AstraZeneca

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Not applicable
ACTIVE INGREDIENT: Not applicable

Study No: NIS-GFR-DUM-2008/2
National observational study on GERD through the various ages of life in patients, adults and children, followed by family physicians

Developmental Phase: Not applicable
Study Completion Date: LSLV = 30/10/2009
Date of Report: 14/09/2010

OBJECTIVES:

Primary

- To describe GERD semeiology according to ages in life: (0 to 23 months old) and (24 months old and over) for children, and for adults (18 to 29); (30 to 39); (40 to 49); (50 to 59) and (over 60).

Secondary

- To describe the characteristics of the patients according to the age range taken into account (gender, medical and/or surgical history, weight, height, smoking…).
- To describe GERD semeiology in 2 to 17 year-old children according to two age brackets: (24 months to 11 years old) and (12 to 17 years old).
- To describe the digestive and extra-digestive symptoms related to GERD.
- To describe the care taking of GERD per age bracket in children and adults (postural, dietetic and hygienic measures, medication, surgery in some cases, possible tests contemplated, medical follow-up contemplated).
- To compare the children's characteristics and GERD symptomatology per age bracket according to the manner of medical follow-up (General Practitioner or private pediatrician).
- To compare the care taking of pediatric GERD per age bracket according to the manner of medical follow-up (General Practitioner or private pediatrician) according to whether the treatment exists or not.
- To describe the general impact of GERD in children and adults: diet, schooling, sociability, social and professional behavior for adults.

METHODS:

Transversal, multicentre, observational study.

RESULTS:

This national, multicentre, cross-sectional, observational survey was designed to describe the clinical signs and management of GERD as a function of age in adults and children followed in office medicine (general practitioners or private paediatricians). The general impact of GERD on daily life was also evaluated in children and in adults by means of the GIS questionnaire adapted to the patient's age.
From January to October 2009, 961 GPs selected 2,866 adult patients and 921 children while 169 paediatricians selected 333 children, i.e. a total population of 4,120 patients with GERD. A total of 331 patients (8.0%) (133 children and 198 adults) were excluded from the analysis population as they failed to meet at least one inclusion/exclusion criterion. The analysis population was therefore composed of 3,789 patients: 2,668 adults included by 947 GPs and 1,121 children including 850 children included by 850 GPs (from a total of 953 active GPs) and 271 children included by 150 paediatricians.

Adult patients (n=2,668) had a mean age of 52 years (56.0% were over the age of 50 years) and were predominantly male (57.9%). The mean BMI increased with age, with 42.1% of overweight patients ($25 \leq BMI < 30$ kg/m^2) and 16.6% of obese patients (≥ 30 kg/m^2).
Two-thirds (66.3%) of adult patients had a history of previous episodes of GERD; the majority (66.6%) of these patients reported a first episode of GERD during the previous 5 years. One quarter of patients (26.1%) had undergone endoscopy during the previous three years with an increasing frequency according to age (34.5% in patients over the age of 60). The most frequent gastrointestinal diseases in the patient's history were hiatus hernia (26.9%) and oesophagitis (21.5%). Almost one half of patients (45.8%) were smokers with a higher proportion among younger patients (aged 18 to 39 years) and 37.1% of patients reported regular alcohol consumption with a higher frequency in the 40 to 59 years age-group (40 to 45%).
The frequency of gastrointestinal symptoms typical of GERD among adult patients was 82.0% for pyrosis, 76.9% for acid reflux and 69.8% for heartburn. The frequency of these symptoms varied according to age-group. They occurred daily in almost one half of patients (42.5%). These symptoms interfered with the patient's daily life in almost 80% of patients, regardless of age-group, and almost one-third of patients younger than 60 reported a negative impact on their ability to work. The other most common gastrointestinal symptoms associated with GERD were eructation and a feeling of gastric distension (56.6% and 46.7%, respectively) which varied only slightly according to age. On the other hand, flatulence was reported more frequently in older age-groups (50 years and older) and abdominal pain and nausea were reported more frequently by younger adults (18-29 years). The main non-gastrointestinal symptoms were chronic cough in 24.0% of patients, chronic sore throat in 18.2% of patients and noncardiac chest pain in 15.6% of patients. The frequency of chest pain increased with age (10% in young adults

to more than 20% in patients 60 years and older), while asthma was reported more frequently by patients aged 18 to 29 years (11.6% vs about 6% in the other age-groups). Analysis of the management of GERD showed that further complementary investigations were requested after the visit for only one quarter of patients (mainly endoscopy) with no major difference according to age-group.
Treatment was considered for almost all patients (99.7%), mainly prescription of anti-reflux medication (86.0%), diet and lifestyle measures (low-fat diet, 70.9%) and postural measures (raising the head of the bed, 70.8%). Among the patients in whom anti-reflux medication was prescribed (n=2,294), the medications most commonly prescribed were PPIs (96.3%), while prokinetics and antacids/alginates were prescribed in 35.9% and 35.7% of treated patients, respectively.

