PEF analysis requiring shorter records for occupational asthma diagnosis

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Introduction

Serial peak expiratory flow (PEF) measurements are recommended as an initial investigation in diagnosing occupational asthma [1]. Analysis of these measurements is best performed by an expert or a computer programme such as Oasys [1,2]. Oasys [2] is a programme with various analysis outputs giving likelihood scores of a serial PEF record demonstrating occupational asthma. The original Oasys score that utilizes the maximum, mean and minimum plot of PEF uses a discriminant analysis; this has been previously validated [3–6] and has been reported to have a sensitivity and specificity of 75 and 94%, respectively. To produce an analysis with high diagnostic sensitivity and specificity, the Oasys score requires a minimum of four readings per day, three consecutive workdays in any work period and ~3 weeks worth of readings (three complexes, a feature of Oasys) [7]. Less data lead to reduced sensitivity and specificity.

The new scoring system utilizes the area between the rest and workday curves in the 2-hourly plot of mean PEF, producing an area between the curves (ABC) score (Figure 1). The plot can be generated using either clock time or time from waking. In an initial study of day-shift workers, both the ABC score by clock time and the ABC score from waking had very similar sensitivities and specificities [8]; therefore, only the ABC score plotted by waking time is being considered in this study. In

Background

The Oasys programme plots serial peak expiratory flow (PEF) measurements and produces scores of the likelihood that the recordings demonstrate occupational asthma. We have previously shown that the area between the mean workday and rest day PEF curves [the area between the curves (ABC) score] has a sensitivity of 69% and specificity of 100% when plotted from waking time using a cut-off score of 15 l/min/h.

Aims

To investigate the minimum data requirements to maintain the sensitivity and specificity of the ABC score.

Methods

A total of 196 sets of measurements from workers with occupational asthma confirmed by methods other than serial PEFs and 206 records from occupational and non-occupational asthmatics who were not at work at the time of PEF monitoring were analysed according to their mean number of readings per day. Measurements from work and rest days were sequentially removed separately and the ABC score calculated at each reduction. The sensitivity and specificity of the ABC score (using a cut-off of 15 l/min/h) was calculated for each duration.

Results

Two-hourly measurements (~8 readings per day) with eight workdays and three rest days had 68% sensitivity and 91% specificity for occupational asthma diagnosis. As readings decreased to ≤4 readings per day, ≥15 workdays were required to provide a specificity above 90%.

Conclusions

To be sensitive and specific in the diagnosis of occupational asthma, the ABC score requires 2-hourly PEF measurements on eight workdays and three rest days. This is a short assessment period that should improve patient compliance.

Key words Data quantity; Oasys; occupational asthma; peak expiratory flow.

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the Oasys programme. Mean PEF measurements taken between 0 and 2, >2 to 4, >4–6 h from waking and so on are plotted based on all workdays and all rest days. The black upper line (square markers) shows the average peak flow for rest days by 2 h segments from 0 to 24 h from waking. The grey lower line (cross markers) shows the same for workdays. The grey area shows information about the times of starting and stopping work (mode, minimum and maximum). The legend shows the start and end of the 2-h time segments, the number of readings used to calculate the work and rest day average PEFs, the area between the rest and workday curves (ABC) on the graph for each time segment and the area per hour (ABC) score. To calculate the ABC/hour score, the total area is divided by the number of hours for which there are measurements (in this case 16 h). In this record, it gives an ABC score of 55 l/min/h (shown on the plot).

this plot, the mean of rest day PEF values and that of workday PEF values are plotted in 2-hourly segments with the first data point representing the mean of all work or rest day readings taken 0–2 h from waking. The next data point represents the mean of all work or rest day readings >2–4 h from the time waking and so on. The area between the rest and the workday curves (ABC) is then calculated in litres/minute and divided by the number of hours contributing to the plot to derive the ABC score; a minimum of three readings per data point is required.

The ABC score has recently been shown to have a sensitivity of 69% and specificity of 100% using a cut-off score of 15 l/min/h for the diagnosis of occupational asthma [8]. The minimum data requirements for maintaining this sensitivity and specificity are unknown. It is likely to need less data quantity compared to the original record and versus when rest days were degraded. After every step of data removal, the ABC score from waking (in l/min/h) and the associated sensitivity and specificity of the score (using the predetermined cut-off of 15 l/min/h) was calculated. This process continued sequentially until data quantity reached a minimum of 3 days, as Oasys analysis could not be computed with fewer days.

