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Pramipexole in restless legs syndrome

Evaluation by suggested immobilization test

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Sirs: The Restless Legs Syndrome (RLS) is characterized by a disagreeable sensation in the limbs and motor restlessness occurring at rest, especially in the evening and at night, which improves temporarily with activity [1]. More than 80 % of RLS patients have periodic legs movements (PLM) during sleep (PLMS) and wakefulness (PLMW) [2, 3]. D3-receptors non-ergoline dopaminergic agents, such as pramipexole and ropirinole, are commonly used in RLS therapy, although detailed data on their effect on PLM are lacking. The aim of our study was to determine pramipexole efficacy on RLS symptoms and motor component by means of the Suggested Immobilization Test (SIT).

Twenty-four never treated patients (mean age 62.4 ± 7.1 years; 13 females, 11 males) were selected according to the standard diagnostic criteria defined by the International RLS Study Group (IRLSSG) [2]. On the basis of the medical history, neurological examination, laboratory tests, electroneurography and F-wave, 20 patients were classified as having primary RLS, and 4 as secondary RLS (2 renal failure, 1 peripheral neuropathy, 1 paraneoplastic peripheral neuropathy). The initial dose of pramipexole was of 0.125 mg/d at 7 p. m., and it was increased every 3 days by 0.125 mg/d until a satisfactory control of symptoms was achieved or until side effects began to appear. At evaluation time therapy ranged from 0.25 to 0.50 mg/d. The subjective assessment of the global RLS severity was performed between 30 and 60 days (mean 39) after reaching the final dosage of pramipexole by using the IRLSSG Rating Scale [4]. This is a recently validated scale consisting in a clinician-administered questionnaire ranging from 0 to 40 points (1 to 10 points = mild, 11 to 20 points = moderate, 21 to 30 points = severe and 31 to 40 points = very severe). SIT was validated in 1998 as a polygraphic test able to identify and score PLMW [5]. During the test the patients were asked to sit at a 45-degree angle in bed with their legs outstretched, and were instructed not to move. Sleep was scored by a standard method; if any patient fell asleep he was awakened after 20 seconds of any stage of sleep [6]. Coleman's criteria were used to score PLMW, whereas duration criterion was considered for any single movement that ranged from 0.5 to 10 seconds, because during wakefulness movements may often exceed 5 seconds [5, 7]. The following measures were made: Movement Index (MI = number of leg movements per hour of SIT), number of leg movements during the first 30 minutes of recording (MIF30), number of leg movements during the last 30 minutes of recording (MIL30), Lateralization Index (LI = left + right movements/MI), Mean Interval between Movements in seconds (MIM), Mean Duration of single movements in seconds (MD), the minute of appearance of first movement (M^{st}). According to Montplaisir et al. MI > 40 was considered abnormal [5]. Ten patients (mean age 61.2 ± 8.6 years; 5 females, 5 males) affected by primary RLS underwent SIT at baseline (without medication) and between 30 and 60 days (mean 46 days) after reaching the final dosage of pramipexole. Comparison between IRLSSG Rating Scale and SIT data, recorded before and after treatment, was made by using the paired-sample t-test.

All 24 patients completed the study. The mean IRLSSG Rating Scale score was 22.6 (SD±6.3) at baseline, and significantly decreased to 11.3 (SD±6.5) between 30–60 days after therapy (Fig. 1). Moreover the mean MI also significantly decreased from 118.8 (SD±74.5) to 54.9 (SD±53.2). PLMW were most prevalent in the second half hour of SIT. Reduction in PLMW occurred mainly in the first 30 minutes (–55 %) as compared with the last 30 minutes (–47 %). Pramipexole significantly increased both the mean M^{st} and MIM, while MD and LI did not change with therapy (Tab. 1). Low doses of pramipexole have significantly improved the subjective symptoms of RLS. Patients reported that the improvement was achieved a few days after treatment, with a good compliance. Pramipexole also produced a significant reduction in PLMW, but

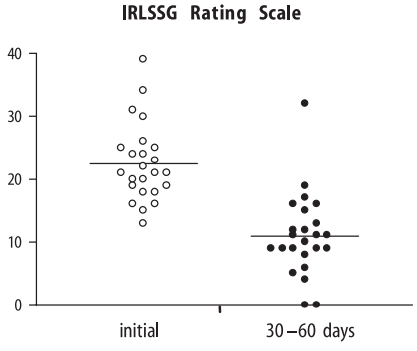

Fig. 1 IRLSSG Rating Scale values in 24 patients affected by primary (20 pts) and symptomatic (4 pts) RLS between 30 and 60 days of therapy

Table 1 MIF30 = Movement Index First 30 minutes; MIL30 = Movement Index Late 30 minutes; M^{st} = the minute of appearance of first movement; MIM = Mean Interval between Movements in seconds

	initial	30–60 days	p-value
IRLSSG rating Scale	22.6 (SD±6.3)	11.26 (SD±6.5)	< 0.001
Movement Index	118.8 (SD±74.5)	54.9 (SD±53.2)	< 0.05
MIF 30	37.4 (SD±43.8)	16.9 (SD±30.1)	n. s.
MIL 30	81.5 (SD±31.9)	42.9 (SD±39.2)	< 0.05
Lateralization Index	0.33 (SD±0.27)	0.33 (SD±0.32)	n. s.
M^{st}	16.4 (SD±11.1)	31.9 (SD±15.8)	< 0.05
MIM	11.9 (SD±6.1)	14.8 (SD±11.4)	< 0.05

not a normalization of the MI values. This finding suggests that the sensitive component of RLS may have a different response to pramipexole from the motor component, and that PLM may still be present also when the patients report a subjective satisfaction with therapy.

Although the number of our patients with secondary RLS was low, pramipexole seems to be effective both in primary and secondary RLS. However this being an open-label study without placebo-control group, a large number of never treated patients was included, and the SIT was firstly used to evaluate the pramipexole efficacy [8–12]. Furthermore our results suggest that pramipexole may be used also in secondary forms of RLS.

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