The Role of Drug Induced Sleep Endoscopy in Paediatric Obstructive Sleep Disordered Breathing

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Tonsillectomy with or without adenoidectomy is one of the most common surgical procedures performed in children. The commonest indication is obstructive sleep disordered breathing (oSDB)/obstructive sleep apnoea in which children stop breathing at night and have reduced oxygen levels in their blood. Whilst a recent well-designed multicentre trial (Marcus *et al*., 2013) showed that watchful waiting may be a useful strategy, there is still debate as to which children would benefit most from surgical intervention (Venekamp *et al*., 2015) and when adenotonsillectomy is indicated, which technique is best to use e.g. coblation tonsillotomy vs tonsillectomy. Likewise, there is debate as to how to approach treatment failures which have been reported in as many as 1/3 of children who experience ongoing problems with OSA.

Obstructive sleep apnoea

Paediatric obstructive sleep disordered breathing is a common condition of childhood that encompasses a spectrum from simple snoring to obstructive sleep apnoea. Approximately 1-3% of children suffer from the severe forms and there is increasing concern about the long-term neurocognitive and cardiovascular outcomes in such cases. The most common aetiology is thought to be adenotonsillar hypertrophy which results in a narrowing of the upper airways, particularly during sleep. Although these lymphoid organs do regress with age, definitive management in the form of surgery to remove or reduce the size of the tonsils and adenoids is commonly performed to prevent long-term neurological and cardiovascular morbidity and the everyday consequences of poor sleep. However, there is a group of children who are considered treatment failures and still have ongoing symptoms of oSDB despite surgery with meta-analysis suggesting this could be in a significant proportion of patients (Bhattacharjee *et al*., 2010; Brietzke & Gallagher, 2006; M. Friedman, Wilson, Lin, & Chang, 2009).

The causes for treatment failure can be broad but patients can be generally followed up in one of two groups. Firstly, children with an underlying comorbid condition such as trisomy 21, craniofacial syndromes, obesity and hypotonia. The second group is children without a clear comorbidity who still have persisting symptoms. Whilst the management requires some careful consideration in both groups, multilevel obstruction that remains untreated despite adenotonsillectomy is hypothesised to be the leading causative factor.

An ongoing question in paediatric otolaryngology is therefore how to proceed in such cases to evaluate the cause of treatment failure and decide on subsequent management. One option is for more rigorous evaluation of the upper airway to localise the cause of persisting obstruction. Various options exist to diagnose persisting obstruction including awake fibreoptic endoscopy, imaging (e.g. drug-induced sleep cine MRI) and endoscopic evaluation of the airway in the sedated child.

A current working definition is that of (Chan, Liming, Horn, & Parikh, 2014) – 'Drug-induced sleep endoscopy (DISE) consists of flexible fiber-optic assessment of the airway from nares to carina under a state of induced simulated sleep using a combination of anesthetic agents and sedatives. Spontaneous ventilation is maintained.' It is performed as an isolated procedure or prior to immediate surgical intervention. It is known by many names including sleep nasendoscopy (SNE)/ drug induced sleep endoscopy/drug induced sedation endoscopy (DISE) amongst others and was first described in the early 1990s by Croft and Pringle for adults with obstructive sleep apnoea. In adults, the assessment has been shown to correlate well with snoring and sleep (Babar-Craig, Rajani, Bailey, & Kotecha, 2012) and validated (Berry, Roblin, Williams, Watkins, & Whittet, 2005) Although there is still a need to standardise the protocol, assessment and reporting (De Vito *et al*., 2014), it is now the most common diagnostic tool for upper airway endoscopic evaluation of snoring and obstructive sleep apnoea in adults.

The first use of DISE in children was reported in 2000 and since then it has been gaining increasing use both for treatment naïve children and children in whom symptoms persist despite adenotonsillectomy. This article will evaluate the current evidence and rationale for the role of drug-induced sleep endoscopy in the management of paediatric obstructive sleep disordered breathing.

