Diagnosis and Treatment of Sleep Apnea in Children

Subjects: Pediatrics | Respiratory System

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Obstructive sleep apnea (OSA) in children is a prevalent, but still, today, underdiagnosed illness, which consists of repetitive episodes of upper airway obstruction during sleep with important repercussions for sleep quality. OSA has relevant consequences in the pediatric population, mainly in the metabolic, cardiovascular (CV), and neurological spheres. However, contrary to adults, advances in diagnostic and therapeutic management have been scarce in the last few years despite the increasing scientific evidence of the deleterious consequences of pediatric OSA. The problem of underdiagnosis and the lack of response to treatment in some groups make an update to the management of OSA in children necessary. Probably, the heterogeneity of OSA is not well represented by the classical clinical presentation and severity parameters (apnea/hypopnea index (AHI)), and new strategies are required. A specific and consensus definition should be established. Additionally, the role of simplified methods in the diagnosis algorithm should be considered. Finally, the search for new biomarkers for risk stratification is needed in this population. In conclusion, new paradigms based on personalized medicine should be implemented in this population.

sleep apnea | cardiovascular | hypoxic burden | children

1. Definition and Prevalence of Obstructive Sleep Apnea in Children

Sleep-disordered breathing (SDB) occurs as a result of upper airway (UA) dysfunction (snoring and/or increased respiratory effort). It ranges from snoring to obstructive sleep apnea (OSA), depending on the degree of intermittent UA obstruction [1], and around 20% of children who snore have OSA [2].

OSA is characterized by recurrent events of partial (hypopnea) or complete (apnea) obstructions in the UA, which disrupt normal oxygenation, ventilation, and sleep patterns [1][3][4][5]. OSA in children has a clear entity with profiles that are very different from adults in terms of etiology, clinical presentation, and consequences (**Figure 1**). For this reason, a specific definition, diagnosis, and treatment approach is needed for this specific population.

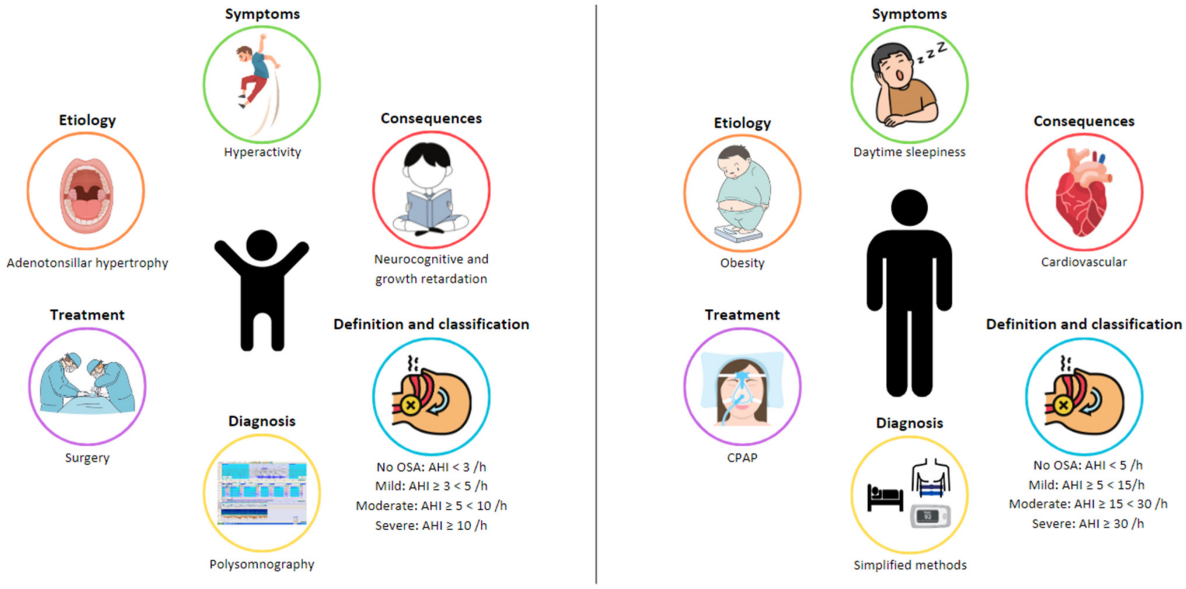

Figure 1. Differences in obstructive sleep apnea (OSA) between adults and children.

