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Role of sleep study in children with Chiari malformation and sleep disordered breathing

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Abstract

Purpose Chiari malformation incorporate numerous forms of congenital or acquired cerebellar herniation through the foramen magnum. This may lead to brain stem, high spinal cord and cranial nerve compression resulting in obstructive and central apneas. This review highlights he high prevalence of sleep-disordered breathing in this population and the importance of refering these patients for sleep studies as part of their workup.

Methods A review of the literature was performed through a PubMed and EMBASE search of original articles and reviews using the key words "chiari" "chiari malformation" "hindbrain herniation" "sleep disordered breathing" "obstructive sleep apnea" "central sleep apnea" "sleep study" and "foramen magnum decompression".

Discussion We highlight the pathophysiology of sleep disordered breathing in patients with Chiari malformation, how it can be diagnosed and what the treatment options are.

Conclusions Sleep-disordered breathing is highly prevalent in patients with CM1. Clinicians caring for these patients should be aware of this and prioritise sleep diagnostic testing to allow for early diagnosis and management particularly in the presence of neurological symptoms and specific brain MRI pointers.

Keywords Chiari malformation · Hindbrain herniation · Foramen magnum decompression · Sleep disordered breathing (obstructive/central sleep apnea) · Sleep studies

Defining Chiari malformations

There is no agreed definition for Chiari malformations, and different descriptions have been proposed. Principally, Chiari malformations entail different clinical entities with variable amount of hindbrain abnormalities. This can range from mild tonsillar ectopia to complete hindbrain hernia through the foramen magnum and in some instances agenesis of the cerebellum. The condition was recognised by the pathologist Hans Chiari, who studied cerebellar changes caused by hydrocephalus of the cerebrum [39].

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Types

Different types of Chiari malformations have been suggested in literature. They are labelled as Chiari 0 to Chiari 5. A main shortcoming of this classification is the inference that these are part of a spectrum of same pathology, whereas in fact, they are distinct pathologies. They can be broadly divided into either acquired or congenital in nature. Acquired types include 0, 1, and 1.5, depending upon amount of tonsillar hernia from no ectopia in type 0 to tonsillar descent along with brainstem in type 1.5. Chiari types 2, 3, 4, and 5 are congenital. They are associated with open neural tube defects and occipital or upper cervical encephalocele.

Pathophysiology

Acquired Chiari malformations can be idiopathic/primary with no obvious cause or secondary. Secondary causes include craniocerebral disproportion (in craniosynostosis, craniometaphyseal dysplasia, and vitamin D deficiency)

[13], raised intracranial pressure (in hydrocephalus, idiopathic intracranial hypertension), and craniovertebral malformations (basilar invagination, assimilation of atlas) [40].

McLone proposed "unified theory" to explain congenital Chiari seen in children with spina bifida. It describes occurrence of neural tube defect first causing leakage of spinal fluid, leading to "pan cranial malformation" including Chiari 2, hydrocephalus, tectal beaking, and medullary kinking.

Symptoms

Chiari can present with classical symptoms of occipital and suboccipital headaches. Additionally due to local bulbar compression, children can develop swallowing difficulty, nystagmus, and sleep apnoea. Obstruction of CSF flow at foramen magnum can lead to formation of the syrinx. This can manifest as sensory disturbance, back pain, and scoliotic deformity of the spine.

Sleep disordered breathing in Chiari malformations

Sleep disordered breathing (SDB) may happen in a form of central or obstructive breathing events with or without hypoventilation. Central breathing disorder most likely results from direct medullary compression. This is more common in neonates with congenital Chiari where medullar kink and hindbrain hernia can lead to stridor. Furthermore, impaired vocal cord function and weak pharyngeal muscles as a result of lower cranial nerve impairment lead to obstructive pattern.

