Preliminary Data on Vitamin D Deficiency and Treatment in a Cohort of Sicilian RLS/WED Patients

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Abstract
Vitamin D deficiency has been noticed to correlate with the occurrence and severity of RLS/WED both in children and in adults. We submit preliminary data on a cohort of 17 (14 females) adult Sicilian patients followed during the last two years in our sleep clinic. All of them had low vitamin D values (mean 15.8 mg/ml), and most of them low ferritin (mean 24 mg/ml), mean IRLS-RS 22.5. Patients were mostly treated by DA-agonists, only two were on pregabalin alone. Eight of seventeen all on Dopamine agonists, mean duration of therapy 12 years, had also augmentation, which was worse for patients with comorbid OSA and females with lower D3. Vitamin D supplementation follow up data (6 months) are available on 5 patients. Severity scores were significantly decreased in parallel with D3 values normalization and augmentation was resolved in 2 out of 5 female patients treated.

ABBREVIATIONS
RLS: Restless Legs Syndrome; WED: Willis Ekbom Disease; OSA: Obstructive Sleep Apnea; IRLS-RS: International RLS Rating Scale; PGB: Pregabalin; PMX: Pramipexole; RTG: Rotigotine

INTRODUCTION
Vitamin D deficiency is known to occur in adult and pediatric patients with RLS/WED [1,2] and in children with growing pains [3]. A significant inverse correlation between vitamin D levels and RLS severity was found and according to some observations [4]. This is particularly relevant in the female gender. Vitamin D is a neuron activating steroid affecting brain development and its functions, among these the development of dopaminergic pathways. Vitamin D receptors are in fact present in the nucleus of tyrosine hydroxylase (TH) neurons in both human and rat substantia nigra. Besides this, hypoxia, whether or not mediated by iron depletion, upregulates, among other factors such as CSF, PG, D2 synthase, cystatin C, and Beta-Hb, also vitamin D binding protein, as lately confirmed by proteomic analysis of CSF of RLS/WED patients [5]. Poor diet, insufficient sun exposure, aging and menopausal effects, all favor a low vitamin D condition, increasing the risk for RLS/WED.

MATERIALS AND METHODS
We enrolled all new RLS patients referred to our Sleep Center in the last two years.

RESULTS AND DISCUSSION
Seventeen (14 females) consecutive RLS patients, mean age 58.4 years, mean BMI 28.3, were enrolled. Co morbidities, vitamin D, ferritin and sideremia values, and IRLS-RS scores according to gender were reported in Figure 1,2, respectively. No statistically significant differences were found between males and females. Eight out of 17 RLS patients (5 F and 3 M) had augmentation. Mean duration of RLS therapy was 12 years; all eight patients were on Dopa-agonists (6 on pramipexole, PMX and 2 on rotigotine, RTG). Patients reporting augmentation had lower ferritin and sideremia values (mean values 15.8 and 24 mg/ml) than patients without augmentation (p<0.5). No difference statistically significant was found regarding vitamin D status in this group. Patients with co-morbid sleep apnea and post-menopausal women reported more augmentation (Figure 3). We have a 6 months follow up with vitamin D therapy on five (F)/17 RLS patients. Original therapy before supplementation were pregabalin (PGB) monotherapy (2 patients), PMX (2 patients), RTG (1 patient). All patients showed reduced severity scores along with increased D3 values. In 2/5 female patient’s augmentation was also resolved by vitamin D
supplementation in addition to Dopa-agonists therapy (Figure 4) our study seems to confirm RLS deficiency as a severity risk factor especially in post-menopausal females. The additive role of comorbid OSA, also known to feature low vitamin D levels [7,8], may be further detrimental and contribute to the development of augmentation. Common hypoxic damage shared by RLS and OSA, partially dependent on vitamin D deficiency, may explain a more severe RLS-OSA comorbid phenotype, exquisitely susceptible to vitamin D supplementation.

CONCLUSION

Our study, albeit preliminary, confirms previous data on the therapeutic effect of vitamin D supplementation to decrease RLS severity and indicates a possible role of vitamin D in the management of augmentation, especially in post-menopausal females with comorbid OSA. More patients and possibly more evenly distributed among genders, with a longer follow up, are certainly needed to confirm these very preliminary data, in order to allow specific therapeutic recommendations.

REFERENCES
