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Are young adults with asthma treated sufficiently with inhaled steroids? A population-based study of prescription data from 1991 and 1994

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1 We conducted a descriptive cross-sectional study of asthma therapy among young adults to assess to what extent the current guidelines for asthma therapy have been implemented. In particular, we examined the use of inhaled corticosteroids in heavy users of inhaled β-adrenoceptor agonists.

2 Data were retrieved from a population-based prescription database. For each of the years 1991 and 1994, all 20 to 44-year-olds who redeemed anti-asthma medication in the Odense area (210 000 inhabitants) were studied.

3 We identified the number of users and total sales volume for specific anti-asthma medications in defined daily doses (DDD) as well as the number of users and median annual doses of common regimens. Combined use of inhaled corticosteroids and inhaled β-adrenoceptor agonists was also described.

4 The annual sales volume of anti-asthma drugs increased by 23% to 927 636 DDD from 1991 to 1994. Inhaled corticosteroids were mainly responsible for this with a 52% increase in number of users and an 88% increase in DDD. Inhaled β-adrenoceptor agonists used in monotherapy remained the most popular regimen in 1994 (1685 users = 39%). Inhaled corticosteroids in combination with inhaled β-adrenoceptor agonist were the second most popular regimen in 1994 (1308 users = 30%), increasing by 64% as compared with 1991. However, among patients with an annual use of inhaled β-adrenoceptor agonist of 200 DDD (1600 'puffs') or more the percent of patients not receiving inhaled corticosteroids at all only fell from 37 to 33%.

5 Though the number of patients being treated with inhaled corticosteroids has increased, there is still evidence of a substantial underuse.

Keywords asthma bronchiale anti-asthma drugs pharmacoepidemiology inhaled corticosteroids

Introduction

Recognition of the importance of the inflammatory component of asthma has been reflected in modern therapeutic principles of treatment of this disease. A number of guidelines and consensus reports suggest a stepwise approach to asthma treatment guided by the severity of the disease [1, 2]. Initiation of inhaled corticosteroid therapy is recommended even in cases of mild asthma.

In a recent publication [3], we presented the results of a population-based analysis of individual utilization of anti-asthma medication in the Odense area. Using the intensity of inhaled β-adrenoceptor agonist treatment as an indicator of the frequency of asthma symptoms, we found a remarkably large fraction of patients who were undertreated with inhaled steroids. The purpose of this study was to examine the development in the use of anti-asthma medication, in particular with respect to a more intensive use of inhaled corticosteroids according to current recommendations.

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Methods

The data were retrieved from the Odense Pharmacoepidemiologic Database (OPED), a prescription database that has been described in detail elsewhere [3]. In brief, OPED has offered full coverage of all prescription refunds in the Odense area since October 1990. OPED covers prescriptions issued by GPs, specialists in private practice and physicians in out-patient units. Medication consumed during hospital admissions is not registered in OPED. The registration of a unique and constant person identifier makes the charting of individual drug consumption histories possible. The database does not contain information on the indication for treatment or the address of the prescription holder.

The study area covering Odense and surroundings (210 000 inhabitants) is an urban/suburban area. The largest fraction of the population is employed in the administrative and service sectors, but also in industrial fields such as shipyard, metalworks, and light industry. Owing to a large university and several other educational institutions, the fraction of the population in the age group 20–30 years is somewhat larger than the average for the whole country.

In Denmark, medical attendance is free of charge. General practitioners (GPs) carry out most of the health care in the Odense area and are responsible for more than 90% of all prescriptions on anti-asthma medications in out-patients. GPs can refer patients to specialists or a large university hospital, which serves as the primary hospital for the area.

For each of the years 1991 and 1994, all prescriptions for anti-asthma medication presented to pharmacies by out-patients aged 20 to 44 years were retrieved. Restriction of the material to data concerning inhabitants of the study area was achieved by only including patients presenting more than half of their anti-asthma drug prescriptions at pharmacies within the study area. Prescriptions presented by these persons outside the Odense area were also included in the analysis.

The denominators used to calculate annual period prevalences were obtained from the Danish Statistical Institute [4]. According to this source, 83 013 persons aged 20 to 44 resided in the study area in 1991, increasing to 85 008 in 1994. Ninety-five per cent confidence intervals for the prevalences were calculated according to the Poisson distribution. We used the χ^2 test to compare the proportion of inhaled steroid users within categories of inhaled β-agonist use in 1991 and 1994.

