

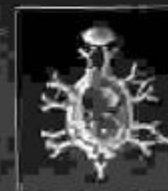
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ASTHMA PREVALENCE AND DRUG PRESCRIPTION IN ASTHMATIC CHILDREN

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Summary

A cross-sectional study was conducted on among 28,856 children aged from birth to 14 years to determine the prevalence of asthma and assess its treatment in a sample of asthmatic children. Children diagnosed with asthma were identified by a sensitive algorithm applied to the information stored in the computerized medical records between 1997 and 1998. Pediatricians then reviewed and validated the diagnosis. Specific information was obtained, after age stratification under 5 ys and over 6 ys, from the medical records and by interview regarding their personal details and treatment of asthmatic patients. In all, 1,263 cases of asthma were identified (64% males) with a prevalence of 6.3% among males and 4% among females in under 5 year-olds, and 3.9% for males and 2.1% for females in over 6 year-olds. The prevalence of asthma diagnosed directly by the pediatrician was consequently higher among under 5 year-olds, in both genders, than among the older children.

Contrary to the international guidelines, pediatricians prescribed more oral corticosteroids and nebulized short-acting β -2 agonists for children under 5 ys olds than for over 6 year-olds (13.3% Vs 4.8% and 25% Vs 10.9%, respectively, $p < 0.001$). For the ≥ 6 year-olds, the most commonly prescribed treatments were oral antihistamines (13.9% Vs 12.6%), inhaled corticosteroids via metered-dose inhaler (30.8% Vs 28.7%) and sodium chromoglycate (12.1% Vs 4.8%, $p < 0.001$).

Key-words: Childhood asthma - Prevalence - Therapy.

INTRODUCTION

Asthma is the most common chronic disease of childhood (1) and its prevalence has been rising in recent decades (2-5), with a considerable variability in industrialized countries (6).

It is the main reason for hospitalization among children in the USA (7), where it is the cause of approximately 1% of all health expenditure (1,8).

In 1997-98, several reports were published containing essentially similar guidelines on the treatment of asthma in adults and children (9-11). These recommendations have undergone further revision by the Global Initiative for Asthma (GINA) (12), demonstrating that the guidelines are continuously evolving. Though they appear to be clear and straightforward, few studies

have been carried out to date to assess adherence to these guidelines (13, 14).

The aim of the present study was to verify the prevalence of asthma cases diagnosed directly by the family pediatrician in a sample of children. Another aim was to analyze the prescription of medication for different age groups.

MATERIALS AND METHODS

SETTING

Within the framework of Health Service, every child is registered at birth and receives free medical care up to 14 years of age from one of the approximately 6,000 family pediatricians working for the Health Service. Our study was based on a population-based database, called "Pedianet", by means of which a national network of pediatricians using a software called "JB 95[®]" took part in a common epidemiological and clinical research project on child care. JB95 is a standardised and validated software used by family pae-

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diatricians to collect and keep clinical information of their patients. Since 1997, Pedianet has collected demographic, clinical and prescription data on the children in the care of the pediatricians belonging to the network. The data are generated from routine patient consultations and include diagnoses, prescriptions, medical examinations, growth measurements, referrals and hospitalizations.

Thirty-two pediatricians (F-PASG) were recruited from among the over 100 belonging to the "Pedianet" network on their interest in participating in this study and their previous involvement in other random Pedianet studies. This cross-sectional study began on April 1st 1999 and the preliminary data collection phase was completed on May 30th 1999. The source population comprised all children aged from birth to 14 years registered as at April 1st 1999 with one of the 32 pediatricians involved. Parents/tutors had given their informed consent to the anonymous treatment of their children's personal data.

DATA COLLECTION

In January 1999 participating paediatricians have been trained on the study procedures, including the electronic form for collecting computerized data on each asthma patient. In March 1999, each pediatrician taking part in the study was given this software application for use in association with the "JB 95[®]" program. The pediatricians were given a month to submit their data to the study centre.