OSA is a very frequent condition in children, with prevalence varying between 1 and 4% [6]. Although there has been an effort to increase knowledge about this entity in childhood, there is less scientific evidence than in adults. Different guidelines establish the definition of SDB and OSA in children, although the criteria are diverse and lack recent updates. The classification of OSA severity in children, through the apnea/hypopnea index-(AHI) (number of respiratory events per hour of sleep) obtained from sleep studies, is the most-commonly used parameter. Generally, an AHI of 1–3/h is accepted as the normal cutoff line for the diagnosis of OSA and is classified as follows: mild OSA if the AHI < 5/h, moderate OSA when the AHI is between 5 and 10/h, and severe OSA when the AHI > 10/h [1][3][5][7]. However, these criteria can vary depending on the guidelines, considering factors such as age, additional comorbidities, and other polysomnographic variables (presence and length of oxygen desaturations, degree of hypoventilation, sleep fragmentation, and decreased total sleep time) [7][8].

2. Etiology of OSA in Children

The etiology of childhood OSA is multifactorial, involving many risk factors, which can increase UA narrowing and collapsibility and which may contribute to the pathogenesis of OSA [8][9][10]. This includes both anatomical and neuromuscular disturbances, leading to increased airway resistance and preventing the normal function of the dilator muscles, respectively [5] (**Figure 2**).

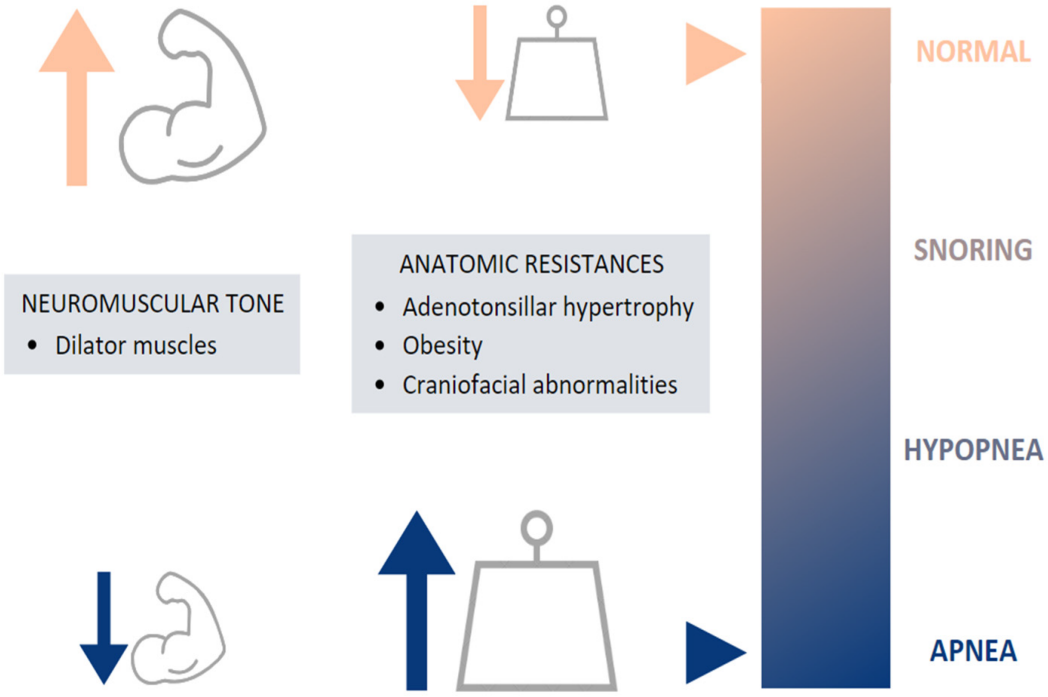

Figure 2. Etiology of pediatric OSA.