The following were considered as anti-asthma medications: inhaled and oral β-adrenoceptor agonists, inhaled anticholinergics, oral xanthines (except caffeine), inhaled glucocorticoids and inhaled cromones. We considered oral glucocorticoid as anti-asthma medication only if it was redeemed by a user of another anti-asthma medication. Anti-asthma medications dispensed as mixtures are used to treat acute bronchitis and were therefore excluded from the analysis. Other dispensing forms (suppositories, injections) only constituting a minor part of the total amount of drugs redeemed were left out for the sake of clarity. Included in the analysis were tablets and inhaled medications.

Users of oral β-adrenoceptor agonist in monotherapy were excluded before calculation of annual period prevalences of use of anti-asthma medication. The low median annual consumption throughout the period observed in this group supported our suspicion that this regimen was primarily used for breathing symptoms associated with respiratory infections and not asthma.

Consumption was described by the Defined Daily Dose (DDD) unit [5]. The DDD is established by a group of experts and represents the typical dose required when the drug is used for its main indication by an adult. Drugs used for the same indication are in principle equipotent when measured in DDD. DDDs for the most frequently used anti-asthma medications in our material are presented in Table 1.

Results

Sales volumes and number of users

In Table 2, the amount of DDD sold for selected anti-asthma medications and the corresponding number of users are presented for the years 1991 and 1994. Sales of the anti-asthma drugs among 20 to 44-year-olds rose from 752 695 DDD in 1991 to 927 636 DDD in 1994, an overall increase of 23%.

Inhaled corticosteroids were responsible for the largest increase in sales volume (DDD) as well as in number of users. As compared with 1991, an 88% increase in sales volume of inhaled corticosteroids and a 52% increase in the number of users of this drug was observed in 1994.

Sales of inhaled β-adrenoceptor agonists (DDD) rose by 13% during the same 4-year period corresponding to a 24% increase in the number of users. Increases in sales volume and number of users were also observed

Table 1 Defined daily doses (DDD) of anti-asthma medications frequently used by young adults in Odense and environs in 1991 and 1994

Route	*Drug*	*DDD*
Inhaled	Salbutamol	0.8 mg
	Terbutaline	2.0 mg
	Fenoterol	0.6 mg
	Salmeterol	0.1 mg
	Budesonide	0.8 mg
	Beclomethasone	0.8 mg
	Fluticasone	0.6 mg
	Ipratropium	0.12 mg
	Cromoglycate	80.0 mg
Nebulized	Salbutamol	10.0 mg
	Terbutaline	20.0 mg
Oral	Salbutamol	12.0 mg
	Terbutaline	15.0 mg
	Bambuterol	20.0 mg
	Theophylline	400 mg
	Prednisolone	10.0 mg

Table 2 Number of individual users of anti-asthma medications and their consumption in the years 1991 and 1994 among residents of Odense and environs aged 20–44 years

		1991		*1994*	
Route	*Drug*	*Number of users*	*Sales volume (1000 DDD)*	*Number of users*	*Sales volume (1000 DDD)*
Inhaled	β-adrenoceptor agonist	2902	469.4	3605	530.6
	Salbutamol	1691	298.8	1463	268.7
	Terbutaline	1127	151.9	1982	237.5
	Anticholinergic	37	3.8	57	8.7
	Corticosteroid	1485	157.4	2255	295.1
	Budesonide	738	78.6	1503	201.5
	Beclomethasone	747	78.7	565	76.2
	Cromone	56	2.8	30	1.4
Oral	β-adrenoceptor agonist	770	41.9	549	32.0
	Salbutamol	291	18.3	165	11.3
	Terbutaline	469	23.2	346	17.1
	Xanthine	268	55.9	136	35.3
	Corticosteroid	172	21.5	207	24.5

for oral corticosteroids and anticholinergics. For the other anti-asthma medications, a decrease in both sales volume and number of users was observed. For xanthines, the number of users decreased by 49% and the sales volume by 63%.

The fraction of the inhaled drugs taken by dry powder inhalers rose from 58% in 1991 to 70% in 1994 for bronchodilators, and from 79% to 92% for anti-inflammatory drugs. These increases occurred largely at the expense of metered dose inhalers. The proportion of medication dispensed as nebuliser solution remained low in 1994 (bronchodilators = 1.7%, anti-inflammatory drugs = 1.9%).

The number of users of anti-asthma medication rose from 3151 in 1991 to 4044 users in 1994, a 28% increase. Correspondingly, the 1 year prevalence of users of anti-asthma medication rose from 3.8% (95% CI = 3.7–3.9) to 4.8% (95% CI = 4.6–5.0). Though the increase in 1-year prevalence was present in both sexes, a gender difference was observed (5.7% and 3.8% for females and males in 1994, respectively).

