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Dip patterns in asthmatic and non-asthmatic children in Benin-city, Nigeria

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Abstract *Objective:* Although the calibre of the airway is kept patent by multifactorial control system, there is evidence that the calibre of the bronchi varies with time of the day in normal subjects. Asthma is now known to be a chronic inflammatory disease and this chronic inflammation causes hyperreactivity and lability in the airway. Therefore, asthma is characterised as a disease where respiratory symptoms are based on large variation in airway calibre leading to variations in resistance to airflow over a short period of time.

Method: Normal non-asthmatic children leaving within 10km of University of Benin Teaching Hospital (UBTH) and whose parents work at UBTH were recruited. These subjects aged 5 – 15 years were initially matched with an index asthmatic case both for sex and age (within six months range). Using a questionnaire the control were screened to exclude any case with history of respiratory, cardiac or any form of active disease or chest deformity or family history of asthma. This was followed by weight and height determination. Both the subject and control were then instructed on the correct use of the mini Wright Peak Flow meter and how to record it in the diary provided. After five days of measurement, the diaries were collected and the PEFR were analysed.

Results: Two hundred and ten (210) asthmatics and one hundred and eighty healthy children completed the study. The two groups were similar for age, weight and height, but the mean daily PEFR was significantly lower for the asthmatic children (P<0.01). The circadian pattern of distribution of PEFR is similar both in asthmatic and the healthy children, the lowest PEFR was at 6am and maximum was at 2pm and thereafter, there was a gradual fall from the 6pm to 10pm, this was the dominant pattern both in asthmatic and the healthy children. Significant difference in magnitude of PEFR between the two groups occurred at 6am, 6pm and 10pm (P<0.01). In all, the asthmatics had lower value. The PEFR in each case at 2pm was similar; 302.6 l/min for normal children as against 3.2 l/min for asthmatic children. Of the asthmatic subject, 205 (97.6%) had a discernable dip pattern compared with 4 (2.2%) in healthy subjects.

Conclusion: Dip pattern exists both in asthmatics and non-asthmatic children, although, more of the asthmatics had a discernable dip pattern. The airway calibre shows a variation with the time of the day, both in asthmatics and normal subjects with lowest values in the morning and highest in the afternoon. But at each time of the day, the asthmatics had lower PEFR values than normal children. This maybe relevant in the management and follow-up of the asthmatics.

Key words: Asthma, dip pattern, circadian rhythm, Peak expiratory flow rate.

Introduction

Bronchial airways remain patent under normal circumstances.[1,2] The mechanisms for maintaining this is complex but it is often through a multifactorial control system acting on the bronchial muscles.[1-3] However, there is evidence that the calibre of the bronchi vary with time of the day.[1-4] This circadian rhythm is reported to be more pronounced in subjects with asthma than in normal, healthy subjects.[5-7] The characteristics of this rhythm is easily demonstrable by serial measurements of peak expiratory flow rate (PEFR) at different times of the day.[6,7] Measurements in adults and recently children reveal significant fluctuations with characteristic patterns.[5,6,8] The most commonly shown is the phenomenon of morning dip which implies significant fall of PEFR during the morning time.[7,8,9] The aim of the study is to define the possible dip patterns in asthmatic Nigerian children and relate these to clinical asthma.

Materials and Methods

Normal non-asthmatic children living within 10km radius of University of Benin Teaching Hospital and whose mother or father or both work at the University of Benin Teaching Hospital were recruited for the study. These subjects, aged five years up to 15 years were initially matched with an index case both for sex and age (within 6 months range) of asthma and agreed to record their own PEFR at home. The list of such subjects were compiled and participation in the study occurred during holidays or work stoppages by teachers. Using a questionnaire, the control subjects were screened to exclude any cases with history of respiratory, cardiac or any form of active disease or chest deformity or family history of allergy or asthma and followed by weight (bath room scale) and height (stadiometer) determination. The subjects were further instructed by the researcher and his trained assistants on the correct use of the min Wright Peak Flow meter and the recording of the measurement in a diary provided for that purpose. This initial contact and teaching took place at the children's homes and in the evenings and lasted three to five days. Having ascertained proficiency in use of the meter and PEFR recording, the actual study comprised five (5) daily measurements of the PEFR, in a standing position at 6am, 10am, 2pm, 6pm and 10pm and for fourteen (14) consecutive days. Three readings of the PEFR were taken at each time period to the nearest 0.5 litres with a minute (60 seconds) rest between readings. Mothers were further instructed to ensure PEFR determination and recording were accomplished not later than 15 minutes of the stipulated time of recording.