The prevalence of SDB in patients with confirmed Chiari type 1 malformation (CM1) reported in the literature is consistently high at 24 to 70% (> 5- to 10-fold higher than the general paediatric population) [33, 36, 48]. This higher prevalence has been confirmed in adult studies [7, 8, 20], mixed adult and paediatric studies [12, 22], and paediatric studies [4, 12, 16, 17, 22, 25, 30]. The lowest prevalence of 24% in the findings of Losurdo et al. may have been a result of their more exclusive study population and the prospective aspect of their study with recruited paediatric patients diagnosed with CM1 on MRI who then had polysomnography, as opposed to examining a population that had polysomnograms done first. Losurdo et al. may have captured some of these patients with CM1 prior to the onset of SDB.

As a result of this high prevalence of SDB, it has been suggested that all children with a diagnosis of CM1 should be offered screening for sleep disordered breathing with a detailed polysomnography/respiratory polygraphy [16, 22, 25, 30]. However, there is no definitive guidelines on when patient with CM1 should undergo polysomnography [6], and there is a potential resource implication in screening all patients in countries where access to sleep diagnostics is limited [4]. Several studies have attempted identifying clinical symptoms and/or radiological findings to determine which patients are at high risk of sleep disordered breathing and would benefit from a more urgent assessment [4, 10, 16, 17, 25].

Clinical sleep history with reported symptoms of sleep disordered breathing and clinical examination are not sensitive or specific enough to establish a diagnosis of sleep apnoea in patients with CM1 [4, 33]. However, the presence of neurological symptoms in patients with CM1 correlated with the presence of SDB in a prospective study by Losurdo et al. [30]. On the other hand, patients may present with SDB before developing any abnormalities on neurological examination, making SDB the only sign of a CM1 for those patients [37, 55].

Contrary to conventional wisdom, obstructive sleep apnoea (OSA) is the more frequent SDB than central sleep apnoea (CSA) even though both are present in cohorts of paediatric patients with CM1 including concomitantly (mixed SDB) [22, 25]. SDB was shown to be predominantly obstructive in several prospective and retrospective studies [4, 12, 25, 30]. Some have suggested that the emergence or worsening of OSA may be a sign of increased intracranial pressure [6, 31]. Conversely, it has been speculated that OSA can cause progression of CM1 through transient rise in intracranial pressure with potential worsening of cerebellar tonsil herniation and development of a syrinx [28, 38]. CSA remains highly prevalent in patients with CM1 with paediatric studies reporting a prevalence between 9 and 18% [4, 17, 25, 30].

Pathophysiology of sleep disordered breathing

OSA is believed to occur as a result of compression of cranial nerves IX and X or their corresponding pontomedullary nuclei resulting in weakness of the pharyngeal and dilating laryngeal muscles [7, 30, 31, 49]. As a result, there may be variability in the neural output to the upper airway dilators, dyssynchrony between neural output to upper airway and ventilatory pump muscles, and impairment of upper airway reflexes and/or vocal cord paralysis [15, 18].

CSA, on the other hand, has the following multiple purported pathophysiological mechanisms:

- Compression or stretching of the glossopharyngeal nerve impairing afferent input from the carotid bodies to the medulla, thereby adversely affecting the chemoreflex [6, 8, 30, 49]
- Dysfunction of the respiratory centre when the medulla oblongata itself is compressed [8, 20, 25, 30, 39, 49] or when compression of the vasculature results in ischemia of the respiratory centre [20, 25, 37]
- Compression of the brainstem resulting in dysfunction of the reticular activating system [8, 20, 30, 37, 49]

- Compression of phrenic motor neurons in the anterior horn of the cervical spinal cord because of a syrinx or compromised vascular supply to the brainstem [39]
- Mechanical stimulation of chemoreceptors leading to overactivity [9, 10]
- Damaged chemoreceptors with decrease responsiveness to CO_2, resulting in central apnoea [12, 20, 31, 37]

It is unclear which CM1 children will develop obstructive, central, or mixed sleep disordered breathing. It has been postulated that it may relate to the site of compression with central apnoea developing because of compression of the pre-Bötzinger complex, whereas obstructive apnoea may develop because of compression of the caudal brainstem [25]. However, as central apnoeas have been reported to be more frequent with a syrinx, other mechanisms are also likely to be involved [35].