The most-common risk factor is adenotonsillar hypertrophy, reaching the peak of development between 2 and 8 years [11], coinciding with the onset of OSA [12]. Nevertheless, some studies have shown a weak or no correlation between the size of the tonsils and adenoids and the severity of pediatric OSA [13][14]. Craniofacial abnormalities can also be a cause of UA narrowing: alterations of the size, position, and geometry of the mandible and the tongue [10]. These anatomical features are often found in children with craniofacial syndromes, achondroplasia, trisomy 21, Beckwith–Wiedemann syndrome, Chiari malformation, and mucopolysaccharidoses [8].

Besides anatomic factors, obesity has also been suggested as a contributor to OSA. Obese children represent a special risk factor, as the prevalence of childhood obesity is progressively increasing (5.6% in girls and 7.8% in boys) [15], also leading to an increase in the prevalence of obesity-associated morbidities including OSA [10][11][16]. This relationship is bidirectional, as OSA is known to worsen weight loss and overweight [17][18].

3. Symptoms of OSA in Children

The symptoms are classically divided into nocturnal and diurnal (**Table 1**). Nocturnal symptoms include snoring, witnessed apneas, gasping, oral breathing, paradoxical thoracic movements, nightmares, restless sleep, and nocturnal enuresis. Snoring is the most-common symptom, along with oral breathing. This population can also present disturbed sleep with frequent changes of position, unusual sleep positions (neck hyperextension), and nightmares [9][19]. Enuresis is another frequent symptom in OSA children related to an altered arousal response and sleep fragmentation, often being resolved when OSA is adequately treated [20].

Table 1. Symptoms of OSA in children.

Nocturnal Symptoms	Daytime Symptoms
Snoring	Behavioral disorders
Witnessed apneas	Neurocognitive disorders
Gasping	Mood instability
Oral breathing	Excessive daytime sleepiness
Paradoxical thoracic movements	
Nightmares	
Restless sleep	
Nocturnal enuresis	

Related to daytime symptoms, a relationship between OSA and behavioral disorders (irritability, aggressiveness, and depression), neurocognitive disorders (difficulty concentrating/learning difficulties and inattention), mood instability, and excessive daytime sleepiness has been demonstrated [5][10][21][22][23].

4. Consequences

OSA in children is associated with a number of adverse morbidities, presented as behavioral and neurocognitive disorders, growth retardation, cardiovascular (CV) diseases, and metabolic consequences, producing a negative impact on quality of life. These consequences are derived from the presence of continuous episodes of hypoxia/resaturation, sleep fragmentation, and/or changes in the intrathoracic pressure. These immediate consequences develop a cascade of intermediate mechanisms, mainly alterations in sympathetic activity, coagulation, inflammation, and oxidative stress (**Figure 3**).

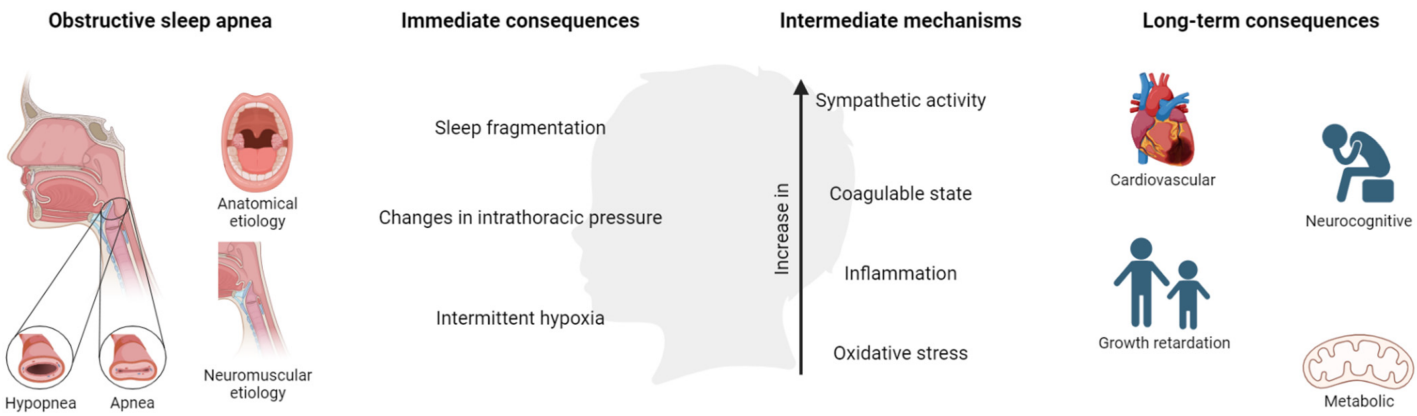

Figure 3. Mechanisms and consequences of OSA in children. Created with BioRender.com. This population is characterized by poor academic performance showing a reduction in memory capacities and difficulties in learning

and attention (especially in specific areas such as mathematics, science, reading, and spelling) [24][25][26], which could be associated with hyperactive behavior during the day.

