Acute asthma during pregnancy

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Abstract

***Background* – Acute asthma during pregnancy is potentially dangerous to the fetus. The aim of this study was to investigate the effect of an acute attack of asthma during pregnancy on the course of pregnancy or delivery, or the health of the newborn infant, and to identify undertreatment as a possible cause of the exacerbations.**

***Methods* – Five hundred and four pregnant asthmatic subjects were prospectively followed and treated. The data on 47 patients with an attack of asthma during pregnancy were compared with those of 457 asthmatics with no recorded acute exacerbation and with 237 healthy parturients.**

***Results* – Of 504 asthmatics, 177 patients were not initially treated with inhaled corticosteroids. Of these, 17% had an acute attack compared with only 4% of the 257 patients who had been on inhaled anti-inflammatory treatment from the start of pregnancy. There were no differences between the groups as to length of gestation, length of the third stage of labour, or amount of haemorrhage after delivery. No differences were observed between pregnancies with and without an exacerbation with regard to relative birth weight, incidence of malformations, hypoglycaemia, or need for phototherapy for jaundice during the neonatal period.**

***Conclusions* – Patients with inadequate inhaled anti-inflammatory treatment during pregnancy run a higher risk of suffering an acute attack of asthma than those treated with an anti-inflammatory agent. However, if the acute attack of asthma is relatively mild and promptly treated, it does not have a serious effect on the pregnancy, delivery, or the health of the newborn infant.**

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Treatment in the pregnant asthmatic patient should aim to keep the mother as free from symptoms as possible. However, acute exacerbations cannot always be avoided. Compensated respiratory alkalosis is frequently seen during normal pregnancy, and in an acute attack of asthma the alkalosis is aggravated and combined with hypoxia. Alkalosis lessens the placental blood flow and thus hypoxia may be more severe in the fetus than in the mother.[1]

Despite this, mothers with severe acute asthma during pregnancy have been delivered of healthy children.[2,3] In previous reports increased incidences of low birth weight and prematurity have been associated especially with severe or undertreated asthma.[4–6]

Our primary aim was to investigate whether an acute attack of asthma during pregnancy influences the course of pregnancy or delivery, or the health of the newborn infant. The secondary aim was to try to identify undertreatment as a possible cause of the exacerbations.

Methods

The patients formed a cohort of 504 pregnant women with asthma who were prospectively followed and treated in our departments between January 1982 and September 1992. All patients satisfied the criteria of asthma set by the American Thoracic Society and American College of Chest Physicians in 1975.[7] The pregnancies resulted in 509 children (five twin births). The controls, originally chosen for another investigation,[8] comprised 237 healthy parturients. This control material was chosen retrospectively from hospital labour records and was matched for age ($\pm$ 2 years) and parity (primiparous or multiparous) with those asthmatic subjects receiving theophylline treatment and/or those who had an acute attack of asthma. The patients and the controls were the same as in one of our previous reports[8] but different from the one published in 1988.[9] The demographic and clinical features of patients and controls are shown in tables 1 and 2.

An acute attack of asthma was defined as an exacerbation of asthma which was not controlled by the patient's normal rescue medication and which was treated as an emergency. Forty seven of the 504 asthmatic subjects had an acute attack of asthma during pregnancy (AA) and 457 subjects did not record acute attacks of asthma during that time (NA). Fifteen of the AA patients had not been seen by us before the acute episode. The acute exacerbation of asthma was treated in our hospital (Helsinki University Central Hospital) in 41 cases. Of these, 10 patients were treated in the outpatient department and considered fit to go home within 12 hours of admission, and 31 were admitted to a hospital ward. Six patients were treated in peripheral outpatient departments and two of these were subsequently admitted to a hospital ward.

The maintenance treatment is shown in table 3 and the timing and dosage of inhaled steroid treatment in table 4. Nasal steroids were used by 25% of the patients during pregnancy, but only six patients used this treatment during the first trimester.

