from all patients. All the sixty patients were suspected to have GERD based on symptoms including acid reflux, Group I: - 40 patients were receiving daily-recommended doses of NSAIDs for at least one month for a diagnosed rheumatological disease, Group II: - 20 patients who were diagnosed as GERD, and were not receiving any NSAIDs for at least one month prior to the present study. The sixty patients were subjected to upper gastrointestinal endoscopy. Patients who were diagnosed as GERD with or without oesophagitis were subjected to ENT fibro-optic laryngoscopy. RESULTS: 42% of all patients with GERD have hoarseness of voice, 30% have recurrent choking, 53% have excessive throat cleaning. Postglottic oedema, arytenoid oedema, vocal fold oedema, were all significantly higher in group I than in group II. CONCLUSION: The chronic use of NSAIDs can be considered as a risk factor for developing GERD, erosive oesophagitis with or without subsequent posterior laryngitis. Laryngoscopy may have a predictive value for the occurrence of GERD in those patients. Patients who were on regular use of NSAIDS, and are symptomatic for GERD are recommended to start medical treatment for GERD to guard against erosive oesophagitis and/or posterior laryngitis.
Introduction:

Non steroidal anti inflammatory drugs (NSAIDs) are known to cause ulcers of the stomach and to a lesser degree, the duodenum (1). Consumption of NSAIDs has been associated with the infrequent occurrence of ulcers at other locations, such as the jejunum, ileum and colon (2 and 3). Several studies have suggested that consumption of NSAIDS also constitutes a risk factor for the development of erosive esophagitis, including esophageal strictures (4). Recently it was concluded that NSAIDS are associated with gastro-esophageal reflux disease (GERD) especially for females, alcohol and tobacco users and patients with asthma, hiatal hernia, or obesity (5).

A recent study concluded that patients with reflux disease can develop severe laryngospasm and possible syncope (6). Furthermore, it was found that GERD felt to be associated with a variety of laryngeal conditions and symptoms of which “reflux laryngitis” is the most common. The most likely mechanism of laryngeal injury and symptoms is secondary to direct acid and mucosal contact, although studies concerning the cause and effect between GERD and laryngeal diseases are conflicting (7).

Laryngoscopy can reveal findings of high predictive value for the presence of GERD. Among these findings, postglottic edema represents up to 70% (8).

 Patients and Methods:

We approached 60 patients, 42 males and 18 females aged between 26 – 52 years old (mean 37.9), during their routine appointments in the outpatients clinics of rheumatology and internal medicine at Ain Shams University Hospitals. A detailed history was taken from all patients. All the sixty patients were suspected to have GERD based on symptoms including acid reflux, retrosternal burning pain, laryngeal symptoms or combination of these symptoms. These patients were divided into 2 groups:

- **Group I:** 40 patients were receiving daily-recommended doses of NSAIDs for at least one month for a diagnosed rheumatological disease [6 patients with rheumatoid arthritis, 18 patients with osteoartheritis and 16 patients with myalgic pain].
- **Group II:** 20 patients who were diagnosed as GERD in internal medicine clinic and were not receiving NSAIDs for at least one month prior to the present study.

**Exclusion Criteria:**

* Smokers.
* Patients with other causes of chronic laryngeal irritation or focal laryngeal lesions.
* Patients with established diagnosis of peptic ulcer or acute gastritis.

The sixty patients were subjected to upper gastrointestinal endoscopy (Olympus GIF – xo 230 videoscopy – Germany) with local anesthetic spray lidocaine 10% as an only used premedication. GERD was diagnosed in the presence of incompetent cardia and/or oesophageal lesion, which was graded by the extent of mucosal breaks into:

- **Erosive oesophagitis grade I:** mild oesophagitis comprised single erosion involving less than 10% of the distal oesophageal circumference.
• Erosive oesophagitis grade II: - moderate oesophagitis comprised confluent erosions involving 10 – 50% of the distal esophageal circumference.

• Erosive oesophagitis grade III: - severe oesophagitis comprised confluent erosions involving more than 50% of the distal oesophageal circumference or oesophageal ulcer identified as large erosions with depth or oesophageal stricture (9).

Gastric and duodenal erosions were not considered in the present study.

Patients who were diagnosed by the above-mentioned criteria as GERD with or without oesophagitis were subjected to ENT fibrooptic laryngoscopy using a rigid telescope (Olympus A 3013, 70 degree, Germany) which was connected to a light source (Karl – storz cold light fountain 488).

