Obstructive Sleep Apnea in Children with Nocturnal Enuresis

There is increasing evidence on the association of monosymptomatic nocturnal enuresis (MNE) with obstructive sleep apnea. In this communication, we share our experience of four patients with Primary monosymptomatic nocturnal enuresis (PMNE) with positive Sleep-related breathing disorder (SRBD) score who underwent detailed polysomnography, and were either refractory to desmopressin treatment or relapsed on discontinuation of desmopressin.

Keywords: *Bedwetting, Polysomnography, Sleep-related breathing disorder*.

There is increasing evidence on the association of monosymptomatic nocturnal enuresis (MNE) with obstructive sleep apnea (OSA) [1]. Although the pathophysiology behind increased frequency of enuresis in patients with OSA is not ascertained, some studies suggest role of Brain-type natriuretic peptide (BNP) that is released from cardiac myocytes after cardiac wall distension. OSA leads to increased intrabdominal pressure and altered systemic blood pressure that induces natriuresis and polyuria by altering levels of brain natriuretic peptides [2-4].

Recently, we reported a high (23.3%) prevalence of sleep related breathing disorders in patients with MNE [5]. In this report, we share our experience of thirty children with MNE visiting our Pediatric Nephrology clinic. Out of these 30 cases, four had positive sleep related breathing disorder (SRBD) score, and thus underwent detailed polysomnography.

Records of thirty patients registered for MNE between September 2014 to September 2015 were retrieved. As per our protocol, every patient with nocturnal enuresis is screened for the presence of obstructive sleep apnea (OSA) through SRBD questionnaire along with detailed history, clinical and neurological examination. The Pediatric SRBD scale contains a total of 22 items and it is validated screening tool to detect sign and symptoms of OSA. Scores >0.33 are considered positive and suggestive of high risk for a pediatric sleep-related breathing disorder. Four children with monosymptomatic enuresis who had positive (SRBD) score were called upon for overnight polysomnography in the sleep laboratory of the institute. Two of these patients had previously taken desmopressin but were refractory to medical treatment while other two patients were referred to us as they had relapse on discontinuation of desmopressin.

Details of the sleep study such as periodic limb movements (PLMS), apnea-hypopnea index (AHI), EEG, snoring index, and saturation dipping and arousal index was noted. Severity of the disease was classified as primary snoring (AHI <1), mild to moderate OSA (AHI 1-5), and severe OSA (AHI >5). Details of the polysomnographic findings are given in the ***Table* I**. Two of the four patients had severe OSA while one each had mild and moderate OSA. PLMS was positive in three out of four cases. Patients with severe OSA underwent adenotonsillectomy and achieved dryness over a period of 4-6 weeks. Other two patients with mild to moderate nocturnal enuresis achieved remission with tapering dose of desmopressin.

Findings from this series show that MNE is associated with OSA, and children with MNE should be screened for presence of OSA. A high index of suspicion is required in the MNE patients who are refractory to medical therapy or develop relapses on discontinuation of desmopressin.

Contributors: GC,SJ,ABG: conceptualized the study and wrote initial draft of manuscript; VG,BD: helped in writing and editing

TABLE I CLINICAL AND POLYSOMNOGRAPHY FINDINGS IN ENURETIC CHILDREN WITH SLEEP-RELATED BREATHING DISORDER

Age/ gender	*Sign and Symptoms*	*BMI (kg/m^2)*	*Tonsils*	*PLMS*	*AHI*	*OSA*	*Lowest oxygen saturation*	*Arousal Index*
15/F	Nocturnal enuresis, restless leg syndrome, sleep talking, acting in dreams	23.3	Grade 2	Positive	1.6	Mild	93%	8.6
10/F	Nocturnal enuresis, snoring	24.2	Grade 3	Positive	4.4	Moderate	94%	16
12/F	Nocturnal enuresis	14.4	Grade 4	Negative	11.5	Severe	95%	8
5/F	Nocturnal enuresis, weight gain	25.8	Grade 2	Positive	7.7	Severe	95%	7

BMI: *Body mass index; PLMS*: *Periodic leg movements; AHI*: *Apneic-hypoapenic index; OSA*: *Obstructive sleep apnea.*

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Subclinical Vitamin D Deficiency in Children from Thrissur, Kerala

This study was conducted to assess the 25-hydroxy vitamin D levels in children (age 1-5 yr) from Thrissur, Kerala, and to find its association with clinical manifestations of vitamin D-deficiency. Among the 79 children included, none had clinical features of rickets. The mean (range) vitamin D level was 18.1 (3.7 - 68.0) ng/mL. All the children had normal serum levels of Calcium, Phosphorous and Alkaline phosphatase. Serum parathyroid hormone levels were normal in 77 children. We conclude that most children with subclinical vitamin D deficiency diagnosed on basis of serum levels of 25 (0H) D do not have clinical symptoms/signs or biochemical evidence of secondary hyperparathyroidism.