Table 1 Patients and controls

	Patients		Controls (n=237)	Statistical significance
	Acute attack (n=47)	No acute attack (n=457)		
Mean (range) age (years)	28·0 (17–43)	28·9 (16–44)	28·9 (17–39)	NS
Primiparae (%)	36·8	49·0	38·0	p1<0·02 p2=NS p3=NS
Age >35 years (%)	6·8	7·6	9·7	NS
Smoking (%)	19·0	10·8	15·2	NS
Mean (range) cigarettes/day	8·2 (2–20)	9·2 (2–20)	11·1 (2–25)	NS
Mean (SD) pre-pregnancy weight (kg)	66·3 (15·4)	63·1 (12·6)	60·3 (9·9)	p1=NS p2<0·01 p3<0·01

p1: Patients (Acute attack) vs Controls
p2: Patients (No acute attack) vs Controls
p3: Patients (Acute attack) vs Patients (No acute attack)

Table 2 Patient characteristics

	Acute attack (n=47)	No acute attack (n=457)
Mean (range) age at onset of asthma (years)	20·3 (0–42)	19·8 (0–43)
Positive skin tests (%)	57·0	69·8
ASA sensitivity (%)	17·0	14·6
Mean (SD) best FEV_1 (% predicted)	95·7 (12·5)	93·4 (13·8)
Mean (SD) PEF variation (l/min)*	48·1 (13·1)	46·4 (9·7)
Mean (SD) best PEF (% predicted)	105·4 (8·4)	102·6 (12·0)

ASA = acetylsalicylic acid; PEF = peak expiratory flow; FEV_1 = forced expiratory volume in one second.
* Mean diurnal variation during two stable weeks.

Table 3 Maintenance anti-asthmatic treatment used before and after the acute episode and in the patients who did not have an acute attack during pregnancy (for inhaled steroids, see also table 4)

Treatment	Acute attack (n=47)		No acute attack (n=457)
	Before	After	
Inhaled β_2 agonist (%)	63·8	100·0	94·0
Inhaled budesonide or beclomethasone (%)	34·0	94·0	61·5
Courses of oral corticosteroids (%)	6·3	74·4*	
Oral theophylline (%)	55·3	74·5	38·5

* Includes the oral steroid given to treat the attack.

Relative birth weight expresses in standard deviation units the difference between the actual infant weight and the mean weight on the corresponding day of gestation in Finnish control material.[10] Neonatal hypoglycaemia was defined as a blood glucose level of 1·8 g/l or less twice during the first 24 hours of life. Jaundice was regarded as being present if treatment with blue light was considered necessary. For other definitions see reference 8.

*Table 4 Mean (SD) and range of doses of inhaled steroids during pregnancy and time of gestation at which medication was started (n=355)**

Inhaled steroid and daily dose	Mean (SD) dose and range (mg)	No. of patients	
		Weeks 1–12	Week 13–term
Beclomethasone	0·86 (0·518), range 0·05–3		
<1 mg		132	48
>1 mg		25	9
Budesonide	0·90 (0·491), range 0·2–4		
<0·8 mg		88	32
>0·8 mg		14	7

* Including the patients in whom inhaled steroids were initiated after the acute attack.

The data were analysed by means of "StatView 512+TM" (Brainpower INC) for Apple Macintosh. For continuous variables the significance of differences between groups was tested by the Mann-Whitney U test. The χ^2 test with continuity correction was used for differences between group frequencies. The relative risk (RR) was calculated according to Campbell and Machin.[11] Shapiro-Wilk's W test was used to test the normality of the distribution of the attacks of asthma during different weeks of pregnancy.

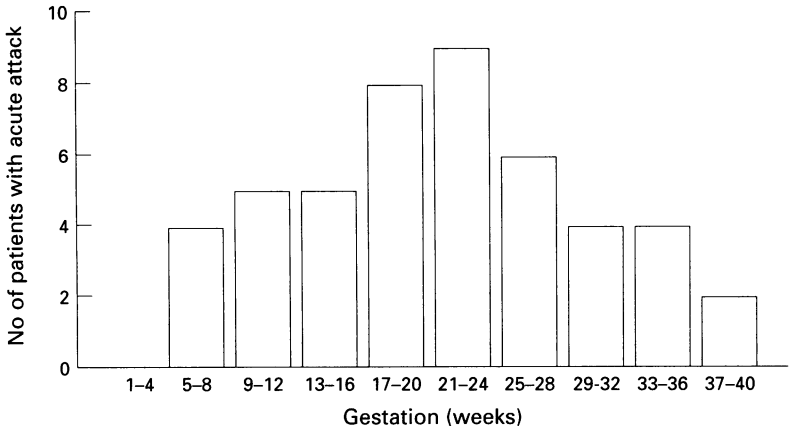
Results

The acute attacks of asthma were not uniformly distributed through pregnancy (figure). The data indicate a normal distribution ($W=0·95$, $p=0·07$), the attacks occurring most frequently between 17 and 24 weeks of pregnancy (mean 20·8, 95% confidence interval 20 to 25·2 weeks). There were no maternal deaths.