The different parts of the glottis were evaluated. The posterior wall of the glottis, the medial surface of the arytenoid cartilages and the cartilaginous part of the vocal folds which together constitute the posterior glottis (10) were analyzed. For all these structures, mucosal thickening, oedema, erythema in comparison to adjacent laryngeal structures were identified. Special attention was given to examine the posterior wall of the glottis when the vocal folds were in full abduction.

Results

As regards symptoms, all study patients (60 patients) were complaining from heart burn and acid reflux, 33 patients complained from retrosternal pain, 18 patients complained from recurrent chocking, 32 patients complained from excessive throat cleaning and 25 patients complained from hoarseness of voice.

Table 1: Shows the prevalence of GERD and Laryngeal Symptoms in the study group (60 patients)

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Number of patients and %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1- Heartburn and acid reflux.</td>
<td>60 (100%)</td>
</tr>
<tr>
<td>2- Retrosternal pain</td>
<td>33 (55%)</td>
</tr>
<tr>
<td>3- Recurrent chocking</td>
<td>18 (30%)</td>
</tr>
<tr>
<td>4- Excessive throat cleaning</td>
<td>32 (53%)</td>
</tr>
<tr>
<td>5- Hoarseness of voice</td>
<td>25 (42%)</td>
</tr>
</tbody>
</table>

As regards upper gastrointestinal endoscopic findings; in group I: - GERD was diagnosed in (26) patients out of the 40 patients (65%). Nine patients (22.5%) had incompetent cardiac (IC) without significant oesophageal lesion, 12 patient (30%) had IC with grade I erosive oesophagitis (single erosion covering less than 10% of the distal oesophageal mucosal circumference) and 5 patients (12.5%) had IC with grade II erosive...
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oesophagitis (diffuse erosion covering 10 – 50% of the distal oesophageal mucosal circumference).

No significant endoscopic findings were noticed in the remaining 14 patients (35%) of group I.

In group II: - GERD was diagnosed in 9 out of the 20 patients (45%). Two patients (10%) had IC with no significant oesophageal lesion while 5 patients (25%) showed IC with grade I erosive oesophagitis and in 2 patients (10%) IC was associated with grade II erosive oesophagitis.

No significant endoscopic findings were noticed in the remaining 11 patients (55%).

Table 2 compares the upper GI endoscopic findings in group I and group II:

<table>
<thead>
<tr>
<th>Finding</th>
<th>Group I No %</th>
<th>Group II No %</th>
<th>P-Value</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Incompetent cardia without oesophageal lesions.</td>
<td>9 (22.5%)</td>
<td>2 (10%)</td>
<td>P=0.05</td>
<td>S</td>
</tr>
<tr>
<td>• Incompetent cardia with grade I erosive oesophagitis</td>
<td>12 (30%)</td>
<td>5 (25%)</td>
<td>P=0.03</td>
<td></td>
</tr>
<tr>
<td>• Incompetent cardia with grade II erosive oesophagitis</td>
<td>5 (12.5%)</td>
<td>2 (10%)</td>
<td>P=0.06</td>
<td>S</td>
</tr>
<tr>
<td>• Symptomatic patients without any significant endoscopic finding.</td>
<td>14 (35%)</td>
<td>11 (55%)</td>
<td>P=0.07</td>
<td>NS</td>
</tr>
<tr>
<td>Total</td>
<td>40 100%</td>
<td>20 100%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

As regards the laryngeal findings; only patients who were endoscopically diagnosed for GERD were subjected to ENT and laryngoscopic examination: -

In group I, 14 out of the GERD +ve 26 patients (53.8%) had positive laryngeal findings: postglottic edema was manifested in 7 patients (26.9%), arytenoids oedema was manifested in 5 patients (19.2%), while vocal fold oedema was seen only in 2 patients (77%).