Figure 1. A 2-hourly plot of average PEF on rest days and workdays from the Oasys programme. Mean PEF measurements taken between 0 and 2, >2 to 4, >4–6 h from waking and so on are plotted based on all workdays and all rest days. The black upper line (square markers) shows the average peak flow for rest days by 2 h segments from 0 to 24 h from waking. The grey lower line (cross markers) shows the same for workdays. The grey area shows information about the times of starting and stopping work (mode, minimum and maximum). The legend shows the start and end of the 2-h time segments, the number of readings used to calculate the work and rest day average PEFs, the area between the rest and workday curves (ABC) on the graph for each time segment and the area per hour (ABC) score. To calculate the ABC/hour score, the total area is divided by the number of hours for which there are measurements (in this case 16 h). In this record, it gives an ABC score of 55 l/min/h (shown on the plot).

**Methods**

A total of 712 serial PEF records were available from the database at the Birmingham Chest Clinic, UK, from patients investigated between 1980 and 2007. These included (i) 389 serial PEF records from workers diagnosed as having occupational asthma based on independent clinical investigations of either specific bronchial challenge test [positive result defined as at least 15–20% fall in forced expiratory volume in 1 s (FEV1) from baseline value in response to exposure to the occupational agent and no significant FEV1 fall in response to exposure to the control agent], 4-fold change in methacholine reactivity related to exposure or positive specific IgE (positive result defined as ≥0.35 kU/l or ≥2.2% binding) plus a relevant history (occupational asthma positives) and (ii) 323 records from patients diagnosed as asthmatics/occupational asthmatics who were not working during their serial PEF measurement period (to ensure that these records could not demonstrate work-related changes in PEF) (occupational asthma negatives). Local ethics committee approval was obtained from the Birmingham East, North and Solihull committee.

To enable analysis by Oasys, PEF measurements in occupational asthma negative records made between 9 a.m. and 5 p.m. from Monday to Friday were analysed as ‘at work’ and compared with readings on Saturday and Sunday that were analysed as ‘off work’.

Occupational asthma positive and negative records were checked to exclude records performed during respiratory tract infections, changes in asthma treatment and those with a mean daily PEF increasing or decreasing >5 l/min/day over the record. Any rest periods >3 days were removed to exclude changes seen only after a long period away from exposure.

Records were grouped by their mean number of readings per day into four groups: ≥7.5 readings per day, ≥6.5 to <7.5, ≥4.5 to <6.5 and ≤4.5 readings per day. Workdays and rest days were then sequentially reduced as outlined below. Records were required to contain a minimum of six workdays when analysing the rest day sensitivity and specificity (taken from an initial analysis of data reduction) and a minimum of three rest days when analysing workdays. Only two records were used from any one worker within each number of readings per day group. Where >2 records were available, the first two (by date) were taken.

Workdays and rest days were removed individually from the end of the record in sequence. When workdays were degraded, the number of rest days was left unchanged as in the original record and vice versa when rest days were degraded. After every step of data removal, the ABC score from waking (in l/min/h) and the associated sensitivity and specificity of the score (using the predetermined cut-off of 15 l/min/h) was calculated. This process continued sequentially until data quantity reached a minimum of 3 days, as Oasys analysis could not be computed with fewer days.

- This plot, the mean of rest day PEF values and that of workday PEF values are plotted in 2-hourly segments with the first data point representing the mean of all work or rest day readings taken 0–2 h from waking. The next data point represents the mean of all work or rest day readings >2–4 h from the time waking and so on. The area between the rest and the workday curves (ABC) is then calculated in litres/minute and divided by the number of hours contributing to the plot to derive the ABC score; a minimum of three readings per data point is required.

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SPSS 15 was used for all analyses. The chi-square test was used to look for differences in occupational asthma negative and positive groups with categorical data. Where outcome variables were expressed as continuous data and the predictors were categorical, the Mann–Whitney U-test was used.

Results

A total of 196 occupational asthma positive records from 124 workers and 206 occupational asthma negative records from 187 patients were available for analysis. Table 1 shows the diagnostic tests used to confirm occupational asthma positive workers and Table 2 shows the demographics for occupational asthma positive and negative patients.

Overall, a greater number of workdays and rest days were required to maintain sensitivity and specificity as fewer readings per day were available. Table 3 shows the results. Two-hourly PEF records (≥7.5 readings per day) with eight workdays and cut down to contain only three rest days showed a sensitivity of 68% and specificity of 91% for the diagnosis of occupational asthma. When all available rest days were used (≥3 rest days), the sensitivity decreased to 62% and specificity remained similar at 92% (as shown in Table 3).

