Sleep related upper airway obstruction in a cohort with Down’s syndrome

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Abstract
The prevalence of sleep related upper airway obstruction (UAO) was studied in a cohort of 34 children with Down’s syndrome from a geographically defined area. Thirty two (94%) of the children, ranging in age between 0·1 and 4·9 years (median 1·4), underwent full clinical assessment for UAO including parental questionnaires and overnight tape recordings of chest wall movements and arterial oxygen saturation (Sao₂). Compared with controls, children with Down’s syndrome had (a) an increased incidence of stridor and chest wall recession during sleep, (b) an increased frequency of a pattern on inspiration indicating increased upper airway resistance, (c) a reduced baseline oxygen saturation (having excluded recordings on four children with potential for right to left intracardiac shunting), and (d) an increased number of episodes with Sao₂<90% despite continued chest wall movements.

At their initial assessment seven children (22%) had evidence of UAO. The 18 youngest children (<1·7 years) underwent repeated recordings and clinical assessment until they had all reached 2 years of age. A further three were found to have developed UAO.

Sleep related UAO is a common problem in children with Down’s syndrome, occurring in 10 of 32 (31%) of this population based sample.

Previous reports have shown that individuals with Down’s syndrome are subject to upper airway obstruction (UAO). Features of the anatomy of the upper airway are thought to predispose to this complication, which when severe may lead to pulmonary hypertension and heart failure. In any child, UAO may be associated with poor growth, sleep disturbance, day time lethargy, chronic upper respiratory problems, and poor developmental progress. If present in a child with Down’s syndrome, these may add to the total load of handicap suffered. As UAO may either increase in severity during, or only be present in, sleep, the patient suspected of suffering this disorder must be investigated while asleep.

The present study aims to determine the prevalence of UAO in a population of children with Down’s syndrome in a well defined geographical area by using questionnaires and overnight multichannel physiological recordings. The subsequent clinical assessment and outcome are also described.

Subjects
The study consisted of three parts: (i) a case-controlled study of signs of UAO obtained by questionnaires administered to parents, (ii) a case-controlled blinded analysis of overnight tape recordings of arterial oxygen saturation (Sao₂) and breathing movements, and (iii) a clinical assessment for the presence of UAO which included the questionnaire, a clinical examination, and open assessment of the overnight tape recordings. This clinical assessment was also performed at the time of repeated recordings on the younger children until they had reached 2 years of age.

The study was approved by the local hospital ethics committee, and all parents of the controls and children with Down’s syndrome gave informed consent.

CHILDREN WITH DOWN’S SYNDROME
All children up to 5 years of age with Down’s syndrome from a well defined geographical area (Oxford Area Health Authority) are enrolled in a programme which offers support, clinical assessment, and coordination of services. Thirty two (94%) of the 34 children with Down’s syndrome in this cohort were recruited to the study; two sets of parents declined. There were 20 boys and 12 girls, whose ages ranged from 0·1 to 4·9 years (median 1·4).

One subject (case 30) had undergone adenoidectomy for recurrent otitis media and one subject (case 14) had severe UAO in the neonatal period, as observed by Mugliston and Mitchell but this had subsequently resolved. No other subject had undergone investigation or treatment for UAO, tonsillectomy, or adenoidectomy for any reason.

Twelve children (38%) were known to have congenital heart disease: five had ventricular septal defects, two had atrioventricular septal defects, three had complex structural defects, and one each had a secundum atrial septal defect and a patent arterial duct. Two of the 12 had undergone palliative surgery. Because cardiac function could have affected the respiratory measurements, a paediatric cardiologist, blind to the study findings, reviewed the case notes of the 12 children. At the time of the recordings, four children had a defect which might have resulted in baseline arterial hypo-xemia (Sao₂<95%) (cases 1, 9, 15, and 22) and five children were considered to be tachypnoeic (cases 1, 2, 9, 15, and 22).

CONTROLS
Two sets of healthy infants and children with-
out Down's syndrome were used as controls. For the questionnaire, 26 controls of similar age to the children with Down's syndrome were selected randomly; they ranged in age from 0·1 to 5·6 years (median 2·0) and there were 15 boys and 11 girls. For the overnight recordings, 32 different controls were selected randomly and matched individually to the subjects' ages; their ages ranged from 0·1 to 5·7 years (median 1·0) and there were 16 boys and 16 girls.

