DISEASES DUE TO AIR POLLUTION IN ORADEA CITY: ASTHMA

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Abstract
In this paper, we present the results concerning the type and the amount of some anti-asthma medicines released by medical prescriptions between 2008-2010, in a public pharmacy in Oradea. The high number of anti-asthma medicines released reveals a high number of patients suffering by asthma in accordance with the low air quality in Oradea city.

Key words: air quality, asthma, anti-asthma medicines, sympathomimetic drugs, parasympatholytic drugs, anti-inflammatory corticosteroids.

INTRODUCTION

Outdoor and indoor air pollution is a major environmental risk to human health. The urbanization, passive smoking, exposure to the air pollutants (e.g. ozone O_3, nitrogen oxides NO_x, sulfur dioxide SO_2, particulate matter) and exposure to environmental allergens (dust, pollen etc.) may cause adverse effects such as respiratory disease, allergy and irritation of the respiratory tract. Because the control of the air quality is often inadequate, the research on its health effects should be strengthened.

Low air quality (exposure to air pollutants) has been associated with asthma development and/or asthma exacerbation, even if the cause of asthma is not fully understood. Thus, excessive ozone in air can cause breathing problems and asthma, as well as lung diseases. Nitrogen dioxide is a toxic gas, which causes significant inflammation of the airways, reduced lung function and asthma after a long-term exposure. Sulfur dioxide can cause inflammation of the respiratory system followed by cough, mucus secretion and aggravation of asthma and chronic bronchitis, since the exposure to particulate matter is associated with increased rates of bronchitis and reduced lung function in children and adults (sources: GINA 2009; http://emedicine.medscape.com; http://www.adevarul, 2007; http://www.who.int; WHO 2005; http://en.wikipedia.org; WHO 2000; WHO 2008; Salam et al., 2008).

Asthma is a chronic disease of the airways characterized by respiratory hypersensitivity, intermittent airflow obstruction, and an underlying inflammation. Asthma commonly causes constriction of the smooth muscles in the airway, cough, wheezing, an increase in the

production of sticky mucus (phlegm) and dyspnoea. The severity of the symptoms varies from person to person.

Asthma is a common illness worldwide. In 2009, asthma affected about 300 million people and it caused 250,000 deaths globally. Currently, asthma affects 22 million persons in the United States. It is the most common chronic disease in childhood, affecting about 6 million children, and it is a common cause of hospitalization for children in the United States. In the UK, 5.4 million people are currently receiving treatment for asthma (sources: http://emedicine.medscape.com; http://www.nhs.uk; GINA, 2009; Miller, Ho, 2008; http://www.ncbi.nlm.nih.gov; http://www.nlm.nih.gov; Oxford dicționar de medicină, 2007; Cristea, 2005).

In Romania, over 2 million people suffer from asthma and chronic bronchitis. The first symptoms usually appear in childhood and generally alleviate with age. In the last years, many cities such as Oradea, Reşița, Slatina or Craiova are characterized by high values for sulfur dioxide in air. More of this, the air in Oradea is also rich in nitrogen dioxide. From 1950 until present, the number of Romanian people who suffer from such diseases has increased by 60%. For children under 15, the prevalence of asthma has increased by 41% in the same period (sources: http://www.adevărul.it; http://www.evenimentul.ro; http://www.adevărul, 2007).

MATERIALS AND METHODS

Research has been made about the release of some anti-asthma medicines prescribed by specialists between 2008-2010 in a public pharmacy in Oradea. We tried to determine the increase or the decrease of using these medicines along three years, watching the turnover of these products. Since these products are released by medical prescriptions that remain at the pharmacy, we could determine exactly the necessary quantity to accomplish the pharmacological effect and not the marketing of these pharmaceutical products, represented through an increase or a decrease in sales.

Three subclasses of anti-asthma medical substances (sympatho mimetics, parasympatholytics, corticosteroids and sympathomimetics in combinations) and the frequency of their release from the pharmacy (18 pharmaceutical products) were studied (tables 1-4, fig. 1-4).