ASTHMA IDENTIFICATION

The asthma patients were identified from the electronic patient records by a sensitive computerized procedure that identified all patients seen by the pediatrician in 1997-1998 and still followed-up at the end of march 1999, registered in the pediatrician's database with a diagnosis of asthma, wheeze bronchitis, recurrent wheezing. The list of potential asthma cases identified by the computerized algorithm was evaluated and confirmed by the pediatrician prior to notification to the study centre according to the following clinical criteria: family history of allergy, age of symptoms appearance, severity of crisis, bronchospasm recovery with or without therapy, bronchospasm triggered by aspecific stimuli (physical activity, passive smoking, cold, etc.) or specific (environmental allergens, etc.). Other criteria considered were: FEV1 increase more than 15% after inhalation of 2 agonist (in collaborating children), elevated IgE levels, plasma eosinophilia, positive RAST test or PRICK test for inhaled allergens (15).

■ The data collected concerned :

- the patient's personal details ; family history of allergy, housing characteristics (country, city centre or suburbs), house heating, parental smoking, presence of pets in the living environment ;
- drug prescribed and taken during the month prior to completing the questionnaire.

These questions were posed in relation to the signs and symptoms as specified by the international guidelines (8-10) and by validated questionnaires (6).

In this paper we have considered only information on prevalence and drug therapy being the most original one.

STATISTICAL ANALYSIS

The prevalence of asthma as at April 1st 1999 was calculated by dividing the number of asthma cases by the number of children registered with the pediatricians. Ninety-five percent confidence intervals were calculated on the basis of the normal distribution. Distributions of categorical and continuous variables were compared using the chi-square test and Student's t-test, respectively.

All the analyses were performed using the SPSS/PC 10 program; p values of < 0.05 were considered statistically significant.

RESULTS

The 32 pediatricians who took part in the study were distributed as follows : 14 in the north (44%), 10 in central Italy (31%) and 8 in the south and islands (25%).

The source population amounted to 28,856 children aged birth to 14 years, (52.4% males, median age 5 years), among which 1,263 confirmed asthma patients (64.2% males) were identified, so the overall prevalence of asthma disease amounted to 4.38%. The prevalence of asthma was higher among males in both age groups and it was also higher in the younger than in the older children (6.3% in males and 4% in females in the group aged under 5 years; 3.9% in males and 2.1% in females in the group over 6 years of age) (table 1).

A significant difference emerged between the various types of medication prescribed in relation to the children's age (table 2) : short-acting nebulized β -2 agonists are prescribed more often in children under 5

years old (25% vs 10.6% in children over 6 years of age), $p < 0.001$), whereas the metered-dose inhaler (MDI) is preferred for children over 6 years old (18.7% vs 7.5% in children under 5 years of age, $p < 0.001$). Nebulized corticosteroids are also used mainly for under 5 year-olds (5.9% vs 4.2% in the older group, $p = 0.19$), as are oral steroids (13.3% vs 4.8% in older children, $p < 0.001$) (table 3).

DISCUSSION

The higher prevalence of asthma recorded among the children under 5 years old was consistent with other reports (16,17). In fact, wheezing is more common up

to 5 years old than in older children because it may also be caused by conditions other than atopy, such as viral infections, which are very common in preschool-age children (18-20). The 3% prevalence recorded among the over 6 year-olds was lower than the 3.9% recently reported in a group of children from the EEC countries (21). The reason could be the climatic and industrial differences in different countries.

As for the type of medication prescribed by the family pediatricians, the most prescribed drugs were beta-2 agonist and inhaled steroids, as recently reported (22).

After age stratification it emerged that nebulized β -2 agonists were preferred for children under 5 years old, despite the literature (23,24) recommending the

	<5 yrs			>6yrs			Total		
	cases	population	prevalence	cases	population	prevalence	cases	population	prevalence
Females	334	8187	4.0%	118	5543	2.1%	452	13730	3.3%
Males	575	9115	6.3%	236	6011	3.9%	811	15126	5.3%
Total	909	17302	5.2%	354	11554	3.0%	1263	28856	4.38%

Table 1 : Prevalence of asthma by gender and age.