It is important to remember that some patients will have CM1 as part of a syndrome (craniosynostosis, velocardiofacial, thoracic dystrophies) or have comorbidities making them more susceptible to develop SDB.

CM1 is common in syndromic craniosynostosis as consequence of the premature fusion of the lambdoid and cranial base sutures resulting in disproportion between hindbrain growth and small posterior fossa. It has been described in 70% of patients with Crouzon's syndrome, 75% with oxycephaly, 50% with Pfeiffer's syndrome, and 100% with the Kleeblattschädel deformity. Raised intracranial pressure (ICP) due to venous hypertension and hydrocephalus is also much more common in these groups. Therefore, additional diagnostic options such as polysomnography with concomitant ICP monitoring may prove important tools and identifying patients needing urgent intervention. This has been developed in our centre with good preliminary results.

Respiratory sleep study

The diagnosis of sleep-disordered breathing requires sleep study in the form of either full polysomnography with electroencephalographic, electroculographic, or electromyographic leads (PSG) or cardiorespiratory polygraphies (CRPG). Both modalities include nasal pressure transducer, thoracic and abdominal excursion via respiratory inductance plethysmography, 2-lead electrocardiography, pulse oximetry, transcutaneous pCO_2 or end-tidal CO_2, and infrared video recording with microphone.

The gold standard test for the diagnosis of SDB and assessment of its severity is an overnight, attended, in-laboratory PSG study. PSGs allow for objective diagnosis and assessment of disturbances in respiratory parameters and sleep architecture. This allows for classification of patients into differential level of SDB severities, which will inform clinical management. It is however not a widely available resource.

CRPG are a limited version of the PSG that can be more easily accessed and also used in the home. When CRP are performed, they can be scored using adapted rules as per the 2012 American Academy of Sleep Medicine (AASM) guidelines for the scoring of sleep and associated events [5]. CRP have previously been demonstrated to be an accurate tool for the detection of sleep-disordered breathing [3, 23]. Sleep stages are scored as either wake, rapid eye movement, or nonrapid eye movement sleep in 30-s epochs by visual analysis of the cardiorespiratory parameters [41, 52].

Interpretation of sleep study results

Different types of respiratory events can be found on a sleep study as follows:

- An obstructive apnoea is scored if there is > 90% fall in nasal pressure transducer for > 90% of the entire event, the event lasted ≥ 2 breaths, and there is continued or increased respiratory effort.
- A mixed apnoea is scored when there is absent respiratory effort during one portion of the event and the presence of inspiratory effort in another portion, regardless of which portion comes first.
- A central apnoea is scored if there is absent respiratory effort for the entire event, and either the event lasted for > 20 s or lasted ≥ 2 breaths and was associated with a ≥ 3% oxygen desaturation.
- A hypopnoea is scored if there was a ≥ 30% reduction in amplitude of the nasal pressure transducer, the event lasted for ≥ 2 breaths, and it was associated with a ≥ 3% oxygen desaturation.

The number of events leads to the determination of the apnoea-hypopnoea index (AHI) by dividing the total number of apnoea and hypopneas by the number of hours of total sleep time [32, 33]. The AHI is the most commonly used PSG parameter for the quantification of SDB severity. It comprises the number of mixed, obstructive, and central apnoea and hypopneas per hour of total sleep time. AHI can then be divided into obstructive AHI (oAHI) and central AHI (cAHI).

An obstructive AHI ≤ 1/hrTST is considered to be normal, 1 < AHI ≤ 5 represents mild OSA, 5 < AHI ≤ 10 represents moderate OSA, and an AHI > 10/hrTST represents severe OSA [33, 54].

With regard to the CAHI, the evidence of what is abnormal is not as clear and requires additional studies. This is currently reviewed by a Taskforce on Paediatric Central Sleep Apnoea set up by the European Respiratory Society. At present, cAHI up to 5/h has been reported in healthy children [36, 48, 51, 52]. Therefore, a cAHI > 5/h is considered by some authors to be outside the normal range although there is no consensus on

what should actually be considered abnormal and the clinical correlation with, for example, a CM1 [19, 26, 34].

