Oxygen consumption during sleep in atopic dermatitis

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Abstract

Measurements of oxygen consumption ($\dot{V}O_2$) were made during sleep in 10 patients with atopic dermatitis. Two groups of healthy children acted as controls. All subjects were studied in bed in an environmental temperature of 24–26°C, and sleep was confirmed during continuous electroencephalographic monitoring. Mean (SD) values of $\dot{V}O_2$ in sleeping patients who were not scratching ranged from 4.0 (0.4) to 7.4 (0.7), which was not statistically significantly different from control values which ranged from 3.24 (0.3) to 5.56 (0.4). During scratching (while asleep), which occurred in nine out of 10 patients with atopic dermatitis, the mean values of $\dot{V}O_2$ ranged from 4.5 (0.04) to 10.4 (2.7), and this was significantly higher than the non-scratching patients and the control values. Scratching during sleep in children with atopic dermatitis is associated with increased $\dot{V}O_2$.

(Arch Dis Child 1995; 72: 144–146)

Keywords: atopic dermatitis, oxygen consumption, scratching, sleep.

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Accepted 18 October 1994

The association of short stature with atopic dermatitis, particularly in cases with widespread skin lesions, is well documented but poorly understood.^{1–4} One of many possible explanations is that limb and body movements during scratching could cause an increase in energy expenditure. If this were associated with an inadequate energy intake, a

negative energy balance would result, and if this persisted this might result in impaired growth.

The aim of this study was to measure oxygen consumption ($\dot{V}O_2$) during sleep in children with dermatitis, during periods of scratching and non-scratching, and to compare it with oxygen consumption of the non-atopic healthy child. We chose to do this study at night, to eliminate confounding variables that affect oxygen consumption such as normal daytime activities and feeding.

Subjects and methods

Children with atopic dermatitis, between the ages of 6 months and 10 years, who were regularly attending the University Department of Child Health at Booth Hall Children's Hospital were studied. All patients fulfilled the diagnostic criteria of Hanifin and Rajka.⁵ Patients were selected on the basis of a parental report of sleep disturbance and not because of the severity of the child's eczema. A sibling or friend without dermatitis was invited to participate in the study as a control subject. The study was approved by the Salford Health Authority research ethics committee.

Each subject was brought to a medical ward in the late afternoon, between 16.00 and 17.00 hours. The child played on the ward until having a meal at 17.30 hours, and was then brought to the study room, a single cubicle, at about 18.00 hours. The subjects' parents accompanied the children. The standing height was measured using a Harpenden stadiometer, and weight was measured using Autoweigh scales, which were calibrated by the company every three months (System IX Industrial Weight Terminal, Ian Fellows Ltd, Frome, Somerset). The dermatitis was assessed using body surface area charts designed for children in the age groups 0–4, 5–10, and 11 years and over. The charts were similar to those used in the assessment of burns in children, but more detailed, and divided the body into 32 separate zones. The surface area of skin affected by dermatitis was multiplied by the degree of erythema to produce a dermatitis severity score.⁶

All subjects were studied in an air conditioned room where the ambient temperature was maintained between 24–26°C. After the meal, the children were occupied with sedentary games and reading. A simple explanation of the study was repeated and the children became familiar with the face mask. The children were clothed in their own pyjamas and covered by one cotton sheet while asleep. Continuous overnight sleep monitoring was

Figure 1 Control range (mean and 95% confidence interval) constructed from pooled data ($n=28$) of sleeping control subjects. Superimposed on control range are the minute by minute measurements of $\dot{V}O_2$ of sleeping patients during scratching.

Figure 2 $\dot{V}O_2$ (ml/min/kg) in sleeping healthy children of different ages acting as a control group. Data from group A published previously in this journal¹ have been combined with new control data from 10 healthy children shown by the 'string' of small circles.

made using electroencephalographic (EEG) recordings. Two leads were placed above, and two below each eye to detect rapid eye movement sleep (REM). For confirmation of non-REM sleep, two leads were placed on right and left temporal regions and two at either side of the vertex. In addition there was an earth and a ground lead. EEG activity was recorded, using a tape recorder, from the time of attaching the leads to their removal the next morning.

Throughout the night each control subject and patient was observed by one of us (MEMJ, CC, or DM). Observations and detailed notes were kept of the sleep state of both patients and controls. For the patients, however, it was important to note periods in which the child's sleep was disturbed by scratching or any other event that caused the child to become restless or wake up. These observations were noted throughout the night and also throughout the period of each measurement of respiratory gas exchange. In this way scratching during sleep could be related to changes in $\dot{V}O_2$.