Thereafter, the homes were visited twice: on the second day, to detect and correct errors if any and, the 15th day to retrieve the diary card(s) and the Peak Flow Meter with plastic mouth piece(s) (multiple participation in some households).

Two hundred and ten normal healthy children were initially recruited of which 30 were excluded from the study: 11 subjects for evidence of falsification of PEFR readings, 19 for irregular and incomplete recordings, lasting less than 10 days, and four for hitherto undiscovered positive asthma history in grandparents.

Using a similar protocol of PEFR measurement to that described for normal healthy children, the study was carried out in 210 asthma children: criteria for selection of asthma patients include aged five years up to 15 years, a history of variable wheezy breathlessness and a demonstration of a more than 20% improvement in PEFR after inhaled or oral salbutamol or a more than 50% improvement of PEFR over the course of hospital admission. They were studied during convalescence at home and recorded their PEFR before taking prescribed medication (where applicable): 150 patients received salbutamol as and when necessary (PRN), 49 on continuous (twice daily) salbutamol while 11 had salbutamol thrice daily. None had corticosteroid during the study period.

Data Analysis

The PEFR values represent the mean of recordings obtained on the 14 consecutive days. A pattern was accepted when it occurred in at least 80% of daily recordings and at least a 5% difference between highest (Acrophase) and lowest (Trough) readings. Daily patterns were defined with reference to the acrophase and trough time.

For statistical analysis, mean and standard deviation (SD) were determined for parametric observations and inter group comparison done with the students t-test. The Chi Square (X^2 test) was used in comparing proportions. The accepted level of statistical significance was P -value less than 0.05.

Results

Two hundred and ten asthmatics and one hundred and eighty normal healthy children completed the study. As shown on Table 1, the two groups were similar for age, weight and height but differed in the mean daily PEFR with significantly lower value for the asthmatic children (P<0.01).

Table 1: Anthropometric Data for Asthmatic and Non-Asthmatic Children

Characteristic	Asthma	Non-Asthma
Mean Age (years)	9.6	9.6
Range	5 – 15	5.3 – 15.0
Sex (M/F)	115/95	82/98
Weight (Mean ± SD) kg	27.2 ± 6.3	28.4 ± 7.9
Height (Mean ± SD) cm	134.6 ± 12.3	132.7 ± 11.9
PEFR (Mean ± SD) L/min	276.21 ± 41.7	288.14 ± 5.2*

* The difference is statistically significant; p<0.01

Figure 1 demonstrates the circadian distribution of PEFR in healthy and asthmatic children. The patterns are similar, with a gradual rise of PEFR from 6am up to maximum values at 2pm and thereafter, a gradual fall in the PEFR through 6pm to 10pm. Significant differences in magnitude of PEFR in the two groups occurred at 6am (P<0.001); 6pm (P<0.01) and at 10pm (P<0.01) with the asthmatic recording lower values. The PEFR values in each case at 2pm was similar; 302.6 for normal children as against 297.2 for asthmatic children. The acrophase tome was 2pm in 150 (71.4%) while trough times was 6pm in 161 (76.7%) asthma cases. None of the asthmatic had trough values at 2pm and none had acrophase PEFR at 6am.

Of the asthmatic subjects, 205 (97.6%) had discernable dip patterns and this compares with 4 (2.2%) cases in healthy subjects.

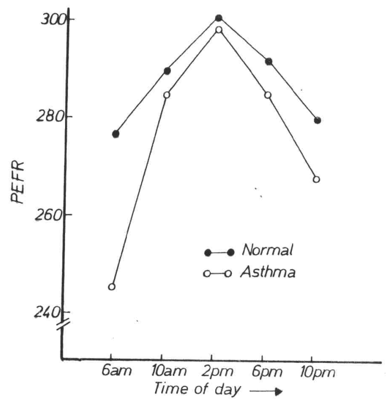

Fig 1: Distribution of PEFR at various times of day in normal and asthmatic children

Figure 2 (a – c) demonstrates the various dip patterns in asthmatic children: Evening dip (2a); Morning dip (2b); Double dip and No dip (2c). The most common pattern was morning dip and occurred in 110 (52.4%) asthma cases; followed by double dip (31%) and evening dip (14.2%) cases. Of the 4 healthy children with dip patterns, 3 had morning dip while the remaining case had evening dip. These dip patterns were however shallow when compared with those in asthmatic children.