RESULTS AND DISCUSSIONS

The anti-asthma medicines reduce the intensity and the frequency of asthma crisis.

1. Sympathomimetic bronchodilators

In this category are included predominant β-adrenergic sympathomimetics used as bronchodilators. Besides the bronchodilator effect, some of them manifest other pharmacological effects also (cardiac stimulation and uterus relaxing). The chemical characteristic of these substances is the bulky substituent for the amino group, which does not allow the fixation on receptors α, which explains the selectivity of receptor activity.

According to the selectivity on β receptors there are:

a) Unselective bronchodilators:

- epinephrine, ephedrine (stimulates the receptors α and β);
- isoprenaline, orciprenaline (stimulates β_1 and β_2 receptors);

b) Selective bronchodilators (β_2-adrenoceptor agonists): terbutaline, fenoterol, salbutamol, salmeterol, hexoprenaline, bambuterol, clenbuterol, formoterol etc. (stimulates β_2 receptors) (Şerban, 2008).

Table 1

Amount of anti-asthma preparations containing substances classed as β_2-adrenoceptor agonists issued in 2008-2010.

Item No.	Commercial name	International common name/composition	2008 (boxes)	2009 (boxes)	2010 (boxes)
1.	ASTMOPENT	orciprenaline 750 µg/dose	5	2	0
2.	VENTOLIN Inhaler CFC-Free	salbutamol 100 µg/dose	299	271	258
3.	BEROTEC N	fenoterol 100 µg/dose	18	12	5

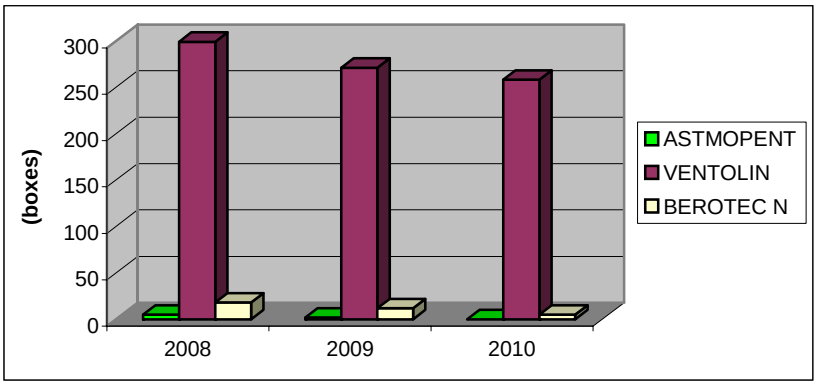

Fig. 1. Variation of release from the pharmacy of sympathomimetic anti-asthma preparations.

2. Anticholinergic bronchodilators

Anticholinergic bronchodilators (parasympatho lytic agents) have antimuscarinic effects by blocking the receptors M_2, M_3 of the smooth muscles of bronchi and reducing the bronchospasm.

Tiotropium, a semisynthetic derivative of scopolamine, is an anticholinergic bronchodilator with unselective action on receptors M_1-M_5, very useful for the treatment of chronic obstructive bronchopulmonary disease (COBP). The bronchodilator effect is for long term and tiotropium must be administered in daily doses (Cristea, 2005; Şerban, 2008).

Ipratropium, a semisynthetic derivative of atropine, is an anticholinergic bronchodilator, which blocks the M_3 muscarinic receptors from the smooth bronchi muscle and prevents the spastic action of acetylcholine at this level. It is indicated in the prophylaxis and treatment of the acute bronchospasm in chronic obstructive pulmonary disease and asthma, the maintaining treatment of bronchospasm of pulmonary disease, the symptomatic improvement of rhinorrhea in allergic and non-allergic rhinitis. The bronchodilator effect installs in 15 minutes and has a medium duration (3-4 hours) (Şerban, 2008).

Table 2

Amount of anti-asthma preparations containing substances classed as anticholinergic agents issued in 2008-2010.