Method

We performed a systematic review of PubMed and Embase using the search terms 'paediatric' OR 'child' AND 'sleep disordered breathing' OR 'obstructive sleep apnoea' OR 'snoring' AND 'endoscopy' OR 'nasendoscopy' OR 'DISE' OR 'drug-induced sedation endoscopy' OR 'drug-induced sleep endoscopy'.

There were no limits on time or language.

We excluded studies solely of adults or solely of central sleep apnoea.

Outcome measures considered were diagnosis, intervention performed and treatment success measured by any outcome described by the authors. Two authors assessed eligibility for studies and extracted the data.

Results

We found 283 potential hits eligible for inclusion. A summary of the 16 main primary studies included are summarised in **Table 1** displayed in the end of the chapter.

Discussion

There is a pressing need to standardise the algorithm for paediatric airway assessment in oSDB. This is highlighted by a recent survey conducted by Friedman *et al* (N. R. Friedman *et al*., 2016) in America of 44 faculty that performed DISE in which there was only 33% overall agreement in using of DISE, although within institutions this was higher. The results are shown below:

Areas of broad agreement:

1. Cine-MRI was not broadly used for preoperative assessment;
2. OAHI, O_2 nadir, and respiratory event type (hypopnea vs. apnea) were all deemed important PSG parameters to assess; and
3. All airway sites, from the nasal cavity to the glottis, were examined during the performance of DISE, whereas the bronchi were typically not assessed.

There was no agreement regarding the following items:

1. Roles of awake flexible laryngoscopy, child's age, tonsil size, or continuous positive airway pressure (CPAP) in the management of OSA prior to DISE;
2. Importance of the following PSG parameters to perform DISE: O_2 and CO_2 distribution, video characteristics, and rapid eye movement (REM) events;
3. Anesthetic regimen, utility of examination of the subglottis and trachea, and use of adjunctive airway support measures in the performance of DISE; and
4. Post-DISE protocols and decision making.

Whilst the number of studies assessing DISE has increased in the past five years, the majority are relatively small retrospective studies with relatively little evidence from prospective studies with a control group. The majority of the studies have also been performed in tertiary paediatric centres and this is reflected in the high proportion of children with comorbidities and craniofacial disorders or syndromes predisposing to oSDB.

There is still ongoing debate over whether DISE should be performed in treatment naïve children [with tonsillar/adenoid hypertrophy evident on examination] or whether it should be reserved for treatment failures or children in whom the clinical examination does not fit with the history of oSDB. This is reflected in the variance in inclusion criteria of children listed for DISE. A recent review by Galluzzi *et al* (Galluzzi, Pignataro, Gaini, & Garavello, 2015) argues DISE should be reserved for children in whom the clinical evaluation is unremarkable or in treatment failures alone as up to two-thirds of patients present with adenotonsillar hypetrophy and thus this should be addressed first (Galuzzi *et al*., 2015). However, Boudewyns and Verhulst (Boudewyns & Verhulst, 2015) argue that the heterogeneity of patients in the Galuzzi review precludes from making such a statement and when studying surgically naïve children without comorbidities (as in their paper included in our review) DISE helps change the management in 24% of patients. However, Galuzzi *et al* counter that as the architecture may change post adenotonsillectomy, DISE in the treatment naïve child pre adenotonsillectomy may not accurately reflect the multilevel obstruction once the limiting region of the adenotonsillar area has been cleared.

The anaesthetic protocol required to ensure appropriate depth for endoscopy without compromising spontaneous ventilation also requires an experienced anaesthetist. There is still no unity with some units relying solely on inhalational anaesthesia whilst others use small amounts of propofol. This topic has been recently reviewed in detail by Chatterjee *et al*., (Chatterjee, Friedman, Shott, & Mahmoud, 2014).

Reporting of the level of obstruction also varies with groups using individualised descriptors as well as standardised definitions such as the VOTE classification (Kezirian, Hohenhorst, & de Vries, 2011).

However, Chan *et al* counter that the VOTE classification is useful in adults as it encompasses the velum, oropharynx, tongue base, and epiglottis. However in children, this does not include the 2 most common levels of obstruction namely the choana by adenoid hypertrophy and the arytenoid collapse into the glottic airway as seen in sleep-induced, late-onset laryngomalacia.