Children (n=1,121), predominantly male (64.6%), had a mean age of 5.8 months for the 341 children (30.4%) aged 0 to 23 months and 13 years for the 780 children (2-11 years) or adolescents (12-17 years) (69.6%). A very low proportion of children (0.63%) had undergone surgery for their GERD and gastrointestinal endoscopy had been performed in 13.7% of children at a mean age of 8.3 years. The majority of children under the age of 2 years (71.8%) were followed by paediatricians, while children between the ages of 2 and 17 years were predominantly (96.7%) followed by GPs (mean age: 11.6 months for children followed by paediatricians and 11.8 years for children followed by GPs).
One half of children between the ages of 2 and 17 years (50.9%) had been exposed to passive smoking and 10.9% of them smoked (earliest age of smoking: 10 years).
A large majority of the children followed by a paediatrician were treated for their GERD regardless of their age: 79.8% of the (0-23 months) age-group and 80.0% of the (2-17 years) age-group. 84.4% of the children under the age of 2 years and only one half of children between the ages of 2 and 17 years (49.7%) followed by a GP were treated for their GERD on inclusion in the study. Diet / lifestyle measures and postural measures were predominantly prescribed to young children (0-23 months) regardless of the type of medical follow-up. Drug treatment had been prescribed in one half of patients (48.5%), more frequently by GPs in children of the 0 to 23 months age-group and more frequently by paediatricians to children in the 2 to 17 years age-group. Regardless of age, the medications most frequently prescribed were antacids/alginates (57.7% of treated children), prokinetics (49.6%) and PPIs (40.9%). It should be noted that antacids and prokinetics were prescribed more frequently to children of the 0 to 23 months age-group, while PPIs were mainly prescribed to children of the 2 to 17 years age-group, regardless of the type of medical follow-up.
The clinical signs of GERD in children differed from those reported in adults. Regurgitation and vomiting were mainly observed in infants between the ages of 0 and 23 months (90.6% and 46.5%, respectively) regardless of the type of medical follow-up. Heartburn/epigastric pain and pyrosis were mainly observed in children aged 2 to 17 years (74.6% and 70.8%, respectively). It should be noted that heartburn/epigastric pain were significantly more frequent in children of the 0-23 months age-group followed by a paediatrician (56.2% versus 28.1% followed by a GP, $p<0.001$) and in children aged 2 to 17 years followed by a GP (75.1% versus 57.7% followed by a paediatrician, $p=0.045$). The other symptoms most commonly associated with GERD were crying/irritability (77.9%) and feeding difficulties (41.9%) in children aged 0 to 23 months (with crying/irritability reported more frequently in children followed by a GP than by a paediatrician, 85.3% versus 75.0% respectively, $p=0.041$); the associated symptoms most commonly reported in children aged 2 to 17 years were eructation (63.5%), abdominal

pain (58.9%), nausea (48.4%) and a feeling of gastric distension (36.3%). Children aged 2 to 17 years followed by a paediatrician presented a significantly higher proportion of abdominal pain (85.7% versus 58.2% of children followed by a GP, p=0.011). The non-gastrointestinal symptoms most commonly reported in children aged 2 to 17 years were chronic cough (36.3%), chronic sore throat (24.9%), and asthma (13.2%), especially in the 2-11 years age-group. Children followed by paediatricians presented significantly more non-gastrointestinal symptoms than those followed by GPs: asthma (28.6% versus 12.6%, p=0.047), cough (61.9% versus 35.6%, p=0.014) and recurrent laryngitis/otitis (42.9% versus 13.7%, p=0.001).
As for adults, a complementary investigation was recommended after the visit for approximately one quarter of children (23.8%) (mainly endoscopy for children aged 2 to 17 years and pH monitoring for children younger than 2 years). GPs requested more investigations in children younger than 2 years than paediatricians (20.9% versus 11.1%).
A treatment was considered in 97.6% of children, mainly prescription of anti-reflux medication (92.0%), diet and lifestyle measures (86.2%) and postural measures (74.4%). Postural measures were prescribed significantly more frequently by GPs than by paediatricians regardless of the patient's age (in children younger than 2 years: 95.5% versus 82.8%, p=0.003; in children aged 12-17 years: 70.1% versus 45.5%, p=0.014), and drug treatment was prescribed significantly more frequently in children younger than 2 years followed by GPs (89.9% versus 78.0%, p=0.014). The anti-reflux medications most frequently prescribed were PPIs in children aged 2 to 17 years (74.1%) and antacids/alginates (63.6%) in children younger than 2 years. H2 receptor antagonists were prescribed significantly more frequently to children younger than 2 years by paediatricians (24.3% versus 3.3% by GPs, p<0.001). Paediatricians prescribed anti-reflux medications to children aged 2 to 17 years for significantly longer periods that GPs (prokinetics: 60.9% versus 31.7%, p=0.003; duration: 6.9 months versus 4.5 months, p=0.006; antacids/alginates: 60.9% versus 33.8%, p=0.007, duration: 8.5 months versus 4.2 months, p<0.001).
Overall, 27.8% of patients were referred to another specialist, especially a gastroenterologist in order to perform further investigations. GPs more frequently referred children under the age of 2 years to a specialist than paediatricians (25.0% versus 9.2%, p<0.001).

The GIS questionnaire, adapted to age, failed to demonstrate any impact of GERD according to age-group for children and adults : mean values of the scores for the “upper gastrointestinal tract symptoms” and “other gastrointestinal symptoms related to acidity” dimensions were 2.4 ± 0.7 for the overall population. The mean score for the “impact of symptoms on daily life” dimension among the 3,717 GIS questionnaires for the overall population was 2.1 ± 0.6.