

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: No applicable

ACTIVE INGREDIENT: No applicable

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| Study No: NIS-GFR-DUM-2007/3 |
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| Linéa : Evaluation of the impact of abdominal fat mass on the severity and frequency of GERD symptoms in general practice. |
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Developmental phase: No applicable

Study Completion Date: LSLV = 3 December 2008

Date of Report: 18 November 2009

OBJECTIVES:

This survey conducted in 2008 consisted of an evaluation, according to gender, of the impact of abdominal fat mass quantified by waist circumference on the severity and frequency of symptoms in patients with GERD in routine practice.

One of the secondary objectives of the survey was to compare anthropometric characteristics (waist circumference, BMI) of GERD patients with those of non-GERD controls (patients without GERD symptoms, matched for age-group (± 5 years) and gender of GERD patients).

METHODS and RESULTS:

The survey is based on a large study population, with 5,047 patients included and 4,739 patients available for analyses. The control population consisted of 2,456 patients.

Mean age was 52 years in the study population, with more male patients (62.3%). Mean weight was 80.5 kg (± 15.7), versus 77.2 kg (± 14.9) 5 years prior to enrollement. Mean height was 170.2 cm (± 8.4). Mean BMI was 27.7 ± 4.9 kg/m², representing a severe overweight. 74.1% of men had a waist circumference > 94 cm and 81.1% of women had a waist circumference > 80 cm. Almost one half of men had a waist circumference greater than 102 cm (48.1%) and 60.1% of women had a waist circumference greater than 88 cm.

GERD patients had a significantly higher mean weight than non-GERD patients (74.2 ± 12.9 kg for non-GERD patients; $p < 0.001$). GERD patients had a significantly higher mean BMI than non-GERD patients (25.4 ± 3.8 kg/m² for non-GERD patients; $p < 0.001$).

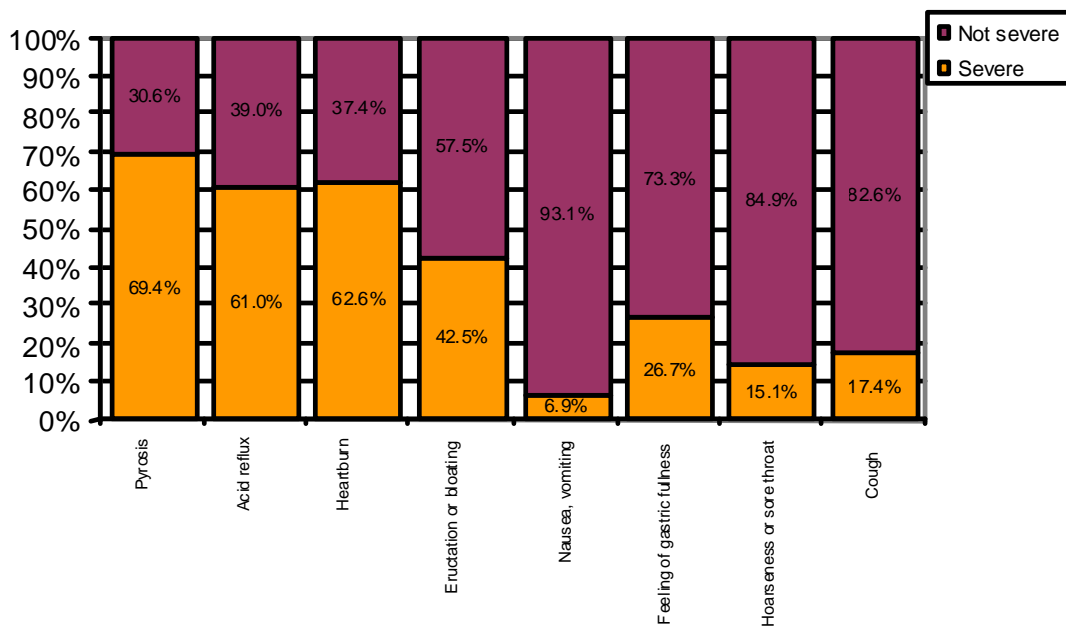
Men with GERD had a higher waist circumference (102.0 ± 13.0) than men without GERD (94.7 ± 11.2) ($p < 0.001$), with similar findings in women (91.4 ± 15.8 vs 85.2 ± 12.1 , $p < 0.001$).