The effects on growth are probably related to factors such as increased energy consumption and reduced production of growth hormone, whose secretion is characterized by wide and frequent peaks during sleep [9]. These adverse results may be recovered after OSA treatment, as suggested by different studies [27][28][29].

In the CV sphere, alterations in the autonomic nervous system, vasomotor tone, systemic inflammation, and atherogenesis associated with OSA are likely to induce functional disruption of the endothelium [30]. In addition, many biomarkers have been evaluated to identify this vascular damage, the C-reactive protein (CRP) being the most-studied marker. This inflammatory indicator is increased in children with OSA, with a recent study indicating that it could be reversed after treatment [31]. It has been reported that children with OSA have increased systolic and diastolic blood pressure (BP), increased BP variability, and decreased BP dipping during sleep. Observing the BP of children with OSA is essential to identifying those at risk for developing clinically significant elevated BP in adulthood [32]. There is an independent effect of OSA on cardiopulmonary function, which improves after the disorder is adequately treated [33][34][35]. Finally, these children may develop an early metabolic syndrome [10][36], this risk being six-times higher than in healthy subjects in adolescents with OSA [37]. A brief literature search of recent evidence in these spheres is described in **Table 2**.

Table 2. Consequences of OSA in children.

Author (Year)	Number of Participants	Age (Years)	OSA Severity Criteria	Outcomes	Results
Behavioral and neurocognitive sphere					
Menzies et al., 2022 [38] Metanalysis of 63 studies	17,834	From 2 to 18 years	Due to the lack of a consensus severity criterion, the subgroup given by the author was used (e.g., mild OSA)	Intelligence, attention, memory, visual spatial skills, and language	Children with SDB had significant impairments in all cognitive domains, intelligence being the most-affected quality. These neurocognitive deficits were found in primary snorers among OSA children.
Growth retardation and metabolism					
Lagravère et al., 2019 [39] Systematic review of 12 studies				Growth mediators (IGF-I and IGFBP-3)	Children with OSA present lower levels of growth mediators, indicating growth retardation, significantly higher cardiovascular disease risk, and decreased cognitive functions compared to healthy controls. Tonsillectomy may improve

Author (Year)	Number of Participants	Age (Years)	OSA Severity Criteria	Outcomes	Results
					all these functions with a great impact on general health.
			Cardiovascular sphere		
Ai et al., 2022 [40] Metanalysis of 14 studies	3081	3 to 17 years	Mild OSA is defined as an AHI between 1 and 5 events per hour Moderate to severe is defined as an AHI ≥ 5 /h.	BP parameters: awake and nighttime SBP and DBP	The mean SBP was higher in children with mild or moderate-to-severe OSA compared to healthy controls, these effects being more pronounced during the night. The results suggest that moderate-to-severe OSA in children is associated with a higher risk of adverse SBP outcomes.

gans and systems is necessary [41]. Therefore, in order to minimize the deleterious consequences related to OSA, early correct diagnosis and treatment management are mandatory. The strongest evidence shows that this population may have a significant impact on CV health in childhood and later in adulthood [42]. Tools to identify children at risk and treatment prevention indication are needed.

Abbreviations: OSA: obstructive sleep apnea; SDB: sleep disordered breathing [30]; IGF-1: insulin-like growth factor 1; IGFBP3: insulin-like growth factor binding protein 3; AHI: apnea/hypopnea index; BP: blood pressure; SBP: systolic blood pressure; DBP: diastolic blood pressure.

5. Diagnosis

The diagnosis of OSA in the pediatric population differs according to the different clinical guidelines and is described according to the Spanish [5], European [1], and American [3] guidelines in **Table 3**.

Table 3. Diagnosis and management of OSA in children.