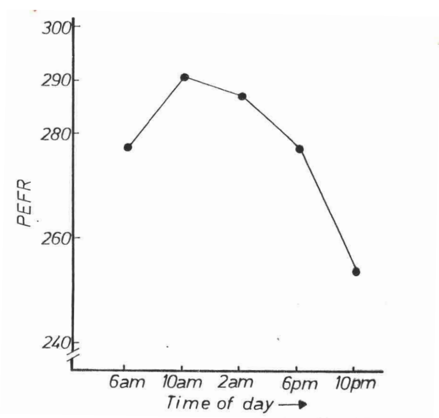

Fig 2a: Dip patterns in asthmatic children showing evening dip

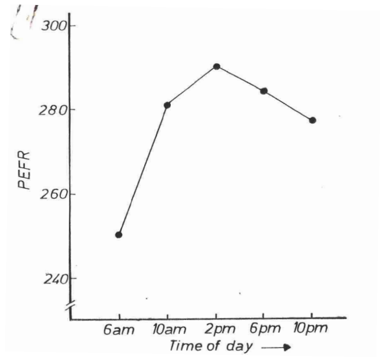

Fig 2b: Dip patterns in asthmatic children showing morning dip

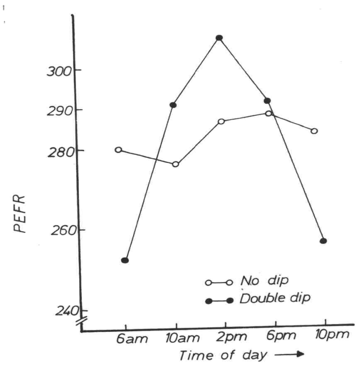

Fig 2c: Double dip patterns in asthmatic children

Figure 3 shows the relationship between times of onset of asthma all attacks or most of the attacks and dip patterns. Of 122 asthma cases with onset of asthma attack in the morning, 102 (83.6%) had morning dip. On the other hand, only seven cases (9%) of those with onset of asthma attack in the evening had morning dip. Furthermore, onset of asthma attack in the afternoon was less common (4 cases) and none had morning or evening dip. Majority of the asthmatic children (61.5%) with onset of attack in the evening had evening dip followed by double dip”. Also from the same figure 3, majority of those with attack in the morning were also morning dippers. Dip patterns correlated significantly with time of onset of asthma attack (X^2 = 104.4; P<0.00001).

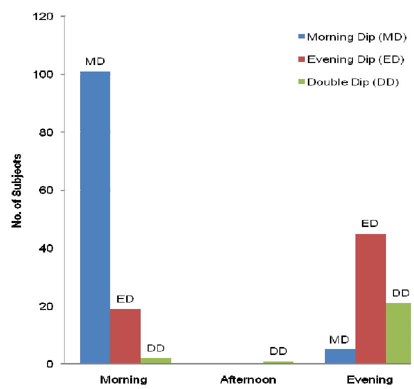

Fig 3: Dip pattern and time of onset of asthma exacerbation

Discussion

This study is in agreement with the fact that a rhythm in respiratory function does exist in asthmatic and non-asthmatic subjects.[5,9,10] However, this rhythm or diurnal variability is less readily detected in healthy, non-asthmatic subjects while more readily detected in asthmatic subjects. In the current study majority of the asthmatic subjects (97.6%) showed a discernable pattern of variability, while only 2.2% of normal controls exhibited this attribute.

The exact mechanism of circadian rhythm in the airways is not clear. It has been found to be unrelated to bronchial calibre,[1,2,11] rather, it represents bronchial reactivity. This is corroborated by the finding of a diurnal variation in airway sensitivity to histamine and to acetylcholine.[1,2,11] This bronchial reactivity is modulated by several inputs and through multifactorial control systems including catecholamines and endogenous steroids.[1,2,3,11]

Various patterns of the rhythmicity are demonstrable, with morning dip being the commonest.[5,6] Generally, the time of trough was at 6am and acrophase at 2pm. As these patterns differ from healthy subjects, determination of dip pattern may aide in the care of asthma.[11-13] This is of particular importance in resource poor areas where sophisticated methods are unavailable for asthma diagnosis since determination of circadian rhythm is performed with the Peak Flow Meter, which is cheap and readily available.[12,13]