Regimens

The five most popular regimens of anti-asthma treatment during the years 1991 to 1994 are presented in Table 3. More than 84% of all users of anti-asthma medication were treated with one of these regimens. Monotherapy with inhaled β-adrenoceptor agonist remained the most popular regimen throughout the period, the number of its users increasing by 19% in 1994. A stable median annual dose of 50 DDD consumed by each individual was observed.

A combination of inhaled β-adrenoceptor agonist and inhaled glucocorticoid was the second most preferred regimen and was used by 1308 patients in 1994, 64% more than in 1991. Approximately 30% of all users of anti-asthma medication in 1994 were given this combination. The median annual consumption of β-adrenoceptor agonist was stable at 100 DDD throughout the period, while median consumption of inhaled glucocorticoid rose from 60 to 90 DDD.

Single therapy with inhaled glucocorticoids increased by 90% during the period, the median annual dose remaining unchanged at 50 DDD. Use of oral β-adrenoceptor agonists as monotherapy declined by 26%. The median annual consumption, however, remained stable at 7 DDD.

The fifth most common regimen consisted of a combination of inhaled β-adrenoceptor agonist, inhaled glucocorticoid and oral β-adrenoceptor agonist with median annual doses of 100–150 DDD, 75–100 DDD and 33–50 DDD, respectively. This combination therapy was used by 84 patients in 1994, 11% less than in 1991.

Use of inhaled steroid among users of inhaled β-adrenoceptor agonist

In Table 4, users in 1991 and 1994 were classified according to their total annual consumption of β-adrenoceptor agonists. Within each category of β-adrenoceptor agonist consumption, the patients were further subdivided in classes depending on the amount of inhaled steroids they redeemed during the year of interest. Overall, the proportion of users of inhaled steroid within classes of inhaled β-adrenoceptor agonist use showed a moderate but statistically significant change from 1991 to 1994 (χ^2 test: $P < 0.001$). There was a general increase in number of patients with a relatively high consumption of inhaled steroids (≥ 175 DDD/year), but this increase was moderate and not clearly related to the amount of inhaled β-adrenoceptor agonists used. Likewise, the decrease in the percentage of non-users of inhaled steroids occurred in all different β-adrenoceptor agonist user groups. Among patients with an annual use of inhaled steroids of ≥ 200 DDD, the percent of patients not receiving inhaled corticosteroids at all only fell from 37% to 33%.

Table 3 The five most popular regimens of anti-asthma medication among 20 to 44-year-olds in Odense and environs, 1991 and 1994

		1991		1994	
Regimen		n *(3575)*	*Median dose DDD (IQR)**	n *(4362)*	*Median dose DDD (IQR)*
1	Inhaled β-adrenoceptor agonist	1417	50 (30–100)	1685	50 (50–100)
2	Inhaled β-adrenoceptor agonist and	799	100 (20–240)	1308	100 (50–200)
	Inhaled glucocorticoid		60 (37.5–125)		90 (50–175)
3	Inhaled glucocorticoid	272	50 (25–62.5)	517	50 (25–100)
4	Oral β-adrenoceptor agonist	428	6.6 (6.6–18.6)	318	6.6 (6.6–18.6)
5	Inhaled β-adrenoceptor agonist and	94	150 (72.5–316.2)	84	100 (50–268.7)
	Inhaled glucocorticoid and		100 (50–153.1)		100 (50–243.7)
	Oral β-adrenoceptor agonist		50 (18.6–130.6)		35.3 (13.7–100)
6	Others	565	–	450	–

* DDD, Defined daily dose. IQR, Interquartile range.

Table 4 Percentage of users of inhaled steroid in different categories of inhaled β-adrenoceptor agonist users, 1991 and 1994. The total number of users in each β-adrenoceptor agonist category is in brackets

	Inhaled β-adrenoceptor agonist use (DDD/year)*									
	1–99		*100–199*		*200–399*		*400–799*		*≥800*	
Inhaled steroid (DDD/year)	*1991* (n = 1528)	*1994* (n = 2049)	*1991* (520)	*1994* (635)	*1991* (379)	*1994* (391)	*1991* (213)	*1994* (236)	*1991* (97)	*1994* (99)
0	73.6	64.4	45.4	38.4	35.6	32.2	42.3	36.0	29.9	29.3
1–174	24.7	31.3	46.0	45.2	43.5	34.8	33.3	25.0	30.9	25.2
175–349	1.4	2.9	6.5	11.5	16.1	19.9	13.1	14.4	17.5	15.2
≥350	0.3	1.4	2.1	4.9	4.8	13.1	11.3	24.6	21.7	30.3
P values[#]	<0.001		<0.001		<0.001		0.002		0.54	

* DDD, defined daily dose. [#] For comparison between 1991 and 1994 within each β-adrenoceptor agonist category.