A control range for $\dot{V}O_2$ was constructed from data obtained from two groups of healthy sleeping subjects. Published data obtained by one of our group⁷ of $\dot{V}O_2$ in 10 healthy sleeping children (group A) was combined with measurements of $\dot{V}O_2$ in healthy siblings and friends of the patients in this study who were recruited as a second control group (B). In

both groups the open circuit flow-through principle of indirect calorimetry was used. The child's expired respiratory gas was collected into a clear plastic face mask, held gently over the nose and mouth.⁸ Measurements were made after the children had settled (awake and at rest) and a series of measurements were made after the children had fallen asleep.

Although the technique of indirect calorimetry used to measure $\dot{V}O_2$ was the same, the two different machines output data rather differently. In group A, measurements were made using a specially designed metabolic cart, designed and constructed for use in infants and children.⁸ The child's exhaled respiratory gas was collected once only during sleep over a period of 15–20 minutes. At the end of the measurement, $\dot{V}O_2$ is given as an average value for the period measured whereas in group B the commercial system used (Deltatrac metabolic monitor, Datex, Instrumentarium Corp, Helsinki, Finland) gives a 'string' of minute to minute values. Thus over a period of 15 minutes, for example, 15 values for $\dot{V}O_2$ are available (see fig 1).

In the sleeping controls and patients measurements of respiratory gas exchange, over 15–20 minute periods, were made approximately every two hours during the night.

Results

Ten healthy children, aged 5.6 to 12.6 years (median 9.2 years) who were the friends or siblings of the patients were studied. Ten patients, aged 3.4–14.1 (median 7.2) years with a dermatitis score ranging from 19–109 (median 61) were studied overnight in an adjacent bed to their respective sibling or friend. This method of recruitment resulted in a difference in the age range of patients and controls but by using the data from the controls in group A, a control range for all the sleeping patients can be constructed.

$\dot{V}O_2$ measured in both groups of healthy sleeping subjects (A, $n=18$ and B, $n=10$) is given in fig 2. Plotting these data from the two groups shows that the pattern of the 'string' of minute by minute measurements of $\dot{V}O_2$ in group B broadly fits with that of the larger group (A, fig 2). $\dot{V}O_2$ in healthy children falls with age, from approximately 8–9 ml/min/kg in the youngest children to approximately 3–6 ml/min/kg in the older ones (fig 2).

The distribution of the plots for $\dot{V}O_2$ in the two groups were examined and these data can be assumed to follow a statistically normal distribution. In each control subject from group B, the mean of 15–20 one minute measurements of $\dot{V}O_2$, obtained approximately four hours after the child had fallen asleep were used. Thus one value from each patient represents sleeping $\dot{V}O_2$ in both control groups. The range of mean $\dot{V}O_2$ in group A was 3.6–9.2 (median 6.8) ml/min/kg and in group B, 3.6–6.0 (median 5.25) ml/min/kg. Multiple regression methods showed that the slopes and intercept of the two lines formed by these data did not differ significantly so data from the two groups were pooled ($n=28$). From this pooled

Table 1 Sleeping $\dot{V}O_2$ during scratching compared with non-scratching

Patient No	Mean (SD) $\dot{V}O_2$ (ml/min/kg) [No of measurements]		No (%) of measurements of $\dot{V}O_2$ which exceeded the non-scratching upper limit*	Significance by paired t test (p value)
	Non-scratching	Scratching		
1	5.2 (0.5) [33]	6.4 (1.0) [25]	11/25 (44)	<0.001
2	7.4 (0.7) [69]	10.4 (2.7) [22]	14/22 (64)	<0.001
3	6.5 (0.4) [70]	9.0 (0.9) [9]	9/9 (100)	<0.001
4	6.9 (0.3) [46]	7.8 (0.8) [43]	23/43 (53)	<0.001
5	4.0 (0.4) [70]	4.5 (0.4) [36]	6/36 (17)	<0.001
6	4.5 (0.2) [51]	5.1 (0.4) [19]	14/19 (74)	<0.001
7	4.8 (0.7) [93]	8.7 (3.3) [28]	18/28 (64)	<0.001
8	4.2 (0.4) [37]	5.0 (0.4) [21]	13/21 (62)	<0.001
9	4.4 (0.3) [47]	4.7 (0.03) [3]	0/3	NS

The 10th patient not included as scratching not observed. *Non-scratching upper limit constructed from mean +2 SD.

