

ASTHMA IN ITALIAN CONSCRIPTS : A FOUR YEAR STUDY

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Summary

■ **Background :** Italian conscripts showed underdiagnosis and undertreatment of asthma in a previous 9-year study (1990-1998).

■ **Methods :** We extended those findings in a new 4-year study (1999-2002) by screening 28,327 18-year old males referred to La Spezia Military Navy Hospital for call-up visit.

■ **Results :** Asthma was diagnosed in 1,847 conscripts (6.52%). Along the observational period there was a significant decrease of mild persistent asthmatic subjects (from 39.6 to 30.1%, $p < 0.01$). The use of inhaled corticosteroids and antileukotrienes significantly increased. However, about one third of the asthmatic subjects did not receive any treatment at all and about 40% of asthmatic subjects showed impaired spirometry.

■ **Conclusions :** In this age, data show a partial success of educational efforts, since underdiagnosis and undertreatment are still present.

Key-words : Asthma - Italian conscripts - Underdiagnosis - Undertreatment.

INTRODUCTION

Numerous studies reported a world-wide increasing prevalence of asthma (1-3). Some epidemiological surveys have shown asthma-like symptoms to be more prevalent than physician diagnosed asthma (4-5) and underdiagnosis of asthma has been repeatedly suspected, especially in children and young adults (4, 6). Consequently, undertreatment of asthma may result from underdiagnosis and/or insufficient prescription of reliever and controller drugs (4-9).

We have previously reported asthma undertreatment in Italian young men, as assessed by medical examination for Navy enrollment during the 1990-98 period (10). Those data derived from a particularly homogeneous population, for age, sex and residence (the "conscript model"), undergoing standardized medical *investigative procedures*. Therefore, the conscript model is suitable for further re-evaluation.

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Aim of the present study was to extend previous data on asthma prevalence and treatment to the 1999-2002 four-year period.

MATERIAL AND METHODS

■ **Call-up visit :** In Italy all men undergo medical examination at the age of 18 to establish their fitness for military service, which is compulsory for those who are fit for it. Navy recruitment occurring in Italy is divided between the two call-up centers of La Spezia and Taranto. Thus, La Spezia call-up concerns about half Italian conscripts for navy recruitment. Geographic distribution of La Spezia call-up pertinence consists of the half part of Italy subdivided longitudinally. Therefore, the cohort visited in La Spezia represents an *important model to study Italian men 18 years old*.

The call-up medical examination is carried out in two stages. Firstly, the conscript is examined by military physicians at the call-up Council (La Spezia). Fitness is assessed on the basis of history and the findings of a clinical examination.

Secondly, if diagnosis of asthma is suspected or need to be confirmed, the conscript is referred to Military Navy Hospital (La Spezia) for further standardized tests (skin prick test, spirometry, and metacholine bronchial challenge).

■ **Standardized procedures for asthma evaluation :** Skin prick test is performed, as stated by the Italian Society of Allergy and Clinical Immunology (11). The panel consists of: mites (*Dermatophagoides farinae* and *pteronyssinus*), cat, dog, grass mix, *Compositae* mix, *Parietaria Officinalis*, birch, hazel tree, olive tree, *Alternaria Tenuis*, *Cladosporium*, *Aspergilli* mix (D (DHS-Bayer Group, Milan, Italy).

Spirometry is performed by using a computer-assisted spirometer (COSMED, Eurasem, Italy), with optoelectronic whirl flow meter. Spirometry is performed as stated by ERS (12), using the European Community for Steel and coal (ECSC) reference equations. and C.E.C.A.

Metacholine bronchial challenge is performed to exclude asthma only if basal FEV1 is equal or more than 80% of predicted. Aerosol is delivered using a dosimetric computerized supply (MEFAR MB3, Marcos, Italy). Subjects inhale increasing doses of metacholine (starting from 200 to 1,590 µg). The test is interrupted if FEV1 value is reduced by more or equal than 20% of control or a maximal cumulative

dose of 1590 µg is achieved. The threshold dose causing a 20% fall of FEV1 (PD20) is calculated. For call-up visit, asthma is excluded if PD20 is > 800 mg.

Study design. We examined data relative to call-up visit at La Spezia call-up Council and Military Navy Hospital from 1999 to 2002. Out of 28,327 examined conscripts 2,966 were referred to Military Navy Hospital to confirm or exclude asthma diagnosis. Asthma was diagnosed according to GINA guidelines (13) by clinical or functional features and not on current medication (14). Subjects answered a questionnaire to investigate asthma treatments relative to the last year.