**Methods**

**QUESTIONNAIRE**

A structured interview was used to question parents about the presence of six clinical signs during sleep which from previous experience were known to be associated with UAO.\(^4\) These were inspiratory stridor (snoring), chest wall recession, sudden wakenings with a startle or gasp, restlessness, breathing through the mouth, and excessive sweating. The significance of differences in the incidence of these signs between children with Down's syndrome and controls was tested by Wilcoxon rank sum or \(\chi^2\) tests.

**RECORDINGS**

Twelve hour overnight tape recordings were performed on each child with Down's syndrome and each control (at the time of the above interviews for the subjects). Recordings included the following signals: (1) \(\text{Sao}_2\) from a pulse oximeter (Nellcor N-100, with software identical to N-200) modified to provide beat-to-beat measurements. (2) The photoplethysmographic pulse waveforms from which \(\text{Sao}_2\) was derived; these were used to identify and exclude \(\text{Sao}_2\) measurements associated with movement artefact. (3) Chest wall movements from respiratory inductance plethysmography (Studley Data Systems) using a purpose made vest over the chest wall (P K Morgan) and from an abdominal volume expansion capsule (Graseby Dynamics). (4) End tidal carbon dioxide concentration, sampling from just below one nostril via a catheter leading to an infrared analyser (Engstrom Eliza). This last signal was collected for clinical assessment only (see below). The full recording technique has been described in detail elsewhere.\(^1\) Records on both the children with Down's syndrome and the controls were performed in their homes, except for that on the youngest subject, who had remained in hospital after biopsy.

Tape recordings were printed out, using an ink jet chart recorder (Siemens 34T), at 3·2 mm/second. Measurements from the recordings were performed manually by two workers without knowledge of the source of the data and working to a protocol established for earlier studies.\(^4\) Breathing patterns were classified as being either regular or non-regular: a regular breathing pattern was signified by periods lasting at least one minute in which breathing movements were steady in rate and amplitude. All other periods of breathing movements, including those interrupted by body movements, frequent sighs or apnoic pauses were classified as non-regular breathing.

Blind analysis of the recordings included an examination for:

(a) The presence of the pattern on the chest wall movement record indicating increased inspiratory resistance (false negative results may be obtained if tachypnoea is present and the five cases with congenital heart disease resulting in this pattern of breathing were, therefore, excluded from this analysis).

(b) Baseline \(\text{Sao}_2\), measured at the end inspiratory peak of five successive breaths in the centre of each period of regular pattern breathing, in an area separated by at least 10 seconds from disturbance of the chest wall movement by sigh or apnoic pause. The mean of these measurements was calculated.

(c) Episodes of desaturation in which \(\text{Sao}_2\) fell to \(\leq 90\%\), the duration of each being measured. Apnoic pauses were identified where there was a cessation of chest wall movement with a duration of \(> 10\) seconds. Episodes of desaturation were discounted if they showed a temporal relationship with such pauses: that is, where the beginnings of a pause and of a subsequent desaturation \(\leq 90\%\) were separated by 2–12 seconds. This excluded the episodic desaturation that has been demonstrated to follow frequently and normally apnoic pauses in healthy infants.\(^1\) The remaining episodic desaturations, that is, those associated with continued chest wall movements, were regarded as probably resulting from UAO. The durations of these episodes were summed in each breathing pattern separately, and expressed as durations per hour of artefact free signal. They were separated because \(\text{Sao}_2\) instability has been demonstrated to be determined by breathing pattern, being reduced in regular pattern breathing.\(^1\)

The significance of the differences for baseline \(\text{Sao}_2\), episodic hypoxaemia, and for the presence of increased inspiratory resistance between the children with Down's syndrome and controls was tested by the Wilcoxon matched pairs signed rank test or McNemar's test. One tailed tests were used throughout.

**CLINICAL ASSESSMENT**

All children with Down's syndrome underwent a clinical assessment which included the questionnaire described above, physical examination both awake and asleep, and an open examination of the overnight tape recordings of \(\text{Sao}_2\), breathing movements, and expired carbon dioxide concentration.\(^4\) A decision was made on the presence and extent of UAO and appropriate action was initiated, investigation and treatment being carried out at the Royal Brompton Hospital or local hospitals. If UAO was considered severe, further investigations might have been indicated (for example, cine barium swallow) before immediate referral was made for assessment in the ear, nose, and throat department. If the UAO was not considered to be severe further recordings were recommended in order to evaluate developmental changes of the impact of respiratory tract infection. The controls were not assessed in this way.

