

CIRCADIAN RHYTHM OF PEAK EXPIRATORY FLOW RATE IN HEALTHY NORTH INDIAN MEN

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Abstract : Peak expiratory flow rate (PEFR) variability follows a specific pattern in asthmatics as well as in healthy individuals. There is scarcity of data for Indian healthy subjects. The PEFR (L/min.) was measured with Wright's portable peak flow meter at 05:00, 8:00, 11:00, 14:00, 17:00, 20:00 and 23:00 hours in 42 healthy, non-smoking adults of age group between 18–26 years. The variability of PEFR revealed a circadian pattern. PEFR levels tend to increase from morning at 5:00 hours till evening at 17:00 hours, with peak PEFR in evening at 17:00 hours, after which there was a progressive fall in PEFR levels, till morning 5:00 hours. This study provides the preliminary reference data of circadian pattern of PEFR in healthy individuals.

Key words : bronchial hyper-reactivity
diurnal rhythm

chronobiology
PEFR variation

INTRODUCTION

The phenomenon of nocturnal asthma has always perplexed clinician's and researcher's mind. Peak expiratory flow rate (PEFR) variability has been suggested as a marker for bronchial hyper-reactivity in

asthmatic individuals (1, 2). PEFR variation has been widely advocated and used in clinical practice and asthma research. The National Heart Lung and Blood Institute (NHLBI) and others have recommended, a diurnal variation of 20% or more, as a diagnostic benchmark for asthma (3, 4).

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Further, comparative studies have not sustained the claim to promote PEFR variability for diagnosing asthma because of the lack of standard cut off value of PEFR variability for labeling a person as asthmatic (5, 6). PEFR shows hour to hour variation that follows a specific pattern in asthmatics as well as in normal individuals as has been identified in earlier studies (7–9). Most of these studies are done in patient population and adequate data is not available for the circadian rhythm in normal individuals. We therefore evaluated the pattern of circadian rhythm of PEFR in healthy North Indian subjects.

MATERIAL AND METHODS

Subjects : The study was conducted on 50 young male volunteers from university population having almost similar daily routine and sleep habits, selected randomly between the age group of 18–26 years. Nature of the study was explained and informed consent was obtained from each subject prior to participation in study. The protocol of the study was approved by institutional ethics committee.

A thorough history was taken and clinical examination of the subjects was performed to rule out any obvious cardio-pulmonary compromise. Subjects with history of smoking, history of severe chest trauma, with obvious chest and spinal deformity, with personal/family history of asthma, chronic obstructive pulmonary diseases and other cardio-respiratory diseases were excluded from the study. All subjects underwent baseline pulmonary function testing to rule out subtle pulmonary dysfunctions (restrictive and obstructive).

Protocol : For the convenience of study, subjects were divided into groups of five and each group was provided one mini Wright's peak expiratory flow meter. Subjects were individually trained for measuring their own PEFR in L/min. and were instructed to record the readings with Wright's portable peak flow meter at 5:00, 8:00, 11:00, 14:00, 17:00, 20:00, and 23:00 on two consecutive days. They were instructed to obtain at least three recordings at a time. Five out of seven sessions each day were under the guidance of the principal investigator and the remaining sessions were under the guidance of a trained captain chosen from each group.

The data sheets were filled for history, clinical examination with height and weight, history of medications and PEFR readings. Only the PEFR readings recorded at 23:00 hour on first day and all readings on the second day were taken into consideration to rule out the remote possibility of training effect. The best of three PEFR readings in a given time was taken for the analysis. The pooled data sheets were scrutinized and those with incomplete test records or data were rejected. Finally, 42 subjects were selected for inclusion into the analysis.

Statistical Analysis : Both original units and normalized data (percent of individual mean 24 hour PEFR) were used to analyze circadian rhythm as a group. Because of large inter-individual differences in mean values of PEFR, individual PEFR values were normalized by re-expressing each value as percentage of its series mean before statistical analyses of grouped data. The original and normalized PEFR values at different time points were analyzed by one

way analysis of variance (ANOVA). Rhythm detection was considered statistically significant with a P value of < 0.05.

Diurnal variation for individual subject was calculated using 2 different indices viz., amplitude percent mean (A%M) and standard deviation percent mean (SD%M) and were calculated as below (9).

$$A\%M = \frac{\text{Highest PEFR value of the day} - \text{Lowest PEFR value of the day}}{\text{Mean PEFR value of the day}} \times 100$$

$$SD\%M = \frac{\text{Standard deviation of PEFR value of the day}}{\text{Mean PEFR value of the day}} \times 100$$

RESULTS

PEFR values of 42 male subjects with mean age of 20.5±1.66 years were measured at 23:00 hour on first day and at 5:00, 8:00, 11:00, 14:00, 17:00, 20:00, and 23:00 hours on second day. The mean PEFR values after a dip in morning at 5:00 hours tend to increase through out the day peaking in evening at 17:00 hours as shown in Table I. The PEFR values were not recorded at 02:00 hours, but trend suggests that after 17:00 hours there is a regular fall in PEFR levels till 5:00 hours as evident in Fig. 1. Identifiable morning dip was observed in 69% subjects and identifiable evening peak was observed in 55% subjects.