Medication	<5 yrs		≥6 yrs		Total		p-value
Short-acting inhaled β -2 agonists	262	32.4%	132	29.1%	394	31.2%	0.23
nebulized	202	25.0%	48	10.6%	250	19.8%	<0.001
aerosol	61	7.5%	85	18.7%	146	11.6%	<0.001
Inhaled corticosteroids	279	34.5%	157	34.6%	436	34.5%	1
nebulized	48	5.9%	19	4.2%	67	5.3%	0.19
aerosol	232	28.7%	140	30.8%	372	29.5%	<0.44
LABACS	42	5.2%	31	6.8%	73	5.8%	0.26
Chromoglycate	39	4.8%	55	12.1%	94	7.4%	<0.001
Anticholinergic agents	17	2.1%	5	1.1%	22	1.7%	0.26
Long-acting β -2 agonists	4	0.5%	15	3.3%	19	1.5%	<0.001

Table 2 : Use of inhaled medication for asthmatic children according to age.

Medication	≤5 yrs		≥6 yrs		Total		p-value
Oral corticosteroids	108	13.3%	22	4.8%	130	10.3%	<0.001
Antihistamines	102	12.6%	63	13.9%	165	13.1%	0.54
Oral β -2 agonists	26	3.2%	9	2.0%	35	2.8%	0.22
Methylxanthine	9	1.1%	1	0.2%	10	0.8%	0.11

Table 3 : Use of oral medication for asthmatic children according to age.

use of short-acting β_2 agonists via MDI in smaller children too, since it has also proved effective in acute asthma (25-27). Moreover, the numerous types of nebulizer on the market have an excessively variable "mass output" (28), making the dose of drug actually inhaled uncertain. The main reason why the nebulizer was still being recommended by the family pediatricians was probably to avoid problems with inhalation techniques for both patient and doctor (29-34).

Oral steroids were prescribed significantly more often for under 5 year-olds than for the older children. In our view, this may be related to the difficulty that some children encounter in taking inhaled corticosteroids, so pediatricians prefer to administer short cycles of oral steroid therapy. This does not seem such a bad idea in the light of authoritative studies demonstrating a reduced risk of hospitalization (35) and re-hospitalization after discharge (36) in patients receiving oral steroid therapy.

Oral antihistamines were prescribed in similar proportions of both age groups. Their use could be influenced by the results of several papers reporting a slowdown in the allergic course of atopic children (37); in the eighties, moreover, it was claimed that antihistamines could have an anti-inflammatory role in asthma disease and a sparing effect on the use of steroids (38) and inhaled β_2 agonists (39).

Some drugs, e.g. long-acting β_2 agonists (40) and antileukotrienes (41, 42) and the association long acting β_2 agonists-corticosteroids inhaled (LABACS) appeared from a short time and their use was not widespread.

On the other hand, methylxanthine seems to have a marginal role (43) and the same goes for chromoglycate (44).

In conclusion, the prevalence of asthma was higher in children, male and female, up to 5 years old than in older children. The medication preferred by pediatricians was MDI-administered drugs for children over 6 years of age, but oral steroids and nebulized β_2 agonists for younger children, despite the recommendations of the international guidelines. Our findings confirm that the use of drugs is continuously changing as suggested by the larger use of LABACS recently reported also in children (45).

REFERENCES

1. Nash D.R., Childs G.E., Kelleher K.J. - A cohort study of resource use by Medicaid children with asthma. *Pediatrics* 1999;104:310-312.