In addition, an oxygen desaturation index (ODI—defined as the number of dips in oxygen saturation ≥ 3% per hour of sleep time), nadir SpO_2, and mean nadir SpO_2 are also calculated during the study analysis. Along with the CO_2 measurements (transcutaneous or end-tidal), they help determine the impact of sleep disordered breathing on gas exchange. Hypoventilation is defined as $PaCO_2 > 50$ mmHg for > 25% of sleep time [5].

Management of sleep disordered breathing

Foramen magnum decompression (FMD) is the mainstay of treatment of CM1. Despite the variability of SDB in CM1 patients and the fact that SDB may be the only symptom of CM1, there is however no study to determine the degree of SDB warranting FMD. The majority of studies focusing on SDB outcomes have been done following FMD. Case reports and retrospective and prospective studies have documented improvement of SDB after FMD (including in syndromic patients) although not always to complete resolution [1, 2, 7, 14, 20, 24, 25]. This absence of complete resolution in some patients may be explained by anatomical factors or possibly by permanent damage from compression that cannot be reversed with surgery. This raises the question of optimal timing of surgery in CM1 patients diagnosed with SDB.

Some patients will have CM1 as part of a craniofacial syndrome, particularly craniosynostosis involving the lambdoid suture. These may require specific surgical interventions combining cranial vault remodelling and FMD [2, 11]. Studies have shown occasional improvement of CM1 following craniofacial repair without FMD but also de novo CM1 after craniosynostosis repair [44, 47].

Use of noninvasive ventilation has been described in several studies with reported improvement on bilevel positive pressure ventilation (BiPAP) [37, 45, 49, 55]. In one of the studies, BiPAP was used as a bridge to surgical intervention (FMD) and subsequently discontinued postsurgical intervention as no longer needed [37].

A retrospective study of 147 children managed conservatively has shown that a proportion of them show spontaneous symptomatic and MRI improvement over a follow-up period of 3.8 years [47].

Due to the possibility of persistent SDB postsurgery, it is important to ensure a follow-up polysomnogram is arranged. There is no consensus on the timing of follow-up PSG, but it is important to leave a certain amount of time before reassessing the presence of SDB. This will allow for resolution of oedema as this has been shown to cause persistent SDB [43]. Some patients have been shown to have normalisation of PSG after 1 to 2 months [24, 29]; some took up to 15 months to achieve complete resolution [45]. Serial sleep studies may therefore be required to monitor gradual improvement over time. Recurrence of SDB can also happen and may indicate recurrence of herniation and brainstem compression such as the one described by Zolty et al. [56]. Long-term sleep follow-up has been advocated by some especially in the presence of high clinical suspicion [14, 28, 56].

There is now a large body of evidence that children with SDB show deficits in neurocognitive performance, behavioural impairments, and school performance [50]. Thus, studies highlighting impaired neurocognitive outcomes in this group [21, 27, 42] emphasise their vulnerability and the importance of the treating SDB adequately.

In summary, the majority of patients will have improvement of SDB following FMD surgical intervention. However, a small proportion will have persistent SDB and may require additional treatment (such as bilevel ventilation support) or additional intervention. Therefore, sleep study follow-up is essential and should be arranged at a minimum of 6 weeks from surgery to ensure accuracy of result (i.e. not affected by perioperative changes like oedema). Some patients will require long-term sleep study follow-up especially in the presence of high clinical suspicion of SDB.

Conclusion

Patients with CM1 have a high prevalence of SDB, and ideally, all should undergo sleep diagnostic testing. However, developing a pathway identifying patients needing prioritisation would allow better use of resources particularly in areas where access to diagnostic services is limited. This pathway should be based on the presence of neurological symptoms and specific brain MRI pointers which have been showed to increase the risk of SDB. The timing of referral is also crucial as SDB also has the potential to cause progression of CM1 and development of a syrinx. All clinicians caring for CM1 patients should be alerted to the high prevalence of sleep disordered breathing so that they can be diagnosed in a timely fashion.