Item No.	Commercial name	International common name/composition	2008 (boxes)	2009 (boxes)	2010 (boxes)
1.	IPRAVENT 20	ipratropium bromide 20 µg/dose	5	5	4
2.	SPIRIVA	tiotropium 18 µg/dose	16	23	13

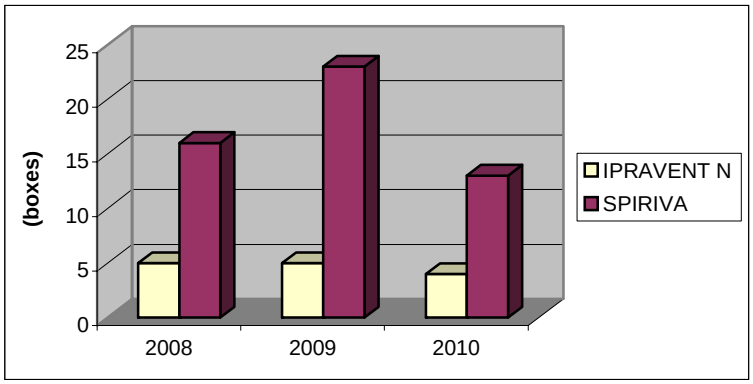

Fig. 2. Variation of release from the pharmacy of anticholinergic agents anti-asthma preparations.

3. Anti-inflammatory corticosteroids

Glucocorticosteroids represent the medication that has maximum of effectiveness. They are chosen in severe crisis of asthma, refractory asthma and status asthmaticus and can be administered: by inhalation, in the prophylaxis and therapy of the crisis; sublingual, in the immediate prophylaxis and therapy of the crisis; by mouth, in the long term prophylaxis; parenteral (s.c., i.m., i.v.) in the therapy of the crisis.

The inhaling method is a current way of administration, both in the long term or immediate prophylaxis and in the therapy of the crisis. The advantages of the inhaling methods are:

- the inhalatory doses represent approx. 10-20% of the systemic ones, and are better tolerated;
- they offer bronchial selectivity, with great improvement;
- the systemic effects are reduced, in comparison with the other ways (by mouth, parenteral) (Cristea, 2005; Cristea, 2009).

In the management of asthma, the active drugs may be administered by inhalation as aerosols, by mouth or by subcutaneous, intramuscular or slow intravenous injection. Inhalation therapy gives some advantages meaning the rapid action of drugs as bronchodilators due to their high selectivity on bronchial receptors (β_2 or M) and low activity on other types of receptors and few side effects. On the other hand, inhalation therapy involves small doses of active drugs in comparison with the same medicines administered by mouth or parenteral route. Taking into account these advantages, all the preparations studied (18) were used as aerosols.

Table 3

Amount of anti-asthma preparations containing antiinflammatory corticosteroids issued in 2008-2010.

Item No.	**Commercial name**	**International common name/composition**	**2008** (boxes)	**2009** (boxes)	**2010** (boxes)
1.	BECOTIDE	beclometasone dipropionate 50 µg/dose	20	7	0
2.	RHINOCORT AQUA	budesonide 32 µg/dose	41	42	16
3.	FLIXOTIDE 50	fluticasone propionate 50 µg/dose	21	16	8
4.	FLIXOTIDE 125	fluticasone propionate 125 µg/dose	28	31	28
5.	FLIXOTIDE Nebules 0.5 mg/2 ml	fluticasone propionate 0.5 mg/2 ml	2	27	43
6.	FLIXOTIDE Nebules 2 mg/2 ml	fluticasone propionate 2 mg/2 ml	1	5	9

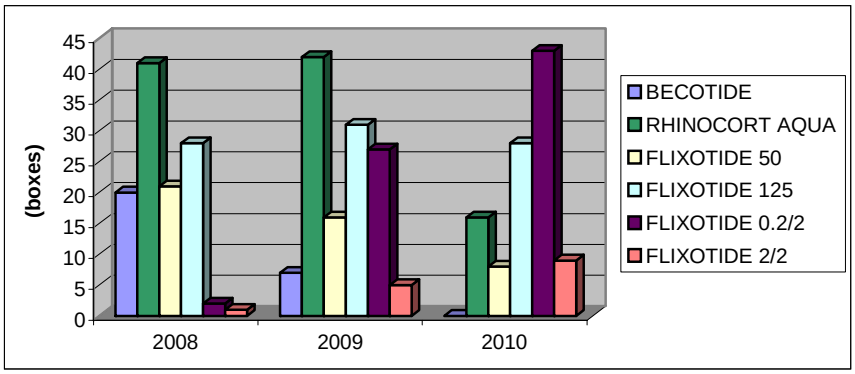

Fig. 3. Variation of release from the pharmacy of antiinflammatory corticosteroids anti-asthma preparations.