The 504 asthmatic subjects were divided into three groups: (1) the 177 patients who had no inhaled steroids at any time during pregnancy, except after an acute attack (NIS), (2) the 257 patients who were on inhaled steroids throughout pregnancy (IS), and (3) the 70 patients in whom inhaled steroids were started at various stages during pregnancy, but before any acute attack (BA). Thus, in the BA group the length of gestation at the start of inhaled steroids varied and the duration of treatment before any acute attack was comparatively short. In the NIS group 31 of the 177 patients (17·5%) had an acute attack compared with only 10 of 257 (3·9%) in the IS group ($\chi^2=17·3$, $p<0·0001$). The risk of having an acute attack during pregnancy in patients treated with inhaled steroids was about 22% of the risk in those not treated with such drugs (RR=0·22, 95% confidence interval 0·11 to 0·44). The corresponding risk for the BA group was 0·49 (95% CI 0·21 to 1·12). Twenty eight of the NIS patients with an acute exacerbation were put on inhaled steroids after the acute attack. None of the AA patients suffered another acute attack of asthma during pregnancy after treatment of the attack recorded in this study.

During the acute attack all the AA patients were treated according to established practice or hospital emergency routine with oxygen and nebulised β agonists (45 patients) and ipratropium (40 patients) immediately on admission until the situation was under control. Twenty three patients also received intravenous theophylline and 13 intravenous glucocorticosteroids. A course of oral glucocorticosteroids was given to 37 patients, the mean initial prednisolone equivalent dose being 35 mg (range 30–40 mg). As judged from the clinical picture described in patients' notes, the exacerbations of asthma were mild or moderate with a mean peak expiratory flow (PEF) of 274 l/min (range 130–430 l/min). None of the patients needed artificial ventilation.

After the emergency incident inhaled steroids were prescribed in 27 of the 31 cases lacking this treatment, a total of 345 patients receiving this treatment at any time of pregnancy. The



Frequency distribution of acute attacks during pregnancy

Table 5 Maternal health during pregnancy

Disorder	*Patients*		*Controls (n=237)*	*Statistical significance*
	Acute attack (n=47)	*No acute attack (n=457)*		
Pre-eclampsia (%)	8.5	12.7	6.4	p1=NS p2=NS p3<0.02
Intrahepatic cholestasis of pregnancy (%)	4.3	3.3	0.4	p1=NS p2=NS p3<0.05
Gestational diabetes (%)	6.4	4.2	3.4	NS
	p1 p2 p3			

Table 6 Complications of pregnancy

Disorder	*Patients*		*Controls (n=237)*	*Statistical significance*
	Acute attack (n=47)	*No acute attack (n=457)*		
Bleeding during 2nd or 3rd trimester (%)	2·1	1·8	6·8	p1=NS p2=NS p3<0·01
Premature rupture of membranes (%)	4·3	3·3	2·1	NS
Premature uterine contractions (%)	15	13	14	NS
Premature separation of the placenta (%)	0	0·9	0·8	NS
Preterm births (<37 weeks) (%)	6·4	5·5	5·5	NS
	p1 p2 p3			

Table 7 Outcome of the newborn infant

Outcome	*Patients*		*Controls (n=237)*
	Acute attack (n=47)	*No acute attack (n=462*)*	
Malformations (%)	4·3	2·5	0·8
Perinatal death (%)	0	0·2	0·9
Median Apgar score at 1 min (range)	9 (4–10)	9 (2–10)	9 (0–10)
Relative mean (SD) birth weight	−0·1 (1·17)	0·005 (0·9)	−0·07 (1·0)
Hypoglycaemia (%)	0	0·2	0·43
Treatment in newborn intensive care unit (%)	2·1	2·0	1·3
Jaundice (%)	6·4	11·3	7·8

* Including five pairs of twins.

overall distribution of treatment with inhaled steroids is shown in table 4. β agonists were added in 17 of the emergency cases and oral theophylline in 19 cases.