Discussion

Our study is based entirely on prescription data. Two important questions that arise are therefore: are users of anti-asthma medication true asthmatics?—and, is the redemption of anti-asthma medication a good measurement of asthma treatment standards? By only including 20–44-year-olds, we believe that we have, to a large degree, excluded patients with chronic bronchitis, which pose a threat to the validity of the study. Anti-asthma medication is probably used in small quantities for other indications than asthma, e.g. as adjuvant treatment in respiratory infections. However, for consumers of large quantities of anti-asthma medication, there seems no obvious reason to doubt the correctness of the diagnosis.

The data in our study are based on presented prescriptions and therefore represent an amalgam of physician and patient behaviour. It is thus conceivable that selective redemption of medication by patients may conceal that physicians prescribe in greater accordance to the guidelines than our study results indicate.

The data were collected in a uniform manner from a population where access to the health services is free of charge and independent of income, employment or social status. Along with the full coverage of the pharmacies in the study area, this secures the completeness of the study. Similar studies concerning other parts of Denmark are not available. National statistics for 1991 concerning the total consumption of anti-asthma drugs show no important differences between the County of Funen and the other Danish counties, indicating that the study also has external validity.

The current guidelines for asthma treatment recommend a stepwise approach to asthma treatment guided by the severity of the disease [1,2]. In the first steps of the British guidelines, inhaled β-adrenoceptor agonists are suggested as the first line of treatment, and if the patient is in need of medication more than once daily, initiation of inhaled steroid therapy is recommended (beclomethasone or budesonide 100–400 μg twice daily) [2]. If adequate control is not achieved, then an increase of the inhaled steroid (800–2000 μg) is proposed, in addition to supplementary treatment. National guidelines regarding asthma therapy have not been published in Denmark. The international guidelines have been presented at postgraduate courses. The Danish Drug Catalogue (Lægemiddelkataloget), which

is sponsored by the medicinal industry, underlines the importance of use of inhaled steroids even in mild cases of asthma.

The increase in sales of anti-asthma medications observed in our study is consistent with previously reported findings [6–12]. Aggregated sales volume figures have indicated a shift towards more extensive use of inhaled steroids [7, 8, 10, 11]. In the UK, the number of prescriptions written in 1992/93 for inhaled steroids was 16% higher than in 1991/92 [12].

In our study, the striking increase in sales of inhaled steroids observed during the period was clearly reflected in an increase in the number of users. Along with inhaled β-adrenoceptor agonists, sales of inhaled steroids seem to have increased partly at the expense of other anti-asthma medications, e.g. theophylline. The bulk of the increase can, however, be ascribed to new users.

Judging by the intensity of their treatment, most patients seemed to have received regimens in accordance with the guidelines. While patients using inhaled β-adrenoceptor agonist in monotherapy, for example, received a median annual dose of 50 DDD, patients who also received inhaled steroids had a median consumption of β-adrenoceptor agonists of a 100 DDD in spite of the steroid treatment, suggesting that the asthma of the latter group of patients was more severe. We were puzzled by the existence of a fairly large group of individuals only receiving inhaled steroids. This group could—at least in part—represent persons, who having been treated with sufficient doses of inhaled steroids, could drastically reduce their use of β-adrenoceptor agonist inhalers. As mentioned earlier, we regarded monotherapy with oral β-adrenoceptor agonists as representing adjuvant therapy for ailments other than asthma.

Judged from the guidelines, all users of 200 DDD (on average 4 'puffs' per day) or more of β-adrenoceptor agonists should be receiving inhaled steroid treatment. For users with an annual consumption of β-adrenoceptor agonist ranging from 200 to 799 DDD, treatment was more in accordance with the guidelines in 1994. However, there was still room for improvement. The patients' heavy β-adrenoceptor agonist use in the last category ($\geq$800 DDD per year or 18 'puffs' per day) indicates that they have severe asthma. Yet their steroid therapy—if any—is often half-hearted.

Our results are in line with those of a large British study based on general practice data from 1990/91 concerning prescribed treatment for children with asthma [13]. An increase in the proportion of children prescribed inhaled steroids was found, but among children using short acting inhaled β-adrenoceptor agonists 4–8 times daily only 14.5% seemed to receive prophylactic treatment regularly.

Though heavy reliance on β-adrenoceptor agonists has been associated with excess death or near death [14], these are still rare outcomes for young asthmatics [15]. Increased morbidity is more probably the price such patients have to pay [16–18]. We conclude that outpatient asthma treatment has improved only moderately since 1991. Current guidelines for asthma treatment have not been implemented for a large group of heavy users of β-adrenoceptor agonists. There is a need for further studies which elucidate the reasons for undertreatment with inhaled steroids and point out potential areas of intervention.

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