Compliance with ethical standards

Conflict of interest The authors state that there are no conflicts of interest arising from the research reported in this paper.

References

1. Aarts LA, Willemsen MA, Vandenbussche NL, Van Gent R (2011) Nocturnal apnea in Chiari type I malformation. *Eur J Pediatr* 170(10):1349–1352
2. Addo NK, Javadpour S, Kandasamy J et al (2013) Central sleep apnea and associated Chiari malformation in children with syndromic craniosynostosis: treatment and outcome data from a

supraregional national craniofacial center. *J Neurosurg Pediatr*. 11(3):296–301
3. Alonso Álvarez ML, Santos JT, Guevara JAC, Egüia AIN, Carbajo EO, Jiménez JFM, Pelayo R (2008) Reliability of respiratory polygraphy for the diagnosis of sleep apnea-hypopnea syndrome in children. *Arch Bronconeumol* 44:318–323
4. Amin R, Sayal P, Sayal A et al (2015) The association between sleep-disordered breathing and magnetic resonance imaging findings in a pediatric cohort with Chiari 1 malformation. *Can Respir J* 22(1):31–6. 18
5. Berry RB, Brooks R, Gamaldo CE, Harding SM for the American Academy of Sleep Medicine (2012) The AASM manual for the scoring of sleep and associated events: Rules, terminology and technical specifications, Version 2.0. www.aasmnet.org, Darien, IL: American Academy of Sleep Medicine
6. Botelho RV, Bittencourt LR, Rotta JM, Tufik S (2000) Polysomnographic respiratory findings in patients with Arnold-Chiari type I malformation and basilar invagination, with or without syringomyelia: preliminary report of a series of cases. *Neurosurg Rev* 23(3):151–155
7. Botelho RV, Bittencourt LR, Rotta JM, Tufik S (2010) The effects of posterior fossa decompressive surgery in adult patients with Chiari malformation and sleep apnea. *J Neurosurg* 112(4):800–807
8. Botelho RV, Bittencourt LR, Rotta JM, Tufik S (2003) A prospective controlled study of sleep respiratory events in patients with craniovertebral junction malformation. *J Neurosurg* 99(6):1004–1009
9. Bokinsky GE, Hudson LD, Weil JV (1973) Impaired peripheral chemosensitivity and acute respiratory failure in Arnold-Chiari malformation and syringomyelia. *N Engl J Med* 28818:947–948
10. Bullock R, Todd NV, Easton J, Hadley D (1988) Isolated central respiratory failure due to syringomyelia and Arnold-Chiari malformation. *BMJ* 2976661:1448–1449
11. Cinalli G, Spennato P, Sainte-Rose C et al (2005 Oct) Chiari malformation in craniosynostosis. *Childs Nerv Syst* 21(10):889–901
12. Dauvilliers Y, Stal V, Abril B et al (2007) Chiari malformation and sleep related breathing disorders. *J Neurol Neurosurg Psychiatry* 78(12):1344–1348
13. Davis AA, Zuccoli G, Haredy MM et al (2019) The Incidence of Chiari Malformations in Patients with Isolated Sagittal Synostosis. *Plast Reconstr Surg Glob Open* 7(2):e2090
14. Doherty MJ, Spence DP, Young C, Calverley PM (1995) Obstructive sleep apnoea with Arnold-Chiari malformation. *Thorax*. 50(6):690–691
15. Doherty MJ, Spence DP, Young C, Calverley PM (1995) Obstructive sleep apnoea with Arnold-Chiari malformation. *Thorax* 50:690e1 discussion 696-7
16. Dhamija R, Wetjen NM, Slocumb NL, Mandrekar J, Kotagal S (2013) The role of nocturnal polysomnography in assessing children with Chiari type I malformation. *Clin Neurol Neurosurg* 115(9):1837–1841
17. El-Kersh K, Cavallazzi R, Fernandez A, Moeller K, Senthilvel E (2017) Sleep Disordered Breathing and Magnetic Resonance Imaging Findings in Children With Chiari Malformation Type I. *Pediatr Neurol* 76:95–96
18. Ely EW, McCall WV, Haponik EF (1994) Multifactorial obstructive sleep apnea in a patient with Chiari malformation. *J Neurol Sci* 126: 232e6
19. Felix O, Amaddeo A, Olmo Arroyo J, Zerah M, Puget S, Cormier-Daire V, Baujat G, Pinto G, Fernandez-Bolanos M, Fauroux B (2016 Sep) Central sleep apnea in children: experience at a single center. *Sleep Med* 25:24–28