Discussion

In this study of serial PEF monitoring on workdays and rest days for diagnosing occupational asthma, we have shown that records containing eight workdays, three rest days and ≥8 readings per day have a sensitivity of 68% and specificity of 91% when using the ABC score of 15 l/min/h. The sensitivity could be increased further to 75% (reducing specificity to 86%) by using a cut-off of 10 l/min/h. This combination of sensitivity and specificity would still be better than pre- and post-shift measurements of PEF or change in non-specific reactivity [9–12]. Lesser data quantity reduces the sensitivity and specificity particularly when fewer readings per day are available. At the minimum data quantity requirement of eight workdays, three rest days and eight readings per day, the ABC score is a useful addition to the analysis system. The system previously only gave a sensitive and specific Oasys score based on the maximum, mean and minimum daily plot for records containing ~3 weeks of readings (three complexes), at least three consecutive workdays in any work period and ≥4 readings per day [7]. The ABC score can also analyse records that do not contain consecutive workdays, thereby making it more useful for workers with intermittent exposure.

The ABC score showed high specificity that mostly remained stable when rest days were reduced, but decreased when workdays were reduced. This may be due to some workers not showing a consistent fall in peak flow on all days at work. Records with long rest periods have not been used in this analysis as many workers only have weekends off work (the exceptions being PEF monitoring at specific times of the year like factory shutdowns or holidays).

The sensitivity of the ABC score was significantly reduced when <7 readings per day were present, and higher numbers of workdays and rest days were then required to maintain sensitivity and specificity acceptable for a diagnostic test. This is partly related to the fact that for calculating the ABC PEF score, there is a requirement for ≥3 readings to be taken within the same 2-h time period across the record for work and rest days. This is a particular problem for the important waking PEF measurements which are likely to vary in time. It would help if workers measured their PEF at consistent times of the day (from waking) to obtain an increased amount of analysable data.

The sensitivity of the ABC score may be further improved by including the analysis of records with a long

Table 1. Diagnostic tests for occupational asthma used for independent validation

<table>
<thead>
<tr>
<th>Test</th>
<th>% (n = 124)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specific bronchial challenge test</td>
<td>60</td>
</tr>
<tr>
<td>4-fold change in methacholine reactivity</td>
<td>27</td>
</tr>
<tr>
<td>Specific IgE plus typical symptom history</td>
<td>13</td>
</tr>
</tbody>
</table>

Table 2. Demographics

<table>
<thead>
<tr>
<th></th>
<th>Occupational asthma positive (n = 124)</th>
<th>Occupational asthma negative (n = 187)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (SD)</td>
<td>42.6 (9.7)</td>
<td>50.5 (9.1)</td>
<td>&lt;0.001a</td>
</tr>
<tr>
<td>% Males</td>
<td>58</td>
<td>59</td>
<td>&gt;0.05b</td>
</tr>
<tr>
<td>% Atopics</td>
<td>57</td>
<td>52</td>
<td>&gt;0.05b</td>
</tr>
<tr>
<td>% Current smokers</td>
<td>20</td>
<td>21</td>
<td>&gt;0.05b</td>
</tr>
<tr>
<td>% Methacholine reactive</td>
<td>62</td>
<td>45</td>
<td>&lt;0.01b</td>
</tr>
<tr>
<td>% Taking ICS</td>
<td>73</td>
<td>83</td>
<td>&gt;0.05b</td>
</tr>
<tr>
<td>Mean FEV1 % predicted (SD)</td>
<td>84.2 (21.6)</td>
<td>84.8 (23.2)</td>
<td>&gt;0.05a</td>
</tr>
<tr>
<td>Mean PEF diurnal variation (SD) (OA positive n = 196; OA negative n = 206)</td>
<td>21.5 (13.7)</td>
<td>19.0 (28.7)</td>
<td>&lt;0.001a</td>
</tr>
<tr>
<td>Mean ABC from waking time score (OA positive n = 196; OA negative n = 206)</td>
<td>23.3 (32.4)</td>
<td>0.7 (7.6)</td>
<td>&lt;0.001a</td>
</tr>
</tbody>
</table>

SD, standard deviation; ICS, inhaled corticosteroids; OA, occupational asthma.

aAnalysed using Mann–Whitney U-test.
bAnalysed using chi-square test.
period off work (these were not included in this analysis). However, as the ABC plots mean values, the first 3 days off work should be excluded in order to ensure that only the days showing improvement in PEF values are analysed (for those workers taking a long time to improve their PEF).

We used a method of grouping records by the number of readings per day that they contained. This enabled us to use real-life measurements which are readily achievable in the clinical setting [7]. These records reflect the fact that subjects often make readings at inconsistent times on work and rest days, which may give less useful data compared to the ideal situation where subjects perform readings at consistent times.

We chose to reduce the record days starting from the end to reflect the real-time situation where subjects get tired of recordings. Thus, this analysis does not necessarily apply to situations where there are gaps in the middle of the recording.