In group II, positive laryngeal findings were seen in 3 out of 9 patients (33.3%). Two patients had postglottic oedema (22.2%) while one patient showed arytenoid oedema (11.1%).
Table 3 shows the laryngeal findings in group I and group II

<table>
<thead>
<tr>
<th>Laryngeal Findings</th>
<th>Group I</th>
<th>Group II</th>
<th>P-Value</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postglottic oedema</td>
<td>7 (26.9%)</td>
<td>2 (22.2%)</td>
<td>P= 0.04</td>
<td>S</td>
</tr>
<tr>
<td>Arytenoid oedema</td>
<td>5 (19.2%)</td>
<td>1 (11.1%)</td>
<td>P= 0.01</td>
<td>HS</td>
</tr>
<tr>
<td>Vocal fold oedema</td>
<td>2 (7.7%)</td>
<td>0 (0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>14 (53.8%)</td>
<td>3 (33.3%)</td>
<td>P= 0.001</td>
<td>HS</td>
</tr>
</tbody>
</table>

As regards the upper gastrointestinal endoscopic finding that associated the positive laryngeal findings, it was as follows:

In group I: - Incompetent cardia (IC) with no oesophaged lesions was seen in 5 patients (36%) of the 14 patients. IC with grade I erosive oesophagitis in 5 patients (36%) and IC with grade II erosive oesophagitis in 4 patients (28%) out of the 14 patients with positive laryngeal findings.

In group II: - IC with grade I oesophagitis was noticed in 2 patients (66.7%) while IC with grade II oesophagitis was seen in one patient (33.3%) out of 3 patients with positive laryngeal findings.

Table 4: shows gastrointestinal endoscopic findings in patients with laryngeal findings in group I and II

<table>
<thead>
<tr>
<th>GI Endoscopic Findings</th>
<th>Group I</th>
<th>Group II</th>
<th>P-Value</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laryngeal findings with IC only</td>
<td>5 (36%)</td>
<td>0 (0%)</td>
<td>P= 0.04</td>
<td>S</td>
</tr>
<tr>
<td>Laryngeal findings with erosive oesophagitis grade I</td>
<td>5 (36%)</td>
<td>2 (66.7%)</td>
<td>P= 0.04</td>
<td>S</td>
</tr>
<tr>
<td>Laryngeal findings with IC and erosive oesophagitis grade II</td>
<td>4 (28%)</td>
<td>1 (33.3%)</td>
<td>P=0.08</td>
<td>NS</td>
</tr>
<tr>
<td>Total</td>
<td>14 (100%)</td>
<td>3 (100%)</td>
<td>P= 0.01</td>
<td>HS</td>
</tr>
</tbody>
</table>

**Discussion:**

In this study, we compared the prevalence of GERD with or without erosive oesophagitis and / or posterior Laryngitis in a group of 40 arthritic patients with GERD symptoms receiving regular NSAIDs to its prevalence in a group of 20 patients with GERD symptoms not receiving NSAIDs to evaluate the NSAIDs as a risk factor for GERD with or without oesophagitis and / or posterior laryngitis.

The patients who were endoscopically diagnosed for GERD in both groups were subjects for Laryngoscopy
to compare the incidence of Laryngeal changes associating GERD in both groups.

The incidence of IC with no oesophageal lesion was 22.5% in group I compared to 10% in group II, which is statistically significant while IC with erosive oesophagitis grade I was 30% in group I compared to 25% in group II, which is statistically insignificant. The incidence of IC with grade II erosive oesophagitis was 12.5%, 10% in group I and group II respectively, with no statistical difference.

These results show a higher incidence of oesophageal damage in group I than in group II which is statistically significant. This supports several previous authors’ suggestions for a possible role of NSAIDs in causing oesophageal damage especially in patients with GERD (11). Avidan et al (12) concluded that patients on chronic NSAIDs for rheumatological disease suffer frequently from erosive oesophagitis, while the risk may be higher in patients with a pre-existing tendency for GERD. Furthermore it was concluded in a recent study that NSAIDs use could be associated with GERD (5).

As regards the laryngeal findings, we noticed a higher incidence of laryngeal findings in group I (patients receiving NSAIDs) than in those of group II (53.8% and 33.3%) respectively, which is statistically significant. The most frequent laryngeal finding in both groups was postglottic oedema (26.9% and 22.2%) respectively which is insignificant statistically. Secondly the arytenoid edema that represented (19.2% and 11.1%) respectively with statistically significant difference, while vocal fold oedema was seen only in group I (7.7%).

The high incidence of laryngeal findings in association with a high incidence of IC and erosive oesophagitis among group I patients may point to NSAIDs as a risk factor for occurrence or exaggeration of GERD which may be complicated with erosive oesophagitis and / or posterior laryngitis.