20. Gagnadoux F, Meslier N, Svab I, Menei P, Racineux JL (2006) Sleep-disordered breathing in patients with Chiari malformation: improvement after surgery. *Neurology*. 66(1):136–138
21. Gonzalez JL, Campa-Santamarina JM (2018) Anomalies in the cognitive-executive functions in patients with Chiari Malformation Type I. *Psicothema* 30(3):316–321
22. Henriques-Filho PS, Pratesi R (2008) Sleep apnea and REM sleep behaviour disorder in patients with Chiari malformations. *Arq Neuropsiquiatr* 66(2B):344–349
23. Jacob SV, Morielli A, Mograss MA, Ducharme FM, Schloss MD, Brouillette RT (1995) Home testing for pediatric obstructive sleep apnea syndrome secondary to adenotonsillar hypertrophy. *Pediatr Pulmonol* 20:241–252
24. Keefover R, Sam M, Bodensteiner J, Nicholson A (1995) Hypersomnolence and pure central sleep apnea associated with the Chiari I malformation. *J Child Neurol* 10(1):65–67
25. Khatwa U, Ramgopal S, Mylavarapu A et al (2013) MRI findings and sleep apnea in children with Chiari I malformation. *Pediatr Neurol* 48(4):299–307
26. Kritzinger FE, Al-Saleh S, Narang I (2011) Descriptive analysis of central sleep apnea in childhood at a single center. *Pediatr Pulmonol* 46:1023–1030
27. Lacy M, Ellefson SE, DeDios-Stern S, Frim DM (2016) Parent-Reported Executive Dysfunction in Children and Adolescents with Chiari Malformation Type 1. *Pediatr Neurosurg* 51:236–243
28. Lam B, Ryan CF (2000) Arnold-Chiari malformation presenting as sleep apnea syndrome. *Sleep Med* 1(2):139–144
29. Levitt P, Cohn MA (1988) Sleep apnea and the Chiari I malformation:case report. *Neurosurgery.* 23(4):508–510
30. Losurdo A, Dittoni S, Testani E et al (2013) Sleep disordered breathing in children and adolescents with Chiari malformation type I. *J Clin Sleep Med* 9(4):371–377
31. Luigetti M, Losurdo A, Dittoni S et al (2010) Improvement of obstructive sleep apneas caused by hydrocephalus associated with Chiari malformation Type II following surgery. *J Neurosurg Pediatr*. 6(4):336–339
32. Marcus CL, Brooks LJ, Draper KA et al (2012) Diagnosis and management of childhood obstructive sleep apnea syndrome. *Pediatrics* 1303:e714–e755
33. Marcus CL, Omlin KJ, Basinki DJ et al (1992) Normal polysomnographic values for children and adolescents. Am Rev Respir Dis 146:1235–1239
34. McLaren AT, Bin-Hasan S, Narang I (2018) Diagnosis, management and pathophysiology of central sleep apnea in children. *Paediatr Respir Rev*
35. Miralbes Terraza S, Garcia Oguiza A, Lopez Pison J et al (2008) Central sleep apnea syndrome as the first sign of type I Chiari malformation. *An Pediatr (Barc)* 68:277e81
36. Montgomery-Downs HE, O'Brien LM, Gulliver TE, Gozal D (2006) Polysomnographic characteristics in normal preschool and early school-aged children. *Pediatrics* 1173:741–753
37. Murray C, Seton C, Prelog K, Fitzgerald DA (2006) Arnold Chiari type 1 malformation presenting with sleep disordered breathing in well children. *Arch Dis Child* 91(4):342–343
38. Pasterkamp H, Cardoso ER, Booth FA (1989) Obstructive sleep apnea leading to increased intracranial pressure in a patient with hydrocephalus and syringomyelia. *Chest* 95:1064–1067
39. Rabec C, Laurent G, Baudouin N et al (1998) Central sleep apnoea in Arnold-Chiari malformation: Evidence of pathophysiological heterogeneity. *Eur Respir J* 126:1482–1485
40. Raza-Knight S, Mankad K, Prabhakar P, Thompson D (2017) Headache outcomes in children undergoing foramen magnum decompression for Chiari I malformation. Arch Dis Child 102(3): 238–243
41. Redmond SJ, deChazal P, O'Brien C, Ryan S, McNicholas WT, Heneghan C (2007) Sleep staging using cardiorespiratory signals. *Somnologie—Schlafforschung und Schlafmedizin* 11:245–256