The fact that it is easier to demonstrate rhythmicity in the changes of the airway calibre among asthmatics than the non-asthmatics may be connected to the initiation and propagation of an acute attack of asthma and the effect of this heightened rhythmicity in asthmatics may become obvious when their airway is exposed to trigger factors (which other individuals may be exposed to without effect). This leads to a cascade of effects, including an initial cholinergic bronchoconstriction and activation of release of bronchoconstrictors and inflammatory peptides from the airway cells and sensory nerves.[14] This will lead to contraction of the smooth muscle and later oedema of the airway due to plasma exudation from the vessels caused by the inflammatory mediators.[14] When this acute response is initiated on an excessively labile airway, there could be rapid onset of acute airway obstruction in a previously stable patient.[14]

Several specific clinical applications and interpretations concerning the diagnosis, monitoring and management of asthmatics, either during acute exercitations or even at steady state are derivable from this study. For instance, acute exacerbations are more likely to occur in the morning or at the time of lowest PEFR values (reduced airway calibre) and as such the dosage of the drugs and use of inhalers should be tailored to reflect this. This confirms contention by Hetzel that there is a pulmonary clock.[1] Interestingly, this pulmonary clock is operation both in disease and in health.[1,9,15]

Furthermore, regular patterns of dip is frequently seen in asthmatics than the control. This reflects the fact that the amplitude of variation is greater in asthmatics than in normal subjects, since wide amplitude is required to demonstrate this regular patterns.[15] Thus, with good control of asthma, the pattern of variability may not be so discernable among the asthmatics. This was further supported by the findings of Connolly, that treatment with bronchodilators reduce the variability in PEFR among asthmatics and the various dip patterns were no longer seen in some of the asthmatics.[15]

The time of dip may be relevant in deciding the possible aetiologic factor in asthmatics and may be relevant in finding the location of the trigger factors. For instance, those who their asthma is attributed to house dust mites in beddings may be more likely to have evening or early morning dip. But this was not supported by the findings of Clark and Hetzel who demonstrated the various dip patterns in both atopic and non-atopic subjects.[9]

Considering the likelihood of patients having an acute attack and in some cases life threatening attack which may start suddenly and become severe within a short time. The analysis of the various dip patterns becomes useful to both the physician and the patient in predicting onset of such life threatening attacks.[14] In this instance, the drug treatment of such patient could be adjusted to adequately cover the period of dip. Drugs like the long-acting bronchodilators being used up to twice daily may effectively do this and reduce the risk of life threatening attacks.[14]

From the foregoing, the dip pattern is a possible indication of the lability of the airway of the asthmatic. In line with this, an asthmatic without a discernable pattern has a more stable airway with less likelihood of an acute attack. Furthermore, a morning dipper has a labile airway in the morning or on waking and such an asthmatic may not have been compliant with his drugs or the drugs may have worn-out from the system, thereby leaving such periods uncovered with drugs. In essence, a double dipper asthmatic has more likelihood of developing possible acute attacks at more times than either the morning or evening dipper and this may show poor asthma control for such a subject. Interestingly, interpretation of the findings of this study could find several use in different aspects of asthma care.[14,15]

Further studies may be needed to correlate some of this findings with the level of control of asthma in these asthmatics and possibly the effects of drugs on the pattern demonstrated.

Study limitations

- We relied on the PEFR recording done at home. Although we tried to authenticate each recording done at home, this was still a limitation as some may be tempted to falsify result if they forgot to do it at the right time.

- We studied children as young as five years, hoping that their parents will supervise them, but instructing children of this age group is difficult.
- In getting time of onset of attack, we relied on the patient's account of such attack. Sometimes, deciding when an attack started is difficult.

Further research areas

- In future, to ensure adequate monitoring, a similar study could be done on recuperating asthmatics on admission in the hospital using other children in the hospital that are non-asthmatics as control.
- Allergic skin test could be included for the asthmatics to find out what they are exposed to that is causing the attack at different times of the day.
- Effect of drugs on these various dip patterns.
- This study can be done on asthmatics during acute attack.

Conclusion

The airway calibre varies with the time of the day both in normal children and in the asthmatics. These variation However, the proportion of asthmatics with dip pattern is far more than that in non-asthmatic children. From this study, the airway calibre measured by the PEFR was smallest in the morning at 6am and largest in the afternoon at 2pm.

At each time of the day, the asthmatics had lower PEFR or smaller calibre than healthy children.

Due to the wider variation in airway calibre among the asthmatics, the difference between the airway at different times of the day reflecting in their dip patterns was more discernable in the asthmatics than in healthy children.

Authors' contribution
Oviawe O : Study design, data collection and analysis, and supervision
Osarogiagbon W: Data collection, analysis and write up
Conflict of Interest: None
Funding: Authors

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