Proprioceptive Focal Stimulation (Equistasi®) May Improve Motor Symptoms in Moderate Parkinson's Disease Patients

Italian Multicentric Preliminary Open Study

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***Abstract*—Object of the study was to evaluate the efficacy of propriocettive Focal Stimulation on Gait in moderate Parkinson (PD) patients by a preliminary open multicentric study, using Equistasi®, nanotechnological device of the dimension of a plaster which generates High Frequency segmental vibration. The efficacy of Gait Analysis (GA) on evaluating gait modification on Parkinson's Disease (PD) Patients is already well known. On the other hand, several studies have shown that Proprioceptive Focal Stimulation seems to be useful in symptoms amelioration in several neurological disease. Therefore, GA was recorded in a group of PD patients. Twenty-one PD patients (age 69,51 years, Duration disease 8.52 years, Duration Therapy 7,19 years; H&Y 2.46) at their best on therapy, were enrolled in the study. Two GA were performed always at the morning, before and after the treatment. Three plaques devices were put on the skin: one at C7, one at the right and the left leg, on soleus muscle. Equistasi® is a nanotechnological device of the dimension of a plaster which generates High Frequency segmental vibration. Clinical state was monitored by MDUPDRS part III. Parametric (One-way ANOVA and paired t-Student) and not – parametric statistic (Freidman ANOVA and Wilcoxon test) were used. The analysis of the Spatial –Temporal variables showed a significant improvement of Mean Velocity (MV) p=.002, Stride Lenght (SL) in right and left respectively p=.0013 and p=.017, Stance (STA) in right and left respectively p=.025 and p=.047 and Double Support Stance (DSS) in left and right stride respectively p=.034 and p=.033. MDUPDRS Part III was statistically reduced with p=0.017; furthermore the items 3.10, and 3.12 were statistically reduced respectively with p=.025 and p=.046. The results, in this group of patients, encourage to investigate the mechanical focal vibration as stimulation of proprioceptive system in PD. The effect of the device on patients may open a new possibility to the management of PD. The data indicates as the device ameliorates postural stability and gait performance and confirms the support that GA gives to underlight the modifications of gait in PD patients.**

Keywords-Parkinson; Rehabilitation; focal vibrations; Equistasi; Gait Analysis.

I. INTRODUCTION

Parkinson's Disease one of more diffuse neurodegenerative disease, second after Alzheimer's disease, present four cardinal motor symptoms: tremor, rigidity, bradykinesia, and postural instability. Last sign is the more influent on the activity of daily living, because it induces falls [10]. Pharmacological therapy as well as surgical therapy are not enough to well control this symptom, and many times the postural instability may induce fear to fall syndrome, and the PD patient are confined in wheelchair [11]. It is already know the Basal Ganglia have golden role in the pathological progression of PD patients, but it is not really true for balance and postural instability, where the Supplementary Motor Area, seems to be an important role specially, on production of Anticipatory Postural Adjustments (APAs). Humans in fact use anticipatory and compensatory postural strategies to maintain and restore balance when perturbed. Inefficient generation and utilization of anticipatory postural adjustments (APAs) is one of the reasons for postural instability [12]. SMA is a relay of many loops, not only cortical-subcortical loop (cortical-BBGG- thalamic- Cortical loop), but also vestibular loop, and proprioceptive loop and is known that gait analysis is important for the clinical evaluation of PD patients [1]. Equistasi®, nanotechnological device of the dimension of a plaster which generates High Frequency segmental vibration. It is not really known how this devise works, there are some studies indicating that this focal stimulation modifies the H wave in the medulla [13] and in PD patients, the presence of Equistasi improves effects of rehabilitation [2]. Object of the study was to evaluate the efficacy of Propriocettive Focal Stimulation in moderate Parkinson disease patients by a preliminary open study.

II. METHOD

A. Design

This is a multicentric, open study. 21 patients diagnosed with hydiopatic PD were enrolled in four rehabilitation

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centers in Italy: S. Lucia Foundation in Rome (principal center), the Auxologic Institute of Piancavallo Verbania, the Villa Margherita Clinic in Vicenza and the Mondino Neurological Institute of Pavia, each received approval from their ethics committee with protocol number respectively CE/PROG 478/15 del 19/11/2015, 58/16, 61/16, 60/16 After screening and enrollment, the patients receive a proprioceptive mechanical stimulation for 8 weeks with the Equistasi method [2], in the absence of any other rehabilitative trials. Informed consent was obtained from the participants.