42. Riva D, Usilla A, Saletti V, Esposito S, Bulgheroni S (2011) Can Chiari malformation negatively affect higher mental functioning in developmental age? *Neurol Sci* 32(Suppl 3):S307–S309
43. Shiihara T, Shimizu Y, Mitsui T, Saitoh E, Sato S (1995) Isolated sleep apnea due to Chiari type I malformation and syringomyelia. *Pediatr Neurol* 13(3):266–267
44. Sofos SS, Robertson B, Duncan C, Sinha A (2017 Jul) Delayed Presentation of Isolated Sagittal Synostosis with Raised Intracranial Pressure and Secondary Chiari Malformation with Cervical Syringomyelia. *J Craniofac Surg* 28(5):1334–1336
45. Spence J, Pasterkamp H, McDonald PJ (2010) Isolated central sleep apnea in type 1 Chiari malformation: improvement after surgery. *Pediatr Pulmonol* 45(11):1141–1144
46. Strahle J, Muraszko KM, Buchman SR et al (2011 Sep) Chiari malformation associated with craniosynostosis. *Neurosurg Focus* 31(3):E2
47. Strahle J, Muraszko KM, Kapurch J, Bapuraj JR, Garton HJ, Maher CO (2011) Natural history of Chiari malformation Type I following decision for conservative treatment. *J Neurosurg Pediatr* 8(2):214–221
48. Traeger N, Schultz B, Pollock AN, Mason T, Marcus CL, Arens R (2005) Polysomnographic values in children 2-9 years old: Additional data and review of the literature. *Pediatr Pulmonol* 401:22–30
49. Tran K, Hukins CA (2011) Obstructive and central sleep apnoea in Arnold-Chiari malformation: resolution following surgical decompression. *Sleep Breath* 15(3):611–613
50. Trosman I, Trosman SJ (2017) Cognitive and Behavioral Consequences of Sleep Disordered Breathing in Children. *Med Sci* 5(4):30
51. Uliel S, Tauman R, Greenfeld M et al (2004) Normal polysomnographic respiratory values in children and adolescents. *Chest* 125: 872–878
52. Vaughn BV, Quint SR, Messenheimer JA, Robertson KR (1995) Heart period variability in sleep. *Electroencephalogr Clin Neurophysiol* 94:155–162
53. Verhulst SL, Schrauwen N, Haentjens D et al (2007) Reference values for sleep-related respiratory variables in asymptomatic European children and adolescents. *Pediatr Pulmonol* 42:159–167
54. Weinstock TG, Rosen CL, Marcus CL, Garetz S, Mitchell RB, Amin R, Paruthi S, Katz E, Arens R, Weng J et al (2014) Predictors of obstructive sleep apnea severity in adenotonsillectomy candidates. *Sleep*. 37:261–269
55. Yosunkaya S, Pekcan S (2013) Complex sleep apnea syndrome in a child with Chiari malformation type 1. *Turk J Pediatr* 55(1):107–111
56. Zolty P, Sanders MH, Pollack IF (2000) Chiari malformation and sleep-disordered breathing: a review of diagnostic and management issues. *Sleep*. 23(5):637–643