70.9% of GERD patients had at least one episode of GERD prior to inclusion. For the largest cohort (41.1%), the first episode of GERD had occurred 1 to 5 years prior to inclusion. 5.9% of patients presented *Helicobacter pylori* infection. The majority of these patients had received *Helicobacter pylori* eradication therapy. In terms of complications of GERD, 22.6% of patients had a history of oesophagitis, 5.0% had a history of a gastroduodenal ulcer and 0.1% had a history of oesophageal and/or gastric cancer. During the 3 years prior to inclusion, one third of patients had undergone gastrointestinal endoscopy and a similar proportion had consulted a gastroenterologist.

Concerning risk factors other than obesity, 35.1% of patients had a hiatal hernia, 43.6% smoked and 41.3% reported regular alcohol use. Most severe symptoms were the typical symptoms of GERD (pyrosis, acid reflux) with a similar intensity of heartburn.

Figure 1 indicates the severity of symptoms in men, but similar results were observed in women.

Fig. 1 Symptom severity in men.



The frequency of symptoms presented a relatively homogeneous distribution. Symptoms were present for at least 5 days a week in only about 20% of the population, with no marked difference across symptoms or genders.

Results : In men age-adjusted analyses did not show any correlation between waist circumference and severity of acid reflux, or most atypical symptoms (heartburn, eructation and bloating, nausea and vomiting, hoarseness or sore throat and cough). Only

the severity of pyrosis and feeling of gastric fullness were correlated with waist circumference. More severe symptoms were reported by patients with a waist circumference ≥ 94 cm (OR = 1.4 for pyrosis, $p < 0.001$ and OR = 1.3 for gastric fullness, $p = 0.016$). Analysis of symptom frequency did not provide any conclusive results. Only the frequencies of pyrosis and heartburn were correlated with waist circumference, with a lower frequency for patients with a waist circumference > 94 cm (OR = 0.8 for pyrosis, $p = 0.0248$ and OR = 0.8 for heartburn, $p = 0.0427$). Age-adjusted analysis in women did not show any correlation between waist circumference and severity of the two typical symptoms or most atypical symptoms (feeling of gastric fullness, hoarseness or sore throat and cough). In contrast with men, the severity of pain and heartburn, eructation and bloating and nausea and vomiting were correlated with waist circumference. More severe symptoms were reported by women with a waist circumference > 80 cm (OR = 1.3 for pain and heartburn, $p = 0.027$, OR = 1.7 for eructation and bloating, $p < 0.001$ and OR = 1.7 for nausea and vomiting, $p = 0.038$). Analysis of symptom frequencies did not reveal any correlation with waist circumference.

The impact of GERD on frequency of symptoms and discomfort was assessed using the GIS self-administered questionnaire. The three dimensions studied showed mean scores between 2.0 and 2.3: "Upper gastrointestinal symptoms" (2.3 ± 0.7); "Other gastrointestinal symptoms related to acidity" (2.2 ± 0.7) and "Impact of symptoms on daily life" (2.0 ± 0.6). The most frequent symptoms were acid reflux, heartburn and epigastric pain. The main symptom in terms of impact on daily life was, surprisingly, the need to frequently take medication followed, more logically, by sleep disorders, that were frequently or daily disabling for one third of the patients.

Analysis of concomitant diseases according to waist circumference showed fairly logically a higher proportion of diseases related to overweight in the group of men with waist circumference greater than 94 cm: cardiovascular disease, hypertension, diabetes (x 3), sleep apnoea, sleep disorders, snoring and joint diseases. In contrast, the prevalence of coronary disease, peripheral vascular disease, asthenia or daytime sleepiness was in men independent of waist circumference (less than or greater than 94 cm). A higher prevalence of cardiovascular disease, coronary disease, peripheral vascular disease, diabetes (x 4), sleep apnoea, snoring and joint diseases was observed among women with a waist circumference greater than 80 cm.

In terms of management, the postural and health and dietary measures recommended during the visit were, in decreasing order of frequency, low-fat diet (82.0%), raising the head of the bed (73.9%), weight loss (67.7%), smoking cessation (43.6%) and alcohol abstinence (41.4%). These last three advises were much more frequently given to men than to women. 99.3% of patients went home with a prescription for a GERD treatment, mostly a PPI. Analysis of management did not reveal any difference according to gender or waist circumference.