■ **Data analysis :** Statistical analysis was performed using C square test, calculating confidential limits of the relative risk at 95%. Differences were considered significant if p values were <0.05. Data are presented as means.

RESULTS

The diagnosis of asthma was confirmed or done for the first time in 1,847 young men (6.52%). Distribution of subjects' sensitization to allergens and of FEV1% of predicted values are summarized on table 1 and 2. The percentage of asthmatic subjects with FEV1>80% of predicted values increased significantly along the 4-

SPT	Dermat. <i>farinae</i>	Dermat. <i>Pter.</i>	Grass. mix	Pariet. off.	Comp.	Trees	Molds	Dog dander	Cat dander
1999	75	78	48	36	13	37	9	6	19
2000	71	72	54	34	11	33	9	4	15
2001	67	67	46	36	12	32	7	4	19
2002	89	89	58	36	19	45	12	4	25
Mean value	75.5	76.5	51.5	35.5	13.7	36.7	9.2	4.5	19.5

Table 1 : Percentage distribution of subjects' sensitization to common allergens along the 4-year observational period. SPT, skin prick test; Trees: olive, hazel-nut, birch.

FEV1, % predicted	<60%	≥60% and <70%	≥70% and <80%	≥100% and <80%
1999	5.8	15.4	33.6	45.2
2000	5.3	17.1	28.5	49.1
2001	1.3	10.2	20.6	67.9
2002	2.3	14.2	22.1	61.4
(Mean)	3.7	14.2	26.2	55.9*

Table 2 : Percentage distribution of FEV1% of predicted values along the 4-year observational period in the conscripts.

* significant increase along the 4-year observational period.

year observational period ($p=0.01$). Moreover, about 40% of asthmatic had an impaired spirometry ($FEV1 < 80\%$ of predicted).

Asthmatic subjects were classified according to GINA guidelines (13) as follows: 47.6% intermittent (I), 34.9% mild persistent (II), 10.8% moderate persistent (III), and 6.7% severe persistent (IV).

Along the 4-year observational period (figure 1), there was a significant reduction of mild persistent asthma ($p < 0.01$).

Asthmatics were subdivided in three groups concerning the treatment (figure 2, panel A-C) :

- without treatment ;
- receiving relievers only (i.e. short acting β_2 -agonists) ;
- treated with relievers plus controllers (i.e., long acting β_2 -agonists, inhaled corticosteroids, and leukotrienes antagonists).

Along the 4-year observational period the group of asthmatic subjects without treatment or treated with relievers only were significantly decreased ($p=0.04$ and $p < 0.01$, respectively). On the other hand, the prescription of relievers plus controllers was significantly increased ($p < 0.001$).

Specifically, there was an increased use of long acting 2-agonists ($p < 0.004$), leukotrienes antagonists ($p < 0.005$) and inhaled corticosteroids ($p < 0.001$). Distribution of these antiasthmatic drugs is illustrated in figure 3 (panel A-C). The percentage of asthmatic subjects treated with systemic corticosteroids was unchanged during the 4-year observational period (2%).

Other antiasthmatic drugs were not reported, since the percentages of prescription were very low, ranging

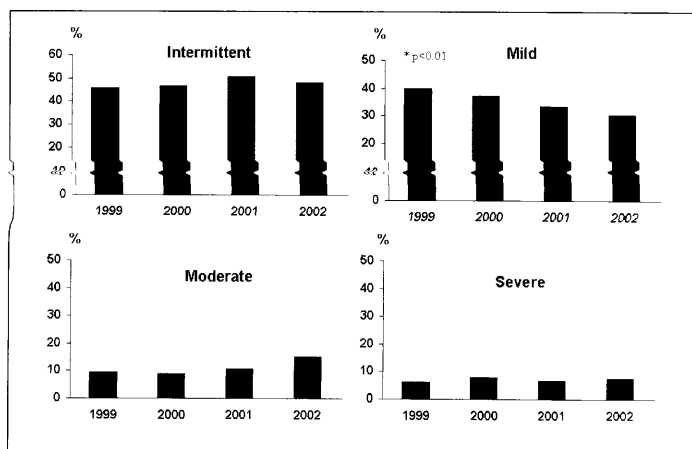


Figure 1 : Distribution of asthma severity according to GINA guidelines during the 4-year observational period in the conscripts. There was a significant reduction of mild asthmatic subjects ($p < 0.01$).