Guide	Diagnosis and Management of OSA in Children
Spanish Society of Pneumology and Thoracic Surgery (SEPAR)	This guide divides the OSA diagnostic methodology between primary care and hospital care in order to increase the diagnostic efficiency. In primary care, the evaluation of the child with suspected OSA (presence of snoring and symptoms or suggestive clinical findings) should include the medical history and complete clinical examination. • Medical history: family history, events related to the child's sleep and breathing, and sleep questionnaire (Chervin). • Complete clinical examination: craniofacial and UA anatomy, cardiopulmonary examination and somatometry. Children with obesity represent a special risk group. Depending on the results, referral of the patient from primary care to the reference sleep unit is considered.

Guide	Diagnosis and Management of OSA in Children
	• If there is suspected OSA in the clinical history and or/Chervin, retrognathia, adenotonsillar hypertrophy and Mallampati ≥ 2, hospital RP is performed. Otherwise, a control visit is carried out 6 months after baseline visit. • When the index of respiratory events is ≥ 5 in the RP, children are referred to adenotonsillar surgery. With an inferior result, a PSG is performed. • An AHI ≥ 5/h on PSG leads to adenotonsillar surgery. If the AHI is < 3/h, an anti-inflammatory therapy or review visit after 6 months is assessed. For an AHI 3–5/h comorbidities are evaluated. The presence of comorbidity leads to adenotonsillectomy and anti-inflammatory therapy is selected when there is absence of comorbidity. • All children should be clinically reassessed after surgery (recommended in the next 6 months), performing a sleep study in children with severe preoperative OSA or when risk factors or OSA symptoms persist, where other treatments such as diet, CPAP, or orthodontics will be assessed.
European Respiratory Society	The diagnosis and management for SDB is described as a stepwise approach in 7 steps. • Identification of risk of SDB: symptoms of UA obstruction, alterations in physical exam, objective findings related to SDB and/or prematurity or family history of SDB. • Identification of comorbidities in CV system, CNS, nocturnal enuresis, growth delay or decreased QoL and conditions coexisting with SDB such as recurrent otitis media and history of tympanostomy tube placement, wheezing or asthma, metabolic syndrome or oral-motor dysfunction. • Recognition of factors predicting long-term persistence of SDB: obesity, male sex, obstructive AHI > 5/h, African-American ethnicity and persistent tonsillar hypertrophy and narrow mandible. • Objective diagnosis and assessment of SDB severity: PSG or RP is indicated in children at risk of SDB. (1) OSA definition 1: obstructive AHI ≥ 2/h or obstructive apnea index ≥ 1/h with SDB symptoms; (2) OSA definition 2: SDB symptoms and AHI ≥ 1/h. No alternative methods can substitute PSG but could be used in low resource settings: ambulatory PSG or RP, nocturnal oximetry, Pediatric Sleep Questionnaire or Sleep Clinical Record. • Indications for treatment of SDB: indicated when AHI > 5/h. When PSG or RP are not available, treatment is considered when positive oximetry or SDB questionnaires or

Guide	Diagnosis and Management of OSA in Children
	morbidity is present. It is unclear whether should treat primary snoring (evaluation annually). • Stepwise treatment approach for SDB is usually implemented until complete resolution of SDB: (1) weight loss in overweight and obese children; (2) nasal corticosteroids and/or montelukast in non-obese and < 6 years children; (3) adenotonsillectomy in children with OSA and adenotonsillar hypertrophy; (4) rapid maxillary expansion or orthodontic appliances in children with OSA and maxillary constriction, retrognathia or malocclusion; (5) CPAP or NPPV when residual OSA after adenotonsillectomy or hypoventilation; (6) craniofacial surgery when syndromic craniofacial abnormalities; (7) tracheostomy in severe OSA when other nonsurgical or surgical interventions have failed or are contraindicated. • Recognition and management of persistent SDB: outcomes monitored after intervention are: symptoms, PSG (or RP, oximetry/capnography when not available), QoL, CV or CNS morbidity, enuresis and growth rate. PSG or RP should be performed, between 6–12 weeks after treatment, in children at risk of persistent OSA, after adenotonsillectomy, in children with persistent symptoms or children with mild OSA treated with corticosteroids and/or montelukast. PSG should be performed 12 months after rapid maxillary expansion and after 6 months when oral appliance treatment is selected. At least, one PSG or RP annually should be used to titrate CPAP or NPPV.
American Academy of Pediatrics	This practice guideline focuses on uncomplicated childhood OSA, associated with adenotonsillar hypertrophy and/or obesity in an otherwise child who is being treated in the primary care setting. It comprises 8 key action statements. • Screening for OSA. If the child presents signs or symptoms of OSA, clinicians should perform medical history and physical examination. • Snoring and findings in the evaluation should lead to PSG (gold standard test) or alternative tests when PSG is not available (nocturnal video recording, nocturnal oximetry, daytime nap PSG or ambulatory PSG). • Adenotonsillectomy is recommended when the child is determined to have OSA and adenotonsillar hypertrophy (and do not have contraindication to surgery). If the child has OSA but not adenotonsillar hypertrophy other treatment should be considered. • Monitoring of high-risk patients undergoing adenotonsillectomy. • Reevaluation. Clinical reassessment should be performed in all patients with OSA for persisting symptoms after therapy to determine whether further treatment is required (6