2. Burr M.-L., Butland M.-K., King S., Vaughan-Williams E. - Changes in asthma prevalence: two surveys 15 years apart. *Arch Dis Child* 1989;64:1452-1456.
3. Rona R.-J., Chinn S., Burney P.-G. - Trends in the prevalence of asthma in Scottish and English primary school children 1982-1992. *Thorax* 1995;50:992-993.
4. Omran M., Russel G. - Continuing increase in respiratory symptoms and atopy in Aberdeen schoolchildren. *BMJ* 1996;312:334.
5. Hartert T.-V., Peebles R.-S. - Epidemiology of asthma: the year in review. *Curr Opin Pulm Med* 2000;6:4-9.
6. The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. - Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. *Lancet* 1998;351:1225-1232.
7. Kelly C.-S., Andersen L.-C., Pastian J.-P., Wenger A.-D., Finch A.-B., Strope G.-L., Luckstead E.-F. - Improved outcomes for hospitalized asthmatic children using a clinical pathway. *Ann Allergy Asthma Immunol* 2000;84:509-516.
8. Weiss K.-B., Gergen P.-J., Hodgson T.-A. - An economic evaluation of asthma in the United States. *N Engl J Med* 1992;326:862-866.
9. National Heart, Lung and Blood Institute. - Guidelines for the diagnosis and management of asthma: expert panel report 2-1997. Bethesda MD: National Institutes of Health, 97-4051.
10. Warner J.-O., Naspitz C. K., Cropp G.-J. - Third international pediatric consensus statement on the management of childhood asthma. *Pediatr Pulmonol* 1998;25:1-17.
11. The British guidelines on asthma management. *Thorax* 1997; 52(S):1-21.
12. National Heart, Lung, and Blood Institute. - Global strategy for asthma management and prevention. National Institute of Health Pub No 02-3659.
13. Legorreta A.-P., Christian-Herman J., O'Connor R.-D. - Adherence with national asthma management guidelines and specialty care: a health maintenance organization experience. *Arch Intern Med* 1998;158:457-464.
14. Jabulis D.-E., Meng Y.-Y., Elashoff R.-M. - Preventive pharmacologic therapy among asthmatics: five years after publication of guidelines. *Ann Allergy Asthma Immunol* 1998;81:82-88.
15. ATS. - Standards for diagnosis and care of patients with chronic obstructive pulmonary disease (COPD) and asthma. *Am Rev Respir Dis* 1987;136:225-244.
16. Sears M.-R. - Evolution of asthma through childhood. *Clin Exp Allergy* 1998;28 (55):82-89.
17. Senthilselvan A. - Prevalence of physician-diagnosed asthma in Saskatchewan, 1981 to 1990. *Chest* 1998;114:388-392.
18. Silverman M. Out of the mouths of babes and sucklings-lessons from early childhood asthma. *Thorax* 1993;48:1200-1205.
19. Martinez F.-D., Wright A.-L., Taussig L.-M., Holberg C.-J., Halonen M., Morgan W.-J. - Asthma and wheezing in the first six years of life. *N Engl J Med* 1995;332:133-138.
20. Godden D.-J., Ross S., Abdalla M., McMurray D., Douglas A., Oldman D., Friend J.-A., Legge J.-S., Douglas J.-G. - Outcome of wheeze in childhood. Symptoms and pulmonary function 25 years later. *Am J Respir Crit Care Med* 1994;149:106-112.
21. Leonardi G.-S., Houthuijs D., Nikitorof B., Volf J., Rudnai P., Zejda J., Gurzau E., Fabianova E., Fletcher T., Brunekreef B. - Respiratory symptoms, bronchitis and asthma in children of Central and Western Europe. *Eur Respir J* 2002;20:890-98.
22. Kuehni C.-E., Frey U. - Age-related differences in perceived asthma control in childhood: guidelines and reality. *Eur Respir J* 2002 Oct;20(4):880-889.
23. Child F., Davies S., Clayton S., Fryer A.-A., Lenney W. - Inhaler devices for asthma: do we follow the guidelines? *Arch Dis Child* 2002;86:176-179.
24. The British guidelines on asthma management 1995. Review and position statement. *Thorax* 1993;48(S):s1-s24.
25. Fuglsang G., Pedersen S. - Comparison of nebulizer and nebulizer treatment of acute severe asthma children. *Eur J Respir Dis* 1986;69:109-113.
26. Lin Y.-Z., Hsieh K.-H. - Metered dose inhaler and nebulizer in acute asthma. *Arch Dis Child* 1995;72:214-218.
27. Rubilar L., Castro-Rodriguez J., Girardi G. - Randomized trial of salbutamol via Metered-Dose Inhaler with spacer versus nebulizer