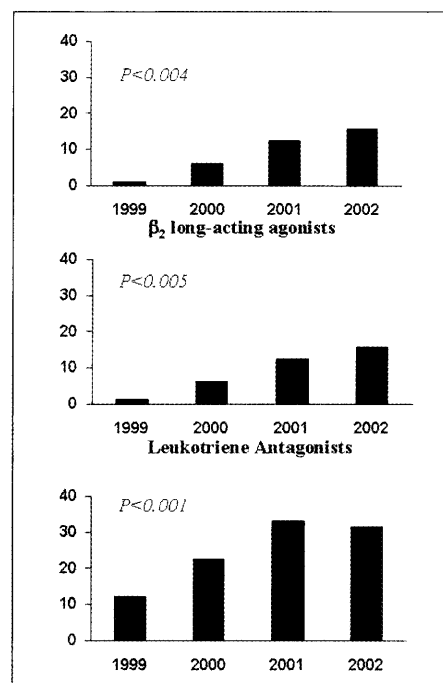


Figure 3 : Distribution of therapeutic classes according to GINA guidelines during the 4-year observational period in the conscripts. The percentage of asthmatic subjects without therapy (A) or using relievers (B) decreased ($p < 0.04$), but increased the percentage of them using reliever plus controller drugs (C, $p < 0.001$).

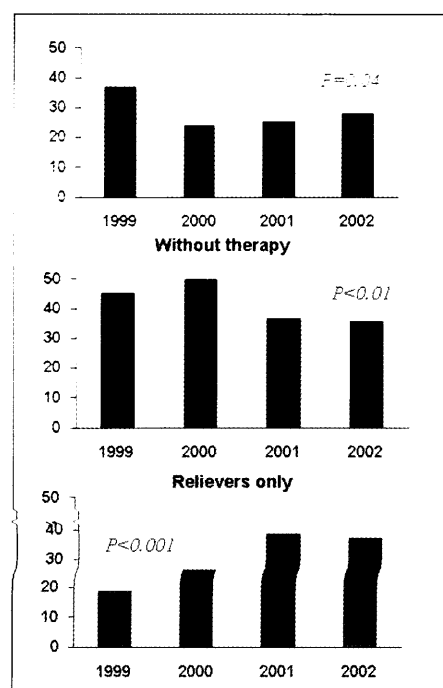


Figure 2 : Distribution of different antiasthmatic drugs in the conscripts during the 4-year observational period in the conscripts. The percentage of asthmatic subjects using β_2 long-acting agonists (A), leukotriene antagonists (B), and inhaled corticosteroids (C) was increased ($p < 0.005$).

from 0.2% to 1.6% for cromones and from 0.1% to 0.8% for theophylline.

DISCUSSION

Asthma prevalence is continuously increasing in the industrial countries, as reported by numerous world-wide surveys, based essentially on questionnaires conducted in both school children and adult populations (1-3).

We believe that our epidemiologic study of conscripts is of interest for the high number of subjects studied, their homogeneity, and the standardized investigational procedure (medical visit, skin prick test, spirometry, metacholine) (10). Particularly, our study offers an important split concerning epidemiologic data on Italian Navy recruitment, and consequently about Italian young men.

Our 4-year observational period on conscripts shows a similar percentage of asthmatic subjects (about 6.5%) to other European surveys and previous findings on the 1990-1998 period (15-17). A new data is the reduction of the percentage of mild asthmatic subjects (GINA II class), associated with an increased use of reliever plus controller drugs during this observational period and compared to the previous 5-15% data (10). Moreover, during the 4-year observational period, the percentage of asthmatic conscripts with a FEV1% of predicted values >80% increased significantly ($p=0.01$).

The decrease of mild asthma probably is the result of educational efforts and increased prescriptions of reliever drugs strictly associated to controller drugs. It is important to note that recently new anti-asthmatic drugs have been introduced in GINA guide-lines (13): the antileukotrienes, approved for chronic asthma treatment and for long term prophylaxis of exercise-induced asthma. The role of leukotriene antagonists in asthma outcomes is well established and their anti-inflammatory properties are supported by several studies (18-19). In Europe antileukotrienes were considered a third line treatment, particularly in moderate asthma, and consequently licensed to be used as additional therapy in patients taking already inhaled and/or oral corticosteroids (18). Very recently, a meta-analysis was published about the bronchoprotective effects of leukotriene receptor antagonists in asthma (20). This study confirmed the role of antileukotrienes as anti-inflammatory therapy in asthma.