Although no other studies have looked at the data quantity requirements for the ABC PEF score calculated by the Oasys programme, studies have assessed requirements for PEF analysis in general. Malo et al. [13] assessed data requirements for peak flows plotted as a graph in four different ways analysed by three different readers and showed that four readings per day were adequate when carried out for at least 2 weeks at work and 2 weeks away from work, giving a sensitivity of 73% compared to positive specific bronchial challenge (agreement of at least two of three expert physicians) and specificity of 78% compared to negative specific bronchial challenge.

We have found that the Oasys score requires at least three complexes of data [2,3] (i.e. ~3 weeks of recording), four readings per day for 75% of the record and three consecutive days in any work period to give a sensitivity of 78% and a specificity of 92% [7]. If the data quantity is any less, the sensitivity and specificity of the Oasys score falls to 64 and 83%, respectively. Achieving three consecutive workdays in any work period is the commonest reason for failing these data quantity requirements [7]. In the PEF records used for sequential reduction in this study, the work and rest days were not required to be consecutive. Although all the occupational asthma negative records contained at least three consecutive workdays, 43% of the occupational asthma positives contained at least one period of 3 workdays before reduction. When the criteria for consecutive workdays was investigated, the sensitivity was 70% for those who had three consecutive workdays and 68% for those with at least one period of <3 workdays. This means that when the data quantity needed for a sensitive and specific Oasys score is not reached, the ABC score can still be a reasonably sensitive and highly specific diagnostic tool for occupational asthma.

Using an ABC PEF score of ≥15 l/min/h as the cut-off point, a sensitivity of 68% and specificity of 91% for occupational asthma diagnosis are achieved when the PEF record contains eight workdays, three rest days and at least eight readings per day. When the mean number of readings per day is less than this, a greater number of work and rest days are required to maintain appropriate sensitivity and specificity. The ABC PEF score therefore requires a shorter serial PEF record for diagnosing occupational asthma compared to the original Oasys score, which should make the diagnosis of occupational asthma easier in workers finding it difficult to comply with the original requirements of longer record keeping.

### Table 3. Sensitivity and specificity for records according to reducing duration of PEF monitoring grouped by the mean number of readings per day

| Number of work or rest days | Mean readings per day (mode) | Wse | Wsp | Rse | Rsp | Wse | Wsp | Rse | Rsp | Wse | Wsp | Rse | Rsp |
|----------------------------|------------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| All available              | 76                           | 97  | 77  | 96  | 57  | 100 | 64  | 100 | 58  | 97  | 67  | 95  | 59  | 97  | 67  | 97  |
| 15                         | 75                           | 95  | 64  | 100 | 57  | 97  | 60  | 97  | 54  | 86  | 60  | 96  | 58  | 97  | 60  | 96  |
| 10                         | 66                           | 94  | 55  | 95  | 39  | 89  | 54  | 86  | 54  | 86  | 54  | 86  | 54  | 86  | 54  | 86  |
| 9                          | 64                           | 92  | 52  | 96  | 37  | 92  | 54  | 86  | 54  | 86  | 54  | 86  | 54  | 86  | 54  | 86  |
| 8                          | 62                           | 92  | 77  | 95  | 57  | 96  | 47  | 100 | 34  | 89  | 68  | 100 | 60  | 81  | 60  | 96  |
| 7                          | 62                           | 89  | 75  | 95  | 59  | 96  | 60  | 100 | 33  | 89  | 56  | 95  | 56  | 78  | 59  | 96  |
| 6                          | 65                           | 87  | 81  | 97  | 60  | 96  | 67  | 100 | 28  | 89  | 58  | 97  | 57  | 78  | 55  | 91  |
| 5                          | 64                           | 83  | 75  | 96  | 56  | 93  | 65  | 91  | 36  | 82  | 54  | 100 | 59  | 78  | 61  | 91  |
| 4                          | 65                           | 84  | 72  | 93  | 52  | 93  | 52  | 88  | 34  | 77  | 55  | 100 | 59  | 71  | 64  | 89  |
| 3                          | 62                           | 82  | 71  | 92  | 47  | 89  | 48  | 94  | 40  | 72  | 46  | 100 | 55  | 77  | 57  | 90  |

Wse, workday sensitivity; Wsp, workday specificity; Rse, rest day sensitivity; Rsp, rest day specificity. Bold numbers highlight the number of rest days and workdays required to keep the sensitivity at ≥60% (where possible) and specificity at ≥90%.
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Conflicts of interest

None declared.

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8. Moore VC, Jaakkola MS, Burge CBSG et al. A new diagnostic score for occupational asthma; the area between the curves (ABC score) of PEF on days at and away from work. *Chest* 2009;135:307–314.