Table 2 Changes in sleeping $\dot{V}O_2$ during scratching

Patient No	Age (years)	Eczema score	Hours asleep	No of times $\dot{V}O_2$ measured during the night*	% Of measurement time spent scratching†	% Increase in $\dot{V}O_2$ ‡	Sleep stages during scratching§	Sedation (trimeprazine tartrate)
1	4.2	31	22.52–06.46	7	43	23	2, REM	60 mg at 19.30
2	4.2	109	21.41–06.36	6	24	40	REM, 2	60 mg at 19.45
3	4.3	83	22.25–05.55	5	11	39	2, 3	
4	4.5	41	22.26–07.01	5	48	13	1, 2, REM	50 mg at 19.30
5	9.9	23	23.02–07.30	6	34	13	1, 2, 3	50 mg at 18.30
6	10.4	72	00.43–07.08	6	27	12	No EEG record	30 mg at 20.10
7	12.0	61	00.57–07.03	7	23	82	1, 2, 3	
8	13.9	18	00.01–05.51	5	36	20	1, 2	
9	14.1	74	01.23–06.07	5	6	Within range	2	
10	3.4	19	21.23–07.32	3	None			

*Each measurement was made over a 15–20 minute period.

†The time spent scratching as a % of the total measurement period.

‡Mean sleeping $\dot{V}O_2$ during scratching as a % above mean sleeping $\dot{V}O_2$ when not scratching.

§The sleep stages given here are in numerical order and not in the pattern they were recorded in the patient.

data a single regression line with its 95% confidence interval was constructed to give a control range for $\dot{V}O_2$ (see fig 1).

Superimposed on this control range are the measurements of $\dot{V}O_2$ of nine patients who scratched during sleep. In four patients, $\dot{V}O_2$ was variable with measurements of $\dot{V}O_2$ within the control range as well as above it (fig 1). Using the Student's *t* test there was no significant difference in individual mean values for $\dot{V}O_2$ in sleeping controls and sleeping, non-scratching patients. The range of $\dot{V}O_2$ for the patients was between 4.0 ± 0.4 and 7.4 ± 0.7 ml/min/kg. However, during sleep, scratching caused a significant increase in $\dot{V}O_2$ compared with values measured when the patients were asleep and not scratching (table 1).

Patients scratched at all times of the night but most scratching occurred during the early morning. One child scratched during the late evening (22.00–24.00), 17 children scratched between the hours of 02.01 and 04.00, and 14 children during the early morning (04.01–08.00).

Each child was measured for approximately 15 minutes on three to seven separate occasions during the night (table 2). The time spent scratching during these measurements was between 11% and 48% of the total measurement period. During scratching $\dot{V}O_2$ was within the normal range for one child only (table 2) but for the other eight patients the mean $\dot{V}O_2$ during scratching was 12–82% (median) above non-scratching mean $\dot{V}O_2$. Scratching occurred more usually during sleep stage 2. Few patients scratched during REM sleep and no children were observed to be scratching during sleep stage 4.

Discussion

Energy expenditure rises with increased movement. If measurements of energy expenditure are made while an individual is awake, complete cooperation is required. This is difficult to obtain from children, particularly if they are very young and it was for this reason that

measurements during sleep were made. EEG recording was used to confirm that the child was indeed asleep during the time when the measurements were taken. This was particularly important when measuring the metabolic rate of children with eczema during periods of scratching, when it is difficult for an observer to know whether or not a child is asleep. However, there are limitations to the approach used here. Although many measurements were taken from each child throughout the night and a rise in energy expenditure identified during scratching, it is only possible to quantify this rise if continuous measurements of $\dot{V}O_2$ are made throughout the night. The variability of $\dot{V}O_2$ and the small number of subjects made it difficult to seek an association between episodes of nocturnal scratching, oxygen consumption, and short stature.

Negative energy balance would result if energy intake fails to match energy expenditure, and it is possible that the increased energy expenditure associated with scratching may interfere with growth. Further quantification of the overall rise in oxygen consumption associated with scratching combined with an assessment of dietary intake⁹ are required.

We thank Professor R A Little, the nursing staff at Booth Hall Children's Hospital, and Mr E B Faragher, department of statistics, Withington Hospital, for their help. The purchase of the Deltatrac monitor was funded by the Peter Kershaw Trust.

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