- for acute wheezing in children less than 2 years of age. *Pediatr Pulmonol* 2000; 29:264-269.
28. Smith E-C., Denyer J., Kendrick A.-H. - Comparison of 23 nebulizer/compressor combinations for domiciliary use. *Eur Respir J* 1995;8:1214-1221.
29. Boe J., Dennis J.-H., O'Driscoll B.-R., Bauer T.-T., Carone M., Dautzenberg B., Diat P., Heslop K., Lannefors L. - European Respiratory Society Guidelines on the use of nebulizers. *Eur Resp J* 2001;18:228-242.
30. Kamps A., van Ewijk B., Roorda R.-J., Brand P.L. - Poor inhalation technique, even after inhalation instruction, in children with asthma. *Pediatr Pulmonol* 2000;29:39-42.
31. Gilles J. - Overview of delivery system issues in paediatric asthma. *Pediatr Pulmonol* 1997;15:55-58.
32. O'Callaghan C., Barry P.-W. - Asthma drug delivery devices for children. *BMJ* 2000;320:664.
33. Amirav I., Goren A., Pawlowski N. -A. - What do pediatricians in training know about the correct use of inhalers and spacer devices? *J Allergy Clin Immunol* 1994;94:669-675.
34. Hanania N.-A., Wittman R., Kesten S., Chapman K.-R. - Medical personnel's knowledge of and ability to use inhaling devices. *Chest* 1994;105:1111-1116.
35. Littenberg B., Gluck E.-H. - A controlled trial of methylprednisolone in the emergency treatment of acute asthma. *New Engl J Med* 1986; 314:150-52.
36. Chapman K.-R., Verbeek P.-R., White J.-H., Rebuck A.-S. - Effect of a short course of prednisone in the prevention of early relapse after emergency room treatment of acute asthma. *New Engl J Med* 1991; 324: 788-794.
37. Warner J.-O. - A double-blinded, randomized, placebo-controlled trial of cetirizine in preventing the onset of asthma in children with atopic dermatitis: 18 months' treatment and 18 months' post-treatment follow-up. *J Allergy Clin Immunol* 2001;108:929-937.
38. Lane D.-J. - A steroid sparing effect of ketotifen in steroid dependent asthmatics. *Clin Allergy* 1980;10:519-525.
39. Varsono J., Volovitz B., Safferman R., Tal A., Schlessinger M., Ratchild M., Tabach E. - Multicenter study with Ketotifen (Zaditen) oral drop solution in the treatment of wheezy children aged 6 months to 3 years. *Pediatr Allergy Immunol* 1993;4:45-50.
40. Bisgaard H. - Long-acting 2-agonists in management of childhood asthma: a critical review of the literature. *Pediatr Pulmonol* 2000;29:221-234.
41. Kemp J.-P. - Role of leukotriene receptor antagonist in pediatric asthma. *Pediatr Pulmonol* 2000;30:177-182.
42. Becker A. - Leukotriene receptor antagonist : efficacy and safety in children with asthma. *Pediatr Pulmonol* 2000;30:183-186.
43. Skoner D.-P. - Balancing safety and efficacy in pediatric asthma management. *Pediatrics* 2002;109:381-392.
44. Konig P., Grigg C.-F. - Cromolyn sodium or nedocromil in childhood asthma: does it matter? *Clin Exp Allergy* 2000;30:164-171.
45. Van Den Berg N.-J., Ossip M.-S., Hederas C.-A., Antilla H., Ribeiro B.-L., Davies P.-L. - Salmeterol/fluticasone propionate (50/100) in combination in a Diskus inhaler (Seretide) is effective and safe in children with asthma. *Pediatr Pulmonol* 2000;30:97-105.

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