The experience of the clinicians performing the endoscopy is also important and two papers have looked at interobserver reliability. Ramji *et al* (Ramji, Biron, Jeffery, Cote, & El-Hakim, 2014) asked three clinicians to rate sixty-one videos (2 weeks apart) and found intra-observer agreement was 0.64 ± 0.08 (95% CI 0.48-0.81), 0.74 ± 0.07 (95% CI 0.60-0.88), 0.59 ± 0.08 (95% CI 0.43-0.74) for the three people assessed.

Fishman *et al* (Fishman *et al*., 2013) asked two otolaryngologists and two pulmonologists to assess the paediatric airway and found the highest correlation in assessment of the nasopharynx and the supraglottis (Kappa score: 0.6 and 0.5, respectively). In addition sleep endoscopy was better than awake endoscopy in assessing airway obstruction caused by collapse of lateral pharyngeal walls and base of tongue (McNemar test for symmetry, P value<0.05). The utility however was less when assessing older children and those with more severe oSDB.

The management of obstructive sleep apnoea has multiple decision making points from when to refer, which specialty should manage the condition, how to diagnose it effectively and how to monitor improvement. DISE is a potent diagnostic tool as we acknowledge that the treatment of oSDB is more complex than adenotonsillectomy alone. Whilst current research shows it's use in single centres is becoming standardised and helping with decision making, the lack of consensus means that future large scale cohort studies will be required to effectively ascertain it's role in decision making in oSDB. In addition, the relative merits of DISE pre-adenotonsillectomy will also need to be evaluated, taking into account the generally acknowledged success of adenotonsillectomy in a large proportion of patients.

Finally for further reading about airway assessment in general in children with oSDB, we recommend the excellent review by Manickam *et al* (Manickam *et al*., 2016).