To assess changes with increasing age,
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related to the complete recordings ranged from 0 to 174.3 seconds/hour (s/h) (median 3.6) compared with 0 to 2.6 s/h (median 0) for the controls (p<0.0001, Wilcoxon). For non-regular breathing pattern alone, the frequency of episodic desaturation ranged from 0 to 219.1 s/h (median 3.45) for the children with Down’s syndrome and from 0 to 4.9 s/h (median 0) for the controls (p<0.0001, Wilcoxon). The frequency of episodic desaturation in regular breathing pattern alone for the 26 children with Down’s syndrome ranged from 0 to 140.7 s/h (median 1.4) but for the controls only one score was greater than 0 (range 0 to 1.3) (p<0.0001, Wilcoxon).

CLINICAL ASSESSMENT FOR UAO
The first assessment indicated UAO in seven of the 32 children with Down’s syndrome (cases 11, 12, 14, 18, 21, 23, and 29). The median age of these seven children was 1.6 years (range 0.7-4.2). At different ages, the proportion of children with Down’s syndrome who demonstrated UAO was as follows: 1/11 (9%) in the first year of life, 4/11 (36%) in the second and third years, and 2/10 (20%) in the fourth and fifth years. The results from these seven children were compared with those from the children with Down’s syndrome (n=25) who had no, or only mild, evidence of UAO. The median number of clinical signs in the children with UAO was three compared with one. Two of the seven had a parental report of chest wall recession and six had inspiratory stridor, and one subject was reported as having no clinical signs (case 14). The seven children, none of whom had a cardiac defect considered to cause baseline hypoxaemia, had a lower median baseline Sao2 (95.5 vs 97.4%). In addition, six of the seven had values below the lowest observed baseline Sao2 in the healthy controls. Compared with the children with Down’s syndrome without UAO, the seven with UAO had more episodic desaturations in both non-regular breathing (median 24.6 vs 2.4 s/h) and regular breathing (9.0 vs 0.5 s/h).

A second clinical assessment was performed in 18 children with Down’s syndrome, and a third in eight of these children. Three additional children (cases 8, 13, and 15) showed UAO at a follow up assessment, having not shown this on their previous recordings. All showed this after infancy (at ages 25, 24, and 18 months respectively). The number of clinical signs these children reported had increased from the number reported at their first recording (from 1, 1, and 3, to 4, 3, and 4 respectively); all showed inspiratory stridor and chest wall recession.

Seven children, followed later by a further three, were thus identified as having UAO (31% of the original cohort). All 10 were offered further investigation, but only eight sets of parents wished to proceed. Three patients underwent repeated clinical assessment and demonstrated no need for immediate intervention, two patients showed apparently spontaneous resolution, and three (9% of the cohort) underwent adenotonsillectomy at 30, 30, and
50 months of age. Six of the 10 children stayed in the programme and their full histories until their fifth birthdays are known. Two of the 10 children with UAO (cases 11 and 14) had moved from the area and were followed up by telephone at around 5 years of age; on contact both were found to need surgery to alleviate UAO (see histories below).

After the end of the formal part of the study two of the younger children, who were considered not to show UAO during the study period, have subsequently developed symptoms and, without formal clinical assessment, underwent adenotonsillectomy at 3 and 4 years of age respectively. Both children had a resultant diminution in their symptoms of UAO. One further child has also undergone adenotonsillectomy, at age 7 years, because of recurrent respiratory infections.

The cohort is now aged between 5 and 10 years. Overall, nine (28%) have undergone adenoidectomy or adenotonsillectomy: one before, and three during, the study period and a further five by the end of the recent follow up.

The case histories of six of the 10 children with UAO, highlighting certain aspects of management, are given below.

Case 8
This boy’s assessments at 8 and 14 months of age had not demonstrated UAO. At 25 months a third assessment was positive and he underwent nasendoscopy, which showed modest adenoidal and tonsillar enlargement (the larynx and trachea were normal). At 30 months, because of an increasing frequency of respiratory tract infections, adenotonsillectomy was performed. An assessment after surgery showed no evidence of UAO and he became free of clinical signs.

