Circadian rhythm of peak expiratory flow in children passively exposed and not exposed to cigarette smoke

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Abstract

Background Because airway calibre shows a circadian rhythm and since exposure to passive smoking reduces lung function this study was undertaken to investigate whether passive smoking affects the circadian rhythm of peak expiratory flow (PEF) in schoolchildren.

Methods Twenty schoolchildren (12 boys and 8 girls, aged 10-11 years) exposed to passive smoking were matched for sex, age, and height with 20 children who had not been exposed to cigarette smoke. Exposure to passive smoking was assessed by questionnaire and by urinary cotinine concentrations. A portable spirometer was used to measure PEF at 16:00, 20:00, 22:00, 06:00, 08:00, and 12:00 hours on a consecutive Saturday and Sunday. The circadian changes in PEF were measured by the cosinor method.

Results Both groups showed diurnal fluctuation in PEF values with a noticeable circadian rhythm. PEF peaks were the same in the two groups and occurred around 15:00 hours. The cosinor mean was approximately 10% lower in children exposed to passive smoking and the amplitude was approximately 60% higher than in the unexposed children.

Conclusion Passive smoking in children is associated with a reduction in the cosinor mean and an increase in the amplitude of the normal circadian rhythm of airway calibre. This increased PEF rhythm amplitude may be considered as an early indication of airway obstruction.

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Passive smoking increases the incidence of respiratory illness and reduces lung function in children.¹⁻³ Airway calibre shows a circadian rhythm^{4,5} that may be related to endogenous biological rhythms or to exogenous cyclical rhythms. Many studies have used the cotinine concentration in saliva³ or in urine⁶ as a quantitative biochemical marker of exposure to tobacco smoke in addition to a questionnaire. The effects of passive smoking on the circadian rhythm of lung function in children have not been determined. This study aimed to investigate whether children exposed to passive smoking, assessed by questionnaire and urinary cotinine values, show greater variation in

the circadian rhythm of the peak expiratory flow (PEF) than children not exposed to cigarette smoke.

Subjects and methods

Questionnaires completed by 60 primary schoolchildren aged 10-11 years were analysed and 20 children (12 boys and 8 girls) exposed to passive smoking were identified. These children were matched for sex and age with 20 respondents who had not been exposed to cigarette smoke. There was no significant difference in the mean (SD) height of the two groups—146.0 (6.8) cm in the unexposed group and 145.6 (7.3) cm in exposed subjects.

Since cotinine is the main metabolite of nicotine,⁶ urine samples were collected from each subject the day before the study for determination of urinary cotinine concentrations. Urinary cotinine values were determined by Tobacco screen kit (Selex Inc, Englewood, NJ, USA), as described.⁶ Subjects who have not been exposed to tobacco smoke have urinary cotinine values less than 2.4 µmol/l.

The children taking part in the study were blind to the hypothesis. Informed consent was obtained from parents or guardians. No child had ever had asthma and none had had an acute respiratory problem or taken drugs in the previous month.

A pocket spirometer (Markos, Monza, Milan, Italy) was used to measure the PEF in each child. Measurement was undertaken with the child standing in the upright posture and wearing noseclips. The best of three measurements was recorded. The PEF was measured at 4:00 pm, 8:00 pm, and 10:00 pm on Saturday, and 6:00 am, 8:00 am, and noon on Sunday. The study was carried out in February and March 1991.

ANALYSIS

The PEF values were subjected to a rhythmic analysis using the cosinor method,⁷ to determine whether there was a statistically significant circadian rhythm and to evaluate the mesor (average level of the rhythm), the amplitude (length from the mesor to the peak of the rhythm), and the acrophase (peak of the rhythm). The cosinor method uses the cosine function:

$g(t) = \text{mesor} + \text{amplitude} \times \cos(\omega t + \text{acrophase})$,
 $g(t)$ being the value at time (t) and ω being the periodic function of angular frequency; in this

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Mean (SD) diurnal fluctuations and results of cosinor analysis of the circadian rhythm in peak expiratory flow (PEF) in schoolchildren unexposed (■) and exposed (●) to passive smoking.

case $\omega = 24$ hours. The mesors of the two groups were compared by the mesor test⁷ and the amplitudes and the acrophases by the amplitude-acrophase test.⁷ p values less than 0.05 were accepted as significant. An analysis using chronograms evaluating the mean (SD) PEF values was also used.

Results

The mean (SD) value of urinary cotinine concentration was 1.85 (0.46) $\mu\text{mol/l}$ in unexposed children and 3.44 (0.52) $\mu\text{mol/l}$ in exposed subjects.

Both groups showed diurnal fluctuations in PEF values with a peak in the afternoon (figure). PEF showed a significant circadian rhythm for both the unexposed and the exposed children ($p < 0.05$). The acrophases were similar in the two groups. The peak of the rhythm occurred at 3:00 pm (range 1:20 pm–4:32 pm) in unexposed children and at 2:40 pm (11:44 am–5:28 pm) in exposed children. Children exposed to smoke had a mesor that was about 10% lower ($p < 0.02$) and an amplitude about 60% higher ($p < 0.02$) than unexposed children.

Discussion

The health hazards attributable to exposure to environmental tobacco smoke have been extensively reviewed in recent years.^{1,28} Passive

smoking in children is associated with reduced pulmonary function, especially in tests of small airway function,^{3,6,9,10} an increased prevalence of phlegm, cough, wheeze, asthma, bronchitis, and chest colds,^{1,2,8,10} more frequent days off school for minor ailments,¹¹ and slowing down in lung growth.^{1,8,9}

This is the first study to investigate the relation of environmental tobacco smoke exposure to the circadian rhythm of PEF measurements. We used a questionnaire and urinary cotinine determination to verify passive smoke exposure. These two measures provide information of past and current exposure respectively.

Our results show a significant circadian rhythm in PEF measurements in school children, whether or not they have been exposed to tobacco smoke. There were significant differences, however, in both mesors and amplitudes between the two groups. The lower mesor in exposed children is consistent with previous data showing that passive smoking is associated with poorer respiratory function.^{1,2,6,8} The increase in PEF amplitude in exposed children, however, is difficult to explain. The circadian pattern of PEF in the children exposed to passive smoking is similar to that observed in asthma in children^{12–14} and adults¹⁵ and adult smokers with normal lung function.¹⁶

The increased circadian amplitude in exposed children could be related to an increase in bronchial reactivity. Tobacco smoke

increases bronchial reactivity in adult smokers with normal lung function¹⁷ and in exposed children.^{9,18,19} There is a close relation between symptomatic asthma in children and parental smoking.²⁰ Increased diurnal variations in PEF have been reported in subjects with increased bronchial reactivity.²¹ The increased amplitude in the PEF circadian rhythm in children exposed to tobacco smoke probably results from amplification of the normal circadian rhythm in airway calibre by the abnormally labile airways.¹⁰ Smokers and those exposed to tobacco smoke may chronobiologically resemble symptomatic asthmatic patients. It has been suggested that exposure to tobacco smoke affects the growth of the respiratory system in childhood^{8,9} and is a major factor responsible for the development of chronic non-specific lung disease in adults.⁸

The circadian rhythm of PEF in the exposed children differed from that of unexposed children, having reduced mesor and greater amplitude. Since any change in the normal circadian pattern of any variable can be seen as abnormal and as a step towards clinically symptomatic disease,²² the increased PEF rhythm amplitude may be a measure of early airway obstruction in response to passive smoking.

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