

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

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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.

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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 osteoarthritis 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 mucosa 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 fiberoptic 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 retrasternal pain, 18 patients complained from recurrent choking, 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)

Symptoms	Number of patients and %
1- Heartburn and acid reflux.	60 (100%)
2- Retrosternal pain	33 (55%)
3- Recurrent choking	18 (30%)
4- Excessive throat cleaning	32 (53%)
5- Hoarseness of voice	25 (42%)

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

Nonsteroidal Antiinflammatory Drugs As A Risk

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:

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

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 and 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 (7.7%).

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

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

As regards the upper gastroin -testinal 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

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

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

Nonsteroidal Antiinflammatory Drugs As A Risk

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 oesophagitis 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

1. Henry D., Lim LL, Rodrigue, LA. Perez S. et al (1996): - "Variability in risk of gastrointestinal complications with individual nonsteroidal anti-inflammatory drugs:

- Results of collaborative meta-analysis". *BMJ* 1996, 312; 1563 – 1566.
2. Safeio S, Zike WL, Surbacher M and Den L, (1974): -"Effect of aspirin, alcohol and pepsin on mucosal permeability of oesophageal mucosa". *Surg Forum* 1974; 25, 335 – 337.
 3. Esslwood GI, Back SO, Costell DO, Brown FC et al., (1991):- "Beneficial effect of endomethacine on acid induced oesophagitis in cats". *Dig Dis Sci* 1991; 28: 601 – 608.
 4. El-Sorag HB, Sannanbarg A, (1997):- "Association of oesophagitis and oesophageal strictures with diseases treated with nonsteroidal antiinflammatory drugs". *Am J Gastroenterol* 1997; 92: 52 – 56.
 5. Kotzan J, Wade W, and Yu HH.,(2001):-"Assessing NSAID prescription use as a predisposing factor for gastroesophageal reflux disease in a Medicaid population". *Pharm Res* 2001; 18 (9): 1367 – 72.
 6. Maceri DR and Zim S, (2001):- "Laryngospasm: An Atypical Manifestation of Severe Gastroesophageal Reflux Disease (GERD). *Laryngoscope* 2001, 111(11 Pt 1): 1976 – 9.
 7. Ormseth EJ and Wong RK, (1999):- "Reflux laryngitis: Pathophysiology, diagnosis, and management". *Am J Gastroenterol* 1999; 94 (10): 2812-7.
 8. Carr,MM, Nguyen A, Poje C, Pizzuto M, et al.(2000):- "Correlation of Findings on Direct Laryngoscopy and Bronchoscopy with Presence of Extra-esophageal Reflux Disease". *LARYNGOSCOPE* 2000; 110: 1560-1562.
 9. Hazol DJ, Dent J, Raad W, Nariolavala FM et al (1989):- "Healing and relapse of severe peptic oesophagitis after treatment with omeprazol". *Gastroenterology* 1989; 95: 903-912.
 10. Hirano M, Kiyokawn K and Sato K (1986):-"Posterior glottis Morphological study in excised larynges". *Ann Otol. Rhinol. Laryngol*, 1986, 95: 576-581.
 11. Wilkina WE, Ridlay MG, and Pozniak AL, (1989):-"Benign strictures of the oesophagus, the rule of non-steroidal antiinflammatory drugs". *Gut* 1984; 25: 478-480.
 12. Avidan B; Sonnenberg A; Schnell T; and Budiman-Mak E; (2001):-"Risk factors of oesophagitis in arthritic patients". *EUROPEAN JOURNAL OF GASTROENTEROLOGY and HEPATOLOGY* 2001; 13: 1095-1099.
 13. Ylitalo R, Lindestad P and Ramel S (2001):- "symptoms, Laryngeal Findings, and 24-Hour PH Monitoring in Patients with Suspected Gastroesophago Pharyngeal Reflux". *LARYNGOSCOPE* 2001; 111: 1735-1741.

خطر استخدام مثبطات الالتهاب الغير كورتيزونية على حدوث الارتجاع البلعومي والتهاب الحنجرة الخلفى فى مرضى التهابات المفاصل

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من المعروف ان مثبطات الالتهاب الغير كورتيزونية تسبب قرح المعدة والى درجة اقل ، الاثنى عشرى . استهلاك مثبطات الالتهاب الغير كورتيزونية ارتبط بحدوث قرح نادرة فى المواقع الأخرى ، مثل المعى الفائى والقولون . وقد اقترحت عدة دراسات ان استهلاك مثبطات الالتهاب الغير كورتيزونية يشكل عامل خطر أيضا لحدوث التهاب المرئ التاكلى ، وقد وجد مؤخرًا ان مثبطات الالتهاب الغير كورتيزونية تسبب الارتجاع البلعومي ، ويرتبط أيضا بالتهاب الحنجرة الخلفى .

هدف العمل : ان يدرس تأثير مثبطات الالتهاب الغير كورتيزونية على تطوير التهاب الحنجرة فى المرضى المصابون بالارتجاع البلعومي .

طرق البحث : تضمنت الدراسة 60 مريض ، 42 ذكر و 18 أنثى بعمر بين 26 – 52 سنة (متوسط 37.9) ، أخذ تاريخ مفصل من كل المرضى . كل المرضى الستون متوقع ان يكون عندهم الارتجاع البلعومي بناء على الأعراض .

قسم المرضى الى مجموعتين :

المجموعة الاولى : 40 مريض كانوا يتعاطون جرعة يومية موصى بها بمثبطات الالتهاب الغير كورتيزونية لشهر واحد على الاقل لمرضى التهابات المفاصل مشخص .

المجموعة الثانية : 20 المرضى الذين شخصوا الارتجاع البلعومي ، ولا يتعاطو اى مثبطات الالتهاب الغير كورتيزونية لشهر واحد على الاقل قبل الدراسة الحالية .

ملاحظة :

- المرضى الستون أخضعوا الى منظار معوى علوى .

• المرضى الذين شخصوا الارتجاع البلعومي مع او بدون التهاب المرء أضعوا الى منظار حنجري بصرى .

النتائج : 42 % كل لمرضى المصابون بالارتجاع البلعومي يعانون من جشاشة الصوت 30 % يعانون من اختناق لحظى متكرر ، 53 % يعانون من تنظيف الحنجرة المفرط .

وقد وجد ان احتقان الحنجرة والاحبال الصوتية كانت جميعا اعلى جدا فى المجموعة الاولى من المجموعة الثانية .

الخاتمة : الاستعمال المزمّن لمثبطات الالتهاب الغير كورتيزونية يمكن ان يعتبر كعامل خطر الارتجاع البلعومي ، التهاب مرئ تاكلى مع او بدون التهاب الحنجرة الخلفى . ربما يكون للمنظار الحنجري البصرى قيمة تنبؤية لحدوث الارتجاع البلعومي فى مرضى التهابات المفاصل .

ينصح للمريض الذى يواظب على الاستعمال المنتظم لمثبطات الالتهاب الغير كورتيزونية ، ويعانى من الارتجاع البلعومي ان يبدأ العلاج الطبى للأرجاع البلعومي للوقاية من التهاب المرئ التاكلى و التهاب الحنجرة الخلفى .