Case 11
This boy showed clinical signs of obstruction, thought to be due to chronic catarrh, and was found to have appreciable UAO at his assessment at age 8 months. At 16 months of age UAO was less noticeable and subsequent assessment during a respiratory infection demonstrated that the UAO did not worsen. He moved home and when recontacted at 56 months of age, he was reported to have a high frequency of respiratory tract infections and a worsening of signs of UAO. A repeated assessment confirmed the presence of severe UAO and nasendoscopy showed adenoidal obstruction of the nasopharynx and oropharyngeal obstruction from palatine tonsils collapsing to the midline. Adenotonsillectomy was performed at age 60 months and was followed by disappearance of both snoring and nocturnal enuresis and a considerable reduction in both sleep disturbance and daytime somnolence. An assessment after surgery showed that UAO had almost completely resolved.

Nasendoscopy showed obstruction at the tongue base, with oropharyngeal shutdown resulting from tongue base and oropharyngeal incompetence. There was no adenotonsillar encroachment and her hypopharynx and larynx were normal. This obstruction would have been difficult to resolve. The treatment options were still under discussion when reassessment at the age of 24 months showed an appreciable lessening of UAO. This confirmed an improvement noted from clinical signs and no action was considered necessary.

Case 13
At 12 months of age this girl showed no evidence of UAO. At 24 months, however, clinical assessment showed severe obstruction that was confirmed by a history of increasing signs during her second year of life. At nasendoscopy it was only possible to examine the airway with the subject on her side because of the severity of the obstruction. The examination showed tonsillar shutdown and obstruction at the tip of the epiglottis, while the larynx and subglottis were normal. Before a routine adenotonsillectomy she suffered a choking and cyanotic episode at home, necessitating resuscitation by an ambulance crew. Surgery was performed urgently at 30 months of age. She was subsequently reported to be more alert, physically stronger, sleeping better, and had a post-operative growth spurt. At age 5 years she presented with sleep disturbance but clinical assessment showed that this was not due to UAO.

Case 14
This boy had severe UAO in the neonatal period but then recovered. An assessment at 15 months showed some UAO but his family reported no clinical signs. By 27 months of age he had developed signs and an assessment at that age showed severe obstruction. He underwent nasendoscopy which showed a significant adenoid pad, with 80% obstruction of the posterior choana, and large palatine tonsils. The epiglottis was posterior, with the aryepiglottic folds being drawn with inspiration into the laryngeal inlet. The vocal cords, subglottic region, and trachea were normal. As he still had few symptoms an expectant policy was adopted. He moved from the area, resulting in no further contact until age 5 years, when he continued to manifest severe symptoms of UAO with snoring, chest wall recession, and frequent wakenings from sleep. An assessment confirmed severe UAO and nasendoscopy showed a modest adenoidal pad obstructing 50% of the nasopharynx. The tonsils were non-obstructive and adenoidectomy alone was, therefore, performed. During the weeks after surgery he had no apparent relief from his signs and his treatment is currently being reviewed.
Assessments at age 2 and 12 months showed no evidence of UAO, but baseline SaO₂ had fallen over time and was thought to be due to his heart disease. At 18 months of age he had signs of UAO, but his recording showed tachypnoea (respiratory rate 51 breaths per minute in regular pattern breathing), making an assessment of inspiratory resistance difficult. A video recording during sleep showed stridor and chest wall recession. He underwent corrective cardiac surgery after which he had fewer clinical signs of UAO. He continued to thrive and develop well with only mild signs of UAO.

Discussion
The prevalence of UAO exacerbated by, or only present during, sleep in young children with Down’s syndrome is high. Overall 10 children (31%) had obstruction identified during the study period: seven on their first recordings and three on repeated recordings. This complication was most prevalent in the second and third years of life. In children without Down’s syndrome, sleep related UAO is related to the emergence of lymphoid hyperplasia, is uncommon in infancy, and most frequent between the ages of 1 and 3 years.14 Our experience with Down’s syndrome reflects this observation and lymphoid hypertrophy did indeed prove to be a major contributing factor. Children clear of UAO in infancy would manifest the problem in early childhood and this sometimes resolved spontaneously at a later stage. Some of this variability in the degree of obstruction could reflect the effect of respiratory tract infections on the size of the lymphoid tissue. It should be noted, however, that adenoidal hyperplasia may occur during infancy and produce UAO (personal observations).