Guide	Diagnosis and Management of OSA in Children
	to 8 weeks after treatment). • Clinicians should refer patients for CPAP management if symptoms persist after adenotonsillectomy or if it is not performed. • Weight loss is recommended in addition to other therapy if the child with OSA is overweight or obese. • Intranasal corticosteroids may be prescribed for children with mild OSA in whom surgery is contraindicated or have mild postoperative OSA (<5/h).

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alternative methods for the diagnosis of OSA in children [42]. As an example, the European guideline accepts hospital RP as a valid alternative for the diagnosis of OSA in children and is considered an adequate screening technique when PSG is not available (**Table 3**).

Abbreviations: OSA: obstructive sleep apnea; UA: upper airway; RP: respiratory polygraphy; PSG: polysomnography; AHI: apnea/hypopnea index; CPAP: continuous positive airway pressure; SDB: sleep-disordered breathing; CV: cardiovascular; CNS: central nervous system; QoL: quality of life; NPPV: non-invasive positive pressure ventilation.

6. Treatment

The goal of OSA treatment is complete resolution of SDB. This may require combining strategies (**Figure 4**), although the first-line treatment for OSA in children is adenotonsillar surgery [5] when adenotonsillar hypertrophy is present. Nonetheless, in the recent past, this treatment has been questioned. Recent publications have shown that the use of adenotonsillectomy in pediatric OSA patients may have variable results, reaching an AHI of 1 or less in about 50–70% of cases, but its efficacy decreases with risk factors such as age (<7 years), severe disease, chronic asthma or obesity. Persistent disease is present in 20–75% of children, with more than half having habitual snoring [7][43][44]. In addition, other surgical procedures may be performed in selected cases, such as septoplasty, uvulopharyngopalatoplasty, epiglottoplasty, glossopexy, and maxillomandibular surgery.