Author	Year	n	Methodology	Age (SD or range as stated)	Inclusion criteria	Comorbidities		Pre-op PSG result (AHI with range/SD unless stated)	Diagnostic result	Intervention	Outcome/post op PSG (AHI unless stated)
Chan	**2014**	16	Retrospective	2.2 years (95% CI, 1.8-2.6; range, 0.5-8.9 years)	Unexplained OSAS, persistent OSAS post adenotonsillectomy, suspicion of synchronous lesions from comorbidities or history/exam.	16 had a medical comorbidity that has been previously associated with obstructive sleep apnea; these included chromosomal abnormalities, hypotonia, and encephalopathy		24.8	Group 1: Single site of obstruction (no or 1 site with a maximum obstructive score ≥2.0); Group 2: Two or more sites of obstruction, but only within either the adenoid-velum-LPW complex or the tongue base–supraglottis complex; or Group 3: Two or more sites of obstruction encompassing both the adenoid-velum-LPW and tongue base–supraglottis complexes.	N/A	N/A
Wootten	**2014**	31	Retrospective	5–18 years (mean 9.7 ± 3.4)	Persistent OSAS post adenotonsillectomy	Down's Syndrome - 14; 22q11.2 deletion Syndrome (Opitz G/BBB) - 1		7.0 (±5.8)	Sleep endoscopy typically revealed multilevel collapse, and 3/26 patients underwent only single-level operation (2 underwent LT; 1 underwent MPG). Twenty-three patients underwent multilevel operation.	Lingual tonsillectomy - 22; midline posterior glossectomy -16; revision adenoidectomy -11; inferior turbinate submucOSASl resection -7; uvulopalatoplasty -2; and supraglottoplasty -2	3.6 (±1.8)
Quante	**2014**	25	Retrospective	5.8, range: 1.9 to 15.7 years	Unexplained OSAS, persistent OSAS post adenotonsillectomy	Morbid obesity - 3; severe physical and mental developmental delay -1		N/A	Most frequent obstructions found in the oropharynx region (n = 22)	Adenotonsillectomy - 20; Supralottoplasty - 2; Mandibular splint - 2; Adenoidectomy -1	N/A
Boudewyns	**2014**	37	Prospective	4.1 years (2.1–6.0),	OSAS and no previous history of adenoidectomy and/or tonsillectomy for OSAS.	Nil - i.e. without craniofacial anomalies or syndromes associated with OSASS		8.6 (6.7–20.7)	Adenotonsillar obstruction was found in 33 cases (89%) as an isolated entity or as part of a multi-level obstruction	Adenotonsillectomy - 28;, adenoidectomy -3, tonsillectomy - 2; non-surgical - 4.	1.0 (0.6-2.0)
Durr *et al*	**2012**	13	Retrospective	7.8 (SD 3.3.) (Range 3-15)	Persistent OSAS post adenotonsillectomy	(85%) of subjects had 1 of the following comorbidities: cerebral palsy, trisomy 21 Syndrome, or overweight or obesity		N/A	multilevel obstruction occurred in all subjects except 2 subjects with obstruction located at the tongue base only. The mean (SD) number of obstructive pathologic conditions per subject was 2.8 (1.6). Tongue base obstruction was the most common diagnosis and was present in 11 subjects (85%). This was followed by adenoid regrowth (69%) and inferior turbinate hypertrophy (54%).	All subjects underwent surgical intervention based on DISE findings.	N/A
Ulualp and Szmuk	**2012**	82	Retrospective	1.5 to 17 years (6 ±3.7 years)	PSG diagnosed SDB	Asthma - 10; Seizure disorder - 3; Down's Syndrome - 2; Congenital heart disease - 1; Sickle cell disease - 1; Chronic lung disease - 1; Neurofibromatosis -1.		28 ±27	DISE showed obstruction at the level of velum in 67 patients, oropharynx/lateral walls in 72 patients, tongue in 10 patients, and epiglottis in 10 patients	Adenotonsillectomy	N/A
Chan	**2012**	22	Retrospective	7.4 (2-18)	Laryngomalacia diagnosed on DISE with subseuquent supraglottoplasty	Down's Syndrome - 2; Cerebral palsy - 2; Sanfilippo Syndrome -1; Duchenne muscular dystrophy - 1; Prader-Willi Syndrome -1; lissencephaly -1; microcephaly -1; neurofibromatosis type I -1		15.4 (1.4-48.4)	supraglottic collapse on inspiration The epiglottis was typically normally shaped, yet slightly retroflexed due to shortened aryepiglottic folds. There was invariably a considerable amount of redundant mucOSAS overlying the arytenoids that prolapsed into the glottis	Supraglottoplasty staged with a second operation for OSASS (adenotonsillectomy, lingual tonsillectomy, adenoidectomy, uvulopalatopharyngoplasty, and/or inferior turbinate reduction) - 13. Supraglottoplasty alone - 9	5.4 (0-24.7)