UAO sufficient to disturb sleep can interfere severely with day time performance. When associated with intermittent or even basal hypoxaemia it may cause pulmonary hypertension.4,7 In addition, it may be life threatening, as in case 13. In children with congenital heart disease with left to right shunts it may hasten the development of pulmonary vascular hypertension.9 All professionals involved in the care of children with Down’s syndrome should be alert to the high incidence of this complication.

Initial investigations, using the methodology outlined above, are non-invasive and minimally disruptive. They give a good assessment of the clinical and physiological severity of UAO, and help in deciding the need for further investigation and/or treatment. In particular they provide objective evidence of the effect of the obstruction on oxygenation. Expertise is required, however, to collect and interpret the physiological information. In the absence of these facilities examination of the child when asleep may show obstruction. Ideally the trunk should be exposed so that evidence of chest wall recession and tracheal tug can be identified; a video recording performed by parents on their child when asleep at home may be particularly helpful.

Examination of the upper airway is indicated once there is evidence of UAO on history, video, or physiological recordings. To assess adenoidal size we recommend a radiograph of the postnasal space. In a patient with severe UAO we would consider performing a cine swallow before endoscopy, thus excluding the presence of a vascular ring. Examination of the upper airway also requires a technique that can judge issues specific to Down’s syndrome, such as the possible multiplicity of sites involved and the relationship between mechanical and functional obstruction, including the impact of marginally enlarged lymphoid tissue on a structurally narrowed airway. This is best accomplished by fibreoptic examination of the upper airway under light general anaesthetic with the child breathing spontaneously. Atropine alone is given for premedication as any form of sedation may precipitate acute worsening of the obstruction, or even respiratory arrest, in patients with sleep related UAO. The fibreoptic examination usually demonstrates the site and mechanism for obstruction, and if the presence of tonsils and adenoids is considered to be contributory, these can be removed under the same anaesthetic. A computed tomogram of the choanal area will be performed if there is evidence of narrowing in this area at endoscopy.

Specific problems arise where UAO coexists with congenital heart disease. Given the high rate of heart anomalies in Down’s syndrome,15 there is a particular need to avoid alveolar hypventilation, hypoxaemia, and the resulting pulmonary hypertension that may result from UAO. It can sometimes be difficult, however, to partition the causes for respiratory signs in patients who have both cardiac problems and UAO, as shown in case 15. In this child it was also interesting to notice a decrease in signs of UAO after cardiac surgery. Before surgery, left to right intracardiac shunting, an increased pulmonary vascular resistance, and hypoxaemia have resulted in compensated increases in negative intrathoracic pressures, thereby exacerbating upper airway closure, a situation that was reversed after corrective surgery.

The site of UAO varied. The role of lymphoid tissue hyperplasia in causing, and therefore of adenotonsillectomy in alleviating, UAO is being increasingly recognised in children without Down’s syndrome,16–18 and surgery was effective in a significant proportion of our cases. Although adenotonsillectomy may be effective for a proportion of children with Down’s syndrome,4 19 20 patients should continue to be assessed in case this is not a complete or permanent solution. Alleviation at other sites is difficult and less effective, particularly if there is a disorder of muscle function in the tongue base and/or a disturbance in the size of the pharynx and hypopharynx, as suggested by Guillemainault and Stoohs21 and demonstrated in Down’s syndrome by Brown et al.22 The rate of adenotonsillectomy in this group of children with Down’s syndrome was high with 28% known to have undergone either this procedure or adenoidectomy alone at some
point in their lives (9% during the study period). This compares with a rate in Britain of 0·8% of the total paediatric population for adenotonsillectomy.23 Our children also appeared to need surgery earlier: the national peak period for adenotonsillectomy is 5 to 9 years of age24 but six of our nine subjects underwent procedures well before their fifth birthday.

A small minority of children with Down's syndrome and life threatening UAO may require tracheostomy. In our limited experience this is successful in overcoming pulmonary hypertension but presents severe difficulties for the children's parents, particularly in relation to the high amount of mucosal secretions associated with Down's syndrome.4 Improvements are needed in surgical and non-surgical alternatives (for example, the use of nasopharyngeal tubes or nasal mask continuous positive airway pressure) if such an extreme, but sometimes essential, solution is to be avoided.

Sleep related UAO is a major and, in most cases, treatable cause of additional morbidity in children with Down's syndrome. Diagnosis is relatively straightforward, but there is a need for better treatment for the severe obstruction that may occur at the base of the tongue.

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