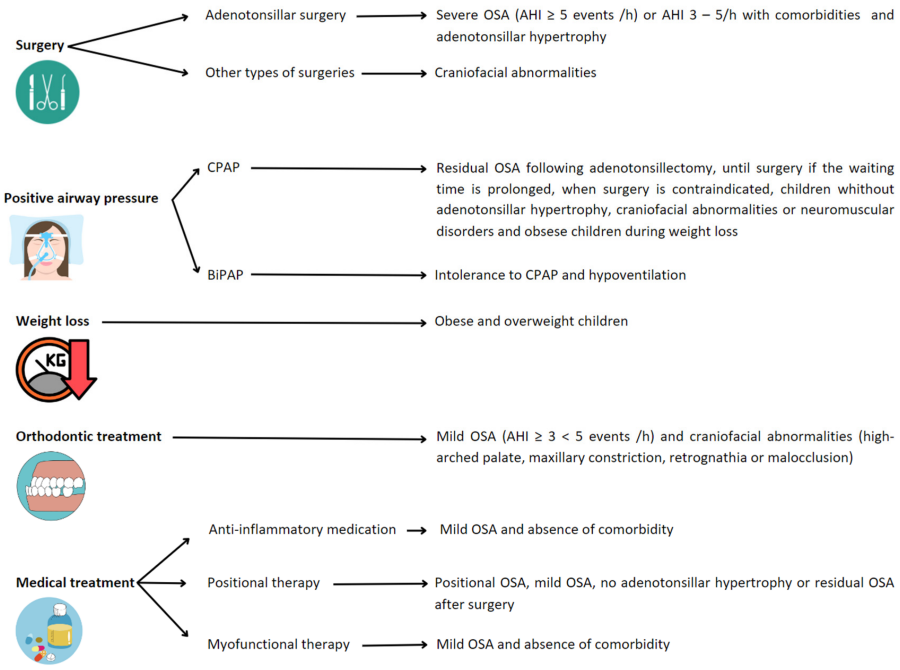

Figure 4. Recommended treatments depending on conditions leading to OSA in children. Abbreviations: OSA: obstructive sleep apnea; AHI: apnea/hypopnea index; CPAP: continuous positive airway pressure; BiPAP: bi-level positive airway pressure.

For those children with residual OSA following adenotonsillectomy or those in whom surgery is contraindicated or without adenotonsillar hypertrophy, positive airway pressure (PAP) therapies can be an effective treatment. The two types of PAP therapies prescribed in children to treat OSA are continuous positive airway pressure (CPAP) and bi-level positive airway pressure (Bi-PAP) [45]. CPAP is the most-commonly used PAP therapy, also recommended in children with craniofacial abnormalities or neuromuscular disorders [1][3][5]. The use of BiPAP is for patients intolerant to CPAP to treat nocturnal hypoventilation [46].

Positional therapy, as an alternative treatment, has been widely studied and relatively implemented in adults for the management of positional OSA. Positional OSA is defined when, spending more than 20% of sleep time in the supine position, the AHI in the supine position is at least double that in the non-supine position. This definition has not been adapted to the pediatric population and is, therefore, assumed in the child. In adults, positional therapy is incorporated in cases of mild–moderate OSA of positional origin and in those with severe OSA in order to lower CPAP pressure or when there is intolerance to first-line treatment. However, the indications in the pediatric population are not clearly established, and the scientific evidence is scarce. In this sense, it seems that children without tonsillar hypertrophy or with residual OSA could benefit from it, mainly in cases of obesity [47][48]. Therefore, randomized studies are necessary to establish the efficacy and indications of this type of therapy in the pediatric patient.

Weight management, orthodontic treatment, or medical therapy are offered as an alternative to surgery, especially in children with mild OSA [7][8][49] or when surgery is not indicated or contraindicated. There are data supporting that weight loss, if the child is overweight or obese, can improve OSA (hence, proposed to be considered first-line treatment in this population) [50]. Rapid maxillary expansion or orthodontic appliances are used to widen the palate and cause flattening of the palatal arch. On the other hand, medical therapies such as anti-inflammatory medications (nasal corticosteroid and/or oral montelukast) can also be used. There is little evidence about anti-inflammatory therapies in children. The results of randomized clinical trials evaluating the efficacy of intranasal corticosteroids for the treatment of OSA are not conclusive. Montelukast has short-term beneficial treatment effects for OSA in healthy, non-obese, surgically untreated children in terms of reducing the AHI, but the clinical relevance remains unclear [51][52]. Finally, myofunctional therapy has been accepted as a non-invasive treatment for OSA in children, as it may improve the AHI and oxygen saturation, at least after tonsillectomy or as an adjunct OSA treatment [53][54].

It is worth mentioning that obstructive SDB can be resolved spontaneously, particularly in children with mild OSA and adenotonsillar hypertrophy. Improvements may be due to the regression of lymphoid tissue or growth of the airway [55].

In summary, current data on the management of pediatric patients with OSA around the world, presented in this research, manifest important discrepancies and the need to be updated and homogenized. An agreed upon definition is needed with specific cutoff points to establish the diagnosis and levels of severity based on the associated risk and comorbidities. Clear diagnostic management algorithms must be settled upon in which it is defined when the simplified methods are useful in pediatric patients, in order to avoid underdiagnosis. It is necessary to identify prognostic markers that set up cutoff points for treatment indications based on objective impact. In addition, new metrics that better evaluate the disease could lead to the establishment of new protocols that improve the treatment management of the child.

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