Postglottic oedema and arytenoid oedema were the most frequent laryngeal findings in this study. This coincides with other investigators who noticed that pharyngeal reflux was significantly more frequent in patients with posterior laryngitis than in healthy control subjects (13). Carr et al 2000, (8) reported that laryngoscopy and bronchoscopy have a high positive predictive value for the presence of GERD.

**Conclusion**

The chronic use of NSAIDs can be considered as a risk factor for developing GERD, erosive oesophagitis with or without subsequent posterior laryngitis. Furthermore Laryngoscopy may have a predictive value for the occurrence of GERD in those patients. So, our study recommends for all patients who are on regular use of NSAIDS and are symptomatic for GERD to start medical treatment for GERD to guard against erosive oesophgitis and / or posterior laryngitis. Also, it is recommended to perform laryngeal examination and laryngoscopy for those patients in order to predict the development of GERD together with the routine upper GI endoscopy.

**References**


خطر استخدام مثبتات الالتهاب الغير كورتيزونية على حدوث الارتجاع البلعومي والتهاب الحنجرة الخلفي في مرضى التهابات المفاصل

*د/ محمود صالح **د/ خالد عبد المجيد **د/ مجدى الشرقاوى

**د/ قدرى السعيد
كلية الطب - قسم إنف - أدن - جامعة المنيا
كلية الطب - قسم الباطنة - جامعة عين شمس

من المعروف ان مثبتات الالتهاب الغير كورتيزونية تسبب قرح المعدة والى درجة أقل، الاثنين عشرة. استهلاك مثبتات الالتهاب الغير كورتيزونية ارتبط بحدوث قرح نادرة في المواقع الأخرى، مثل المعي الفائفي والقولون. وقد اقترحت عدة دراسات ان استهلاك مثبتات الالتهاب الغير كورتيزونية يشكل عامل خطر أيضا لحدوث التهاب المريء التالكي، وقد وجد مؤخرا أن مثبتات الالتهاب الغير كورتيزونية تسبب الارتجاع البلعومي، ويرتبط أيضا بالتهاب الحنجرة الخلفي.

هدف الدراسة: أن يدرس تأثير مثبتات الالتهاب الغير كورتيزونية على تطوير التهاب الحنجرة في المرضى المصابون بالارتجاع البلعومي.

طرق البحث: تضمنت الدراسة 60 مريضا، 42 ذكر و18 أنثى بعمر بين 26 - 52 سنة (متوسط 37.9) ، أخذ تاريخ فصل من كل المرضى. كل المرضى الستون متوقع ان يكون عندهم الارتجاع البلعومي بناءا على الأعراض.

قسم المرضى إلى مجموعتين:

المجموعة الأولى: 40 مريضا كانوا يتعاطون جرع يومية موصى بها مثبتات الالتهاب الغير كورتيزونية لشهر واحد على الأقل لمرضى التهابات المفاصل مشخص.

المجموعة الثانية: 20 المرضى الذين شاركوا في الارتجاع البلعومي ، ولا يتعاطوا اي مثبتات الالتهاب الغير كورتيزونية لشهر واحد على الأقل قبل الدراسة الحالية.

ملاحظة:

المرضى الستون أخضعوا الى منظار معي علوى.

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النتائج: 42% كل لمرضى المصابون بالارتجاع البلعومي يعانون من جشاعة الصوت 30% يعانون من انتفاخ لحظي متكرر، 53% يعانون من تنظيف الحنجرة المفرط.

وقد وجد أن احترقان الحنجرة والالتهاب الصوتي كانت جميعاً أعلى جدًا في المجموعة الأولى من المجموعة الثانية.

الخاتمة: الاستعمال المزمن لمثبطات الالتهاب الغير كورتيزونية يمكن أن يعتبر كعامل خطر الارتجاع البلعومي، التهاب مرئ نكلي مع أو بدون التهاب الحنجرة الخلفي. ربما يكون للمنشأ الحنجرى البصري قيمة تنظيمية لحدوث الارتجاع البلعومي في مرضى التهابات المفاصل.

ينصح للمريض الذي يعاني من الاستعمال المنتظم لمثبطات الالتهاب الغير كورتيزونية، ويعاني من الارتجاع البلعومي أن يبدأ العلاج الطبي للأرتجاع البلعومي للوقاية من التهاب المرئ النكلي و التهاب الحنجرة الخلفي.