OBSTETRIC DATA

There were no differences between the AA group and the NA or control groups as to the incidence of gestational diabetes. Pre-eclampsia and intrahepatic cholestasis of pregnancy were more frequent in the NA group than in controls (table 5). The groups did not differ as to the incidence of premature rupture of membranes, premature uterine contractions, placenta praevia, or premature separation of the placenta. The incidence of prepartum haemorrhage was higher in the controls than in the asthmatic subjects (table 6).

The length of gestation did not differ between asthmatic subjects and controls, being normal in all groups. The incidence of elective caesarean section was 23% in the AA group, 10·7% in the NA group, and 5% in the control group ($p<0·02$ AA versus NA, $p<0·0001$ AA versus controls, and $p<0·0001$ control NA versus controls). The incidence of non-elective caesarean sections in the AA, NA, and control groups was 4·2%, 7·2% and 8·5%, respectively, with no significant differences between any groups. In no case was acute asthma the indication for an emergency caesarean section.

OUTCOME OF THE NEWBORN INFANT

There were no perinatal deaths in the AA group. The Apgar scores, relative birth weight, occurrence of hypoglycaemia and jaundice, and admissions to hospital during the first week of life were similar in all three groups, as were also the incidences of malformations (table 7).

Discussion

In many of the patients who had an acute attack of asthma treatment before the acute exacerbation had not included an anti-inflammatory agent and their treatment may, according to current standards, have been inadequate. Although we have no data on this, we know that many pregnant asthmatic patients decide on their own to refrain from treatment or are advised to do so by doctors or antenatal care nurses. However, treatment with inhaled steroids has not been shown to be harmful during pregnancy.[12] The fact that our results show that treatment with inhaled steroids clearly reduces the risks of having an acute attack of asthma during pregnancy will probably serve as an argument in favour of using these drugs.

In our study the ability of sodium cromoglycate or nedocromil sodium to lessen the risk of acute attacks could not be studied since there were not enough patients treated with these drugs. The exacerbations of asthma were apparently mild or moderate, as judged by the comments in the patients' notes and the available clinical parameters. In the study area asthmatic patients are accustomed to seeking

help promptly at their local health centre or the hospital emergency department. This may be one of the reasons why no severe attacks were seen. The treatment of acute asthma is prbably consistent in this area because of the wide distribution of guidelines in Finnish published by student and medical associations.

Some patients stop or reduce their medication, particularly during the first part of pregnancy, in which case a worsening of the asthma is likely to occur a few weeks later. This may be the most likely explanation for the finding that there was a tendency for acute attacks to occur between the 17th and 24th weeks of pregnancy. Unfortunately we did not investigate this aspect in detail, and we have no reliable data on possible modifications of the antiasthmatic medication by patients or their doctors before they came into our care.

As in our earlier study,[9] our present data failed to confirm the increased incidence of prematurity and low birth weight reported by others[5] in infants of asthmatic mothers. The explanaton for this may be that our patients, despite the acute exacerbations, were better treated and controlled than the more heterogenous groups included in other reports. In fact, intrauterine growth may be related to poor lung function[13] which was not a general feature of our patients. Confirming previous results, the incidence of pre-eclampsia in our study was higher among asthmatics than among controls, although it was not specifically high in the AA group. Contrary to previous results,[9] the incidence of hypoglycaemia in newborn infants was not more common in our study, possibly because of a lower use of systemic corticosteroids.

The high incidence of elective caesarean section in the AA group and in asthmatic subjects in general is in agreement with previous findings.[9] The possible risks connected with asthma may influence the obstetrician when deciding on the mode of delivery.

The health of the newborn infant was generally good. Although there was no significant increase in the incidence of neonatal icterus in the groups analysed in the present study, neonatal jaundice may be connected with the use of oral theophylline as has been reported and discussed elsewhere.[7]

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