Table 4

Amount of anti-asthma preparations containing substances in combinations issued in 2008-2010.

Item No.	**Commercial name**	**International common name/composition**	**2008** (boxes)	**2009** (boxes)	**2010** (boxes)
1.	BERODUAL N	0.05 mg fenoterol + 0.02 mg ipratropium bromide/dose	0	2	13
2.	SERETIDE 50/100	50 µg salmeterol xinafoate + 100 µg fluticasone propionate/dose	6	3	0
3.	SERETIDE 50/250	50 µg salmeterol xinafoate + 250 µg fluticasone propionate/dose	27	44	47
4.	SERETIDE 50/500	50 µg salmeterol xinafoate + 500 µg fluticasone propionate/dose	67	69	74
5.	SYMBICORT 80/4.5	80 µg budesonide + 4.5 µg formoterol fumarate/dose	0	3	4
6.	SYMBICORT 160/4.5	160 µg budesonide + 4.5 µg formoterol fumarate/dose	0	7	20
7.	SYMBICORT 320/9	320 µg budesonide + 9 µg formoterol fumarate/dose	0	4	11

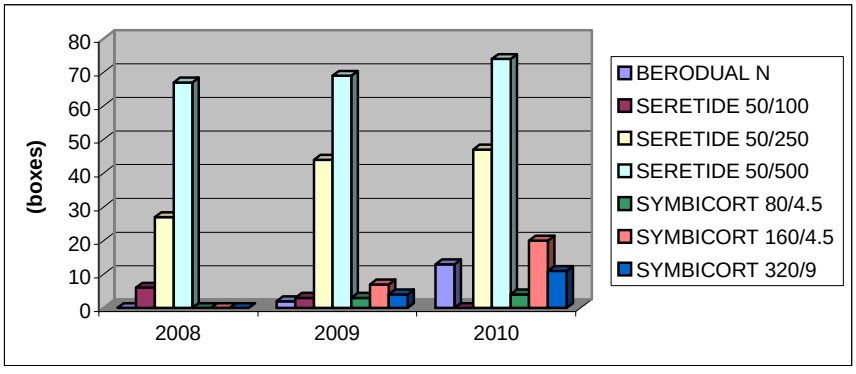

Fig. 4. Variation of release from the pharmacy of anti-asthma preparations (combinations).

CONCLUSIONS

The study of the anti-asthma medicines revealed a decrease in the usage of old sympathomimetic substances with unselective effect (orciprenaline) or dangerous adverse effect (fenoterol), except the products containing salbutamol (Ventolin), a very efficient and selective bronchodilator, the most frequently used in Oradea (fig. 1, table 1).

Very efficient for the treatment of asthma are also those combinations (e.g. Seretide) containing long-acting sympathomimetic bronchodilator agents with high selectivity for β_2 receptors (salmeterol) and anti-inflammatory corticosteroids (fluticasone). Due to complementary effects of the components, these kinds of medicines are particularly rapidly acting agents at low doses with good results in maintenance treatment of asthma (fig. 4, table 4).

Other anti-asthma medicines containing only anti-inflammatory corticosteroids (Becotide, Rhinocort Aqua) or anticholinergic agents (Ipravent, Spiriva) have an intermediate usage among the patients. Even if their components manifest good anti-inflammatory and bronchodilator effect respectively, their significant adverse effects could explain the low popularity of these medicines.

The high number of anti-asthma medicines released by medical prescription in only one public pharmacy in Oradea revealed a high number of patients suffering by this disease in accordance with the low air quality in this city.

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