However, GINA guidelines were revised again (www.ginaasthma.com) and antileukotrienes have been clearly positioned as an alternative to low doses

of inhaled corticosteroids in mild asthma. Their oral administration is of great importance for patients' compliance, particularly in this age range. A recent open-label, randomised, two-period, crossover study on 113 asthmatic subjects aged 12-17 years, reported preferences of asthmatic adolescent (21). The results indicated that adolescents preferred zafirlukast (70%) to low doses of inhaled beclomethasone propionate (27%) and that only 29% of adolescents were able to use their inhaler correctly. Actually, the incorrect use of inhalers is also a well-known cause of poor response in some patients (22). It is well known that when comparing patients' compliance with prescribed oral or inhaled asthma medication, results indicate that oral is superior to inhaled administration (23). Patients' compliance with oral medication ranges from 70% to 80%, while with inhaled medications from 30% to 60% (23,24).

However, even if asthmatic subjects without any treatment are decreasing, there was a discrepancy between the percentage of subjects with intermittent asthma (GINA I class, 34.9%) and of subjects using relievers only (41.1%). Furthermore, asthmatic subjects without any treatment were 28.8%. These findings imply an evident undertreatment: one third of asthmatics is without any therapy (even a reliever as needed) and one tenth of them is without a controller therapy. Moreover, the high percentage of asthmatic subjects (40%) with impaired spirometry is an important signal of possible undertreatment of asthma.

Possible explanations of asthma undertreatment could be insufficient physicians' adherence to asthma guidelines, a reduced compliance in adolescents, an improper use of inhaler drugs, and finally an attitude to denial asthma symptoms in this age range. Nevertheless, a reduction of mild persistent asthma occurs. This evidence might derive from a increased prescription of inhaled corticosteroids (even though still insufficient - only 30% of asthmatics is treated with them in 2002) and the introduction in the market of antileukotrienic drugs since 1998.

In conclusion, our study showed an increased use of controller drugs during the 4-year period study and compared to previous data. However, further educational efforts are necessary attempts to gain an optimal management of asthma, particularly in this age range.

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PRESS RELEASE

New research on trends in asthma treatment ; safe medication for pregnant women*

MILWAUKEE - Asthma treatment over the past decade is increasingly consistent with current asthma guidelines, leading to improved asthma control, according to a study in the April 2003 Journal of Allergy and Clinical Immunology (JACI). The JACI is the peer-reviewed journal of the American Academy of Allergy, Asthma and Immunology (AAAAI).

Asthma is a chronic disease that affects more than 17 million people in the United States. Current asthma guidelines emphasize the importance of long term control of underlying airway inflammation in asthma treatment. Inhaled corticosteroids, either alone or in combination with long-acting inhaled β_2 -agonists, are recommended as the primary treatment for patients with moderate to severe asthma. Short-acting inhaled β_2 -agonists, once the mainstay of asthma therapy, are now only recommended for mild intermittent asthma or the prevention of exercise-induced symptoms.

In the study, Randall S. Stafford, MD, PhD, Stanford Center for Research in Disease Prevention, and colleagues analyzed 25 years of data extracted from the National Disease and Therapeutic Index (NDTI). Researchers tracked trends from 1978-2002 in the frequency of asthma visits and patterns of asthma treatment, focusing on the use of controller and reliever medications.

Researchers noted substantial changes in the number of asthma visits and in asthma treatment over the past 25 years. Among the findings : Asthma hospital visits doubled between 1978 (8.5 million visits) and 1990 (17.7

million visits). However, the number of visits stabilized at an average of 16 million per year between 1991 and 2002.

There is a declining trend in the number of return hospital visits for asthma, an indirect indicator of improved asthma control.

The data indicated an increasing trend in the prescription of controller medications, particularly inhaled corticosteroids, and a decreasing trend in reliever medication use, particularly short-acting oral β_2 -agonists.

In 2001, the prescription rate for asthma controller medication surpassed that of reliever medication for the first time (83% vs. 80%). The difference widened in 2002.

Xanthines, which once dominated asthma therapy, were used in only 2% of visits in 2002.

- Prescribed asthma treatment 1978-2002

- Controller 10% 81%

- Reliever 58% 72%

- Xanthines 63% 2%

Increases in the prescription rates of controllers reflect a rise in the use of inhaled corticosteroids, long-acting β_2 -agonists and leukotriene modifiers. The JACI study contributed to previous findings demonstrating that asthma treatment is evolving to be more consistent with consensus guidelines.

* from the Journal of Allergy and Clinical Immunology