Keywords: *Diagnosis, Hypovitaminosis D, Rickets*.

Hypovitaminosis D and its potential health implications are currently the subject of significant interest and controversy [1]. Though serum level of 25-hydroxyvitamin D (25OHD) is widely used as the marker of the vitamin D status, what level defines its deficiency is still under debate, particularly in children. This cross-sectional study was conducted in a tertiary care hospital in Central Kerala from June 2016 to December 2016 after approval by Institutional Ethics Committee. Children aged 1 to 5 years, attending the immunization clinic, outpatient clinic and well-baby clinic run by Department of Pediatrics were enrolled into the study after obtaining informed consent from parents/caretakers. Children with chronic illness, and those on Calcium or Vitamin D supplements were excluded from the study. Baseline demographic details, detailed clinical history and complete physical examination were performed in all included children. Serum levels of 25-hydroxy Vitamin D (25 (OH) D) were measured in all children using Chemiluminescent Microparticle immunoassay (CMIA, Abbott). Serum parathyroid hormone (PTH) level was assessed by Electro Chemiluminescent Immunoassay (ECLIA, Roche). Serum calcium, phosphorous and Alkaline phosphatase (ALP) were also measured simultaneously. The laboratory reference range for PTH was 15-65 pg/dL, while that for 25 (OH) D was 30-70 ng/mL.

We categorized serum 25(OH)D levels as <12, 12-20, 20-60 and >60 ng/mL. Among the 79 children (42 boys mean age 3.4 y), none had clinical features of rickets. The 25 (OH) D level was normally distributed on visual inspection of curve. The mean (range) Vitamin D level was 18.1 (3.7- 68.0) ng/mL. Majority of children (37.9%) had levels between 12-20 ng/mL. Twenty-two children (27.8%) had a vitamin D level less than 12 ng/mL, suggestive of significant vitamin D deficiency. None of these children had hypocalcemia, and only two of them had high PTH levels (PTH >55 pg/dL). The mean (range) level of PTH was 31.3 (6.5-53.6 pg/mL). Calcium, phosphorus and ALP level had mean (range) values of 9.0 (8.3-10.9) mg/dL, 6.2 (2.8-7.8) mg/dL and 201.7 (100-317) IU, respectively.

Vitamin D deficiency was initially considered rare in India, as the studies were based on serum calcium and alkaline phosphatase in our population [2]. Assessment of serum 25 (OH) D is increasingly being used to assess vitamin D status, resulting in common diagnosis of

subclinical hypovitaminosis D. However, the optimal cut-off levels of 25 (OH) D for diagnosing vitamin D deficiency are not well described in children. In Kerala, there is a good antenatal care system assuming better maternal nutritional status [3]. The children in Central Kerala are adequately exposed to sunlight and have reasonably good health index. However, the mean value of 25 (OH) D in our study was 18.1 ng/dL, which is well below the accepted normal levels. Most of these children neither had clinical features of rickets nor had other laboratory evidence suggestive of Vitamin D deficiency. The present era is witnessing many diseases being etiologically attributed to vitamin D deficiency detected by low levels of 25 (OH) D. Hence, over prescribing Vitamin D, especially in pediatric age group, is quite common. Vitamin D is toxic in large doses and there are sporadic reports of vitamin D toxicity in literature [4]. Despite the concerns for over diagnosis and overtreatment of vitamin D deficiency, the practice, of testing for vitamin D deficiency using 25 (OH) D assay is on the rise. Few studies from Western countries have reported increased testing of 25 (OH) D levels leading to concerns related to quality of care, cost, and potential over-diagnosis [5].

Vitamin D measurement is often inaccurate and imprecise, and majority of tests performed currently fail to reveal vitamin D-deficiency [6]. IAP Guidelines on Vitamin D- and calcium-deficiency [7] do not recommend routine screening of healthy children; it should be performed only in those at risk of vitamin D deficiency. Moreover, there is a need for educating the practitioners as well as public about sun exposure for vitamin D synthesis [8], and dietary intake of vitamin D rich foods rather than promoting high market sales of calcium supplements, which could predispose to toxicity.

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