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Chan	**2012**	84	Retrospective	10.2 (2-18)	Unexplained OSAS, persistent OSAS post adenotonsillectomy, OSAS with medical comorbidities	Neuromuscular dysfunction - 23; 13 were syndromic, including 5 with Down Syndrome; 6 had primary respiratory disease; chromosomal abnormalities (trisomy 21, trisomy 15q), Beckwith-Wiedemann Syndrome, Noonan Syndrome, Opitz Syndrome, fetal hydantoin Syndrome, Prader-Willi Syndrome, Sanfilippo type II, lissencephaly, dermatomyositis with respiratory muscle weakness, Duchenne muscular dystrophy, and severe asthma.		12.8 (1.1)	Lingual tonsil/supraglottic collapse on inspiration	Lingual tonsillectomy or carbon-dioxide laser supraglottoplasty	4.8 (0.7)
Digoy	**2012**	43	Retrospective	4.13 (1.1-14.8)	Unexplained OSAS, persistent OSAS post adenotonsillectomy. Younger children (age <24 months) with laryngomalacia history.	Down's Syndrome - 6; DiGeorge - 6; CHARGE - 1; Two children were suspected of having a syndrome but had not been officially diagnosed. Cerebral palsy - 5.		13.3 (12.9)	Laryngomalacia	Supraglottoplasty	4.1 (5.0)
Fung	**2012**	23	Retrospective case-control	Retrospective case-control	Down's children presenting with persistent snoring or SDB	Down's Syndrome		N/A	S group exhibited significantly more pharyngeal collapses than the controls (O:C:M, 2:6:15 and 12:0:10, respectively; $p < .005$). Lingual collapses were also noted more in DS children (11 vs 4), and a more significant number of collapses were seen ($p < .004$). Whereas nearly equal numbers exhibited tonsillar obstruction, adenoidal obstruction was significantly less in DS children ($p < .05$).	N/A	N/A
Truong	**2012**	80	Retrospective	6 (SD 3.75)	Unexplained OSAS, persistent OSAS post adenotonsillectomy, OSAS with medical comorbidities	21 patients had co-morbidities		Group 1 - 13.8 ± 15.9; Group 2 15.7 ± 13.3	Group 1who were surgically naïve. In this group we observed the obstructive effects of moderately sized adenoids and endophytic tonsils (Sites A and B), and found that these children did well with T&A. Conversely, children with small adenoids with an open velopharynx and tonsils which caused no central oropharyngeal crowding did not benefit much from T&A.	Group 1 - Adenotonsillectomy + pillar closure and radio frequency inferior turbinate cautery. Supraglottoplasty -2. Inferior turbinoplasty - 1. Subglottic cyst excision - 1. Group 2 - endoscopic lingual tonsillectomy - 28; Supraglottoplasty - 4; combined lingual tonsillectomy and supraglottoplast -4; Revision adenotonsillectomy - 5.	Group 1: 8.0 ± 8.0; Group 2 7.9 ± 9.9
Lin	**2009**	26	Retrospective		Persistent OSAS post adenotonsillectomy	14 of the patients (54%) had various disorders such as Down Syndrome, Asperger Syndrome, Beckwith-Wiedemann Syndrome, and velocardiofacial Syndrome. Two patients had isolated craniofacial anomalies		RDI 14.7	Lingual tonsillar hypertrophy	Endoscopic-assisted coblation lingual tonsillectomy	RDI 8.1

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Myatt	**1999**	20	Prospective	4.6 (1 week to 13 years)	1 Children with severe OSAS (A/H index > 30/h) on polysomnography. 2 Children who have undergone previous adenotonsillectomy with severe residual OSAS (A/H index > 30/h) on polysomnography. 3 Children with OAA on continuous CPAP for airway support. 4 Children with OAA requiring but unable to tolerate CPAP.	Cerebral palsy -4; PEHO Syndrome (progressive encephalopathy, hypotonia, EEG changes and oedema) - 1; Trisomy 13 - 1; Pierre Robin Sequence - 2; Down's Syndrome - 3; Morbid obesity - 2; velo-cardio-facial Syndrome - 1; previous cleft palate repair and pharyngoplasty - 1; normal children with severe OSAS - 5		48 (15.5)	1Level 1 - velopharyngeal obstruction -4 2Level 2 - tonsillar obstruction - 4 3Level 3 - tongue base obstruction -6 4Level 4 - supraglottic obstruction -2 Level 2 and 4 - 3; Level 3 and 4 -1.	Guided by DISE - UVPP - 3; Adenotonsillectomy - 6 (1 with division of glottic web); CPAP - 2, Nasopharyngeal tube - 2; CO2 supraglottaplasty 5 (1 with tonsillectomy, 1 with adenotonsillectomy, 1 with mandibular splint); Mandibular splint - 2	4.6 (4.5)
Contencin	**1991**	17	Prospective	N/A	N/A	Craniofacial malformation - 4		N/A	Adenotonsillar (9); Laryngeal (4); Tongue base (3); Oropharynx circular (1)	N/A	N/A
Hagen	**1991**	1	Case report	2	OSAS	N/A		N/A	oropharyngeal wall collapsed at the level of the velopharyngeal sphincter	Nasotracheal tube	Resolved at 1 year
Croft	**1990**	15	Prospective	3.15 years (9 months to 10 years)	OSAS	Down's Syndrome -6; Pierre Robin -1		N/A	Tongue base (3); Adenotonsillar (10); Pharynx (1); Laryngomalacia (1)	Guided by DISE -Tonsillectomy (10); Tongue reduction (1); Tracheostomy (2); CPAP (1); Expectant 1	All had resolution of symptoms and were well

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