The mean PEFR values at different time

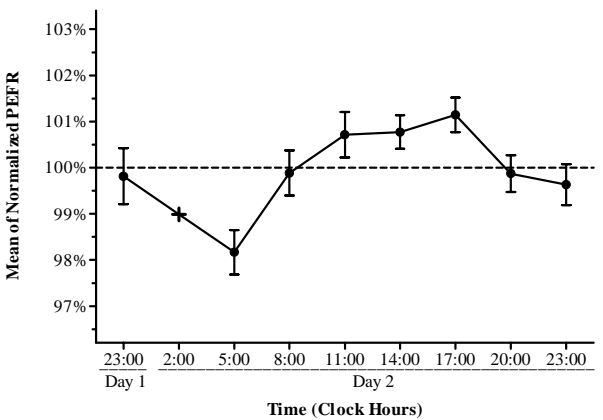


Fig. 1: Circadian rhythm of Peak expiratory flow rate (PEFR). PEFR values are represented as mean ± S.E. of normalized PEFR values, taking 24 hour individual mean PEFR as 100%. Horizontal dashed line at 100% represents population 24 hour mean PEFR corresponding to 538.13 L/min. Values at various time intervals are significantly different (n=42, P<0.001; One way ANOVA).

points were analyzed for variation using one way analysis of variance which did not reveal significant rhythm (P>0.9). After normalizing the data, the circadian rhythm became statistically significant (P<0.001). Assuming equal variance (Levene’s statistics was used to determine the homogeneity of variance, P>0.05) Tukey’s test was applied, which revealed significant differences in the mean percent PEFR values at 05:00 hours and 11:00 hours, 5:00 hours and 14:00 hours, 5:00 hours and 17:00 hours (P<0.05).

Mean diurnal variation, for second day, was 7.55±4.1 (A%M) and 2.79±1.42 (SD%M) in this population. The upper limits of

TABLE I: The PEFR values (mean ± SE; L/Min) at various time intervals between 23:00 hours (day1) and 23:00 (day 2) were obtained from 42 subjects. PEFR at 2:00 hour on day 2 was not measured.

Time (Hours)	23:00	5:00	8:00	11:00	14:00	17:00	20:00	23:00
PEFR (L/Min)	537.1	528.6	537.9	541.8	542.1	543.9	537.4	536.2
± S.E.	9.88	9.98	10.34	9.58	9.43	9.23	9.53	9.75

normal variability A%M at 95% and 99% confidence limits were 15.75 and 19.85, respectively. Similarly, SD%M at 95% and 99% confidence limits were 5.63 and 7.21, respectively.

DISCUSSION

This study provided the preliminary reference data of circadian rhythm of PEFr in healthy individuals. Our results suggest that PEFr in normal subjects exhibits definite circadian rhythm characterized by a morning dip followed by progressive rise peaking in the evening and small fall at bed time. This was the commonest pattern observed in most of the subjects i.e. morning dip in 69% of subjects and evening peak in 55% subjects. In earlier reports lesser percentage of subjects followed this pattern although having overall circadian pattern similar to the present study (10). Higher prevalence of identifiable rhythm in greater percentage of subjects in present study may be because of homogeneity of our subject group. Moreover, subjects were living in same environmental conditions and had almost similar daily routine.

Diurnal variation calculated for this population, expressed as A%M and SD%M are in close approximation to the earlier study in Indian subjects (10) and are lower than

the data for Western subjects (11, 12). These differences in diurnal variation of PEFr from Western subjects may be attributed to different sample characteristics and/or ethnic variation. This may in part also be explained by confounding effects of smoking in these studies. Diurnal variation in this study is found to be lesser than that reported in asthmatics in previous studies. The circadian rhythm in asthmatics although follows almost similar pattern i.e. with PEFr dip in morning and PEFr peak in evening, but the swing of PEFr from the mean value is more than in normal subjects (13, 14).

The exaggeration of normal pattern of PEFr variability may be considered as an useful marker for diagnosing asthma, the normal pattern however, is not found to be universally applicable. Therefore, the use of PEFr variability for population screening and clinical diagnosis of asthma has serious limitations. This conclusion in no way should undermine the utility and credibility of PEFr variation in monitoring and routine management of asthmatic patients. Further, longitudinal studies are required to follow up those subjects who do not confirm to the normal circadian pattern. The knowledge of normal circadian pattern of PEFr in healthy subjects and its variation might help in better understanding of patho-physiology of nocturnal symptoms present in some asthmatic patients.

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