B. Subjects

Participants could be included if they had consented to participation, patients with rigid akinetik form of bilateral idiopatic Parkinsons Diseasei (Hoehn and Yahr 2-3) in according to current criteria [3] for at least four years with a good response to antiparkinsonian therapy and with stable drug therapy for at least 3 months. The exclusion criteria were: presence of co-morbidity that prevent safe mobility or exercise (including clinically evident neuropathy and important medical conditions such as malignant tumors), severe dysautonomia with marked hypotension, major depression of mood, dementia, pregnancy, caridac pacer maker, deep brain stimulation (DBS) or other conditions affecting postural stability (eg poor visual acuity or vestibular dysfunction). In addition, patients had to have a MMSE > 24 points [5].

C. Instrumental assessment

As primary measures of outcome for Gait Analisys 3D the main measures of the linear path (BTS Smart system with Davis Procol in all the Centers) were evaluated: the speed (Velocity), the length of the step (Stride Length), the percentage of support times (Stance) and the percentage of the times of double support (DST).

D. Clinical assessment

Motor impairment was assessed with the parts III (motor examination) of the Unified PD Rating Scale [6] and Items 3.10, 3.11, 3.12, 3.13 were separately evaluated for underlying data on gait, freezing of gait, postural and postural instability of PD patients. Other data collected at baseline included age, gender, body mass index (BMI), disease duration, Hoehn and Yahr scale, anti Parkinsonian treatment expressed as levodopa-equivalent daily dose [7] and cognitive status assessed with the MMSE. All adverse events such as injuries, were verified and recorded during the study.

E. Statistical Analysis

This clinical trial used a sample of convenience, with the assumption that 21 participants would be ample to explore safety and feasibility. Given the small sample and the lack of normal distribution of most of the variables on Shapiro-Wilk test, nonparametric statistics were used. Treatment effect across time points were explored Wilcoxon signedrank test. we have also verified with Montecarlo method (MC) [12] [13], the adequacy of the p-value estimates. Categorical variables were compared by means of chisquare test. All values were expressed as mean and standard deviation were chosen to improve clarity of data presentation. IBM SPSS Statistics ver. 20.0 was used for all statistical analyses. All tests were two-sided with a level of significance set at P,0.05.

III. RESULT

Twenty-one subjects were enrolled in this open study (Table 1) and we have observed the clinical and instrumental assessments before (T0) and after (T1) 8 weeks of treatment. No major adverse events or death were observed during the study period.

TABLE I: BASELINE DEMOGRAPHIC AND CLINICAL VARIABLES. BMI: BODY MASS INDEX; H&Y: HOEHN & YAHR STAGE; LEDD: LEVODOPA EQUIVALENT DAILY DOSE; MMSE: MINI-MENTAL STATE EXAMINATION.

Patients	**Mean**	**stdv**
SEX (M/F)	14/7	
SIDE (R/L)	13/8	
AGE	69,51	10,1
BMI	25,89	3,7
DISEASE DURATION	8,52	3,2
YEARS OF THERAPY WITH L-DOPA	7,19	3,1
DISEASE ONSET AGE	60,04	10,4
LEDDS	697,3	110,4
H/Y	2,46	0,51
MMSE	26,4	1,46

A. Kinematic parameters

In the kinematic variables of the gait, we observed a significant improvement in Speed from 0.694 m/s to 0.756 m s p = .0002; a significant increase in the length of the Stride, both right and left respectively from 0.823 m to 0.902 m p = .0013 and from 0.835 m to 0.895 m p = .0173; Stance right and left significantly decreases, respectively from 64.65% to 62.75% p = 0.0253 and from 64,22%; to 62,75% p = .0342; the right and left DST decreases significantly, respectively from 14.02% to 12.99% p = .0342 and from 14.71% to 13.47% p = .0333 (Table 2).

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TABLE II: DIFFERENCES BETWEEN T0 AND T1 IN THE TEMPORAL SPACE PARAMETERS; WE USED ANOVA FOR REPEATED MEASURES

	Pre (dst)	Post (dst)	p value
Velocity (m/s)	0,694 (0,25)	0,756 (0,24)	.0002
Stride Lenght R (m)	0,823 (0,25)	0,902 (0,22)	.0013
Stride Lenght L (m)	0,835 (0,14)	0,895 (0,19)	.0173
Stance R (%)	64,65 (3,5)	63,46 (3,4)	.0253
Stance L (%)	64,22 (2,3)	62,75 (3,5)	.0473
DST R (%)	14,02(3,2)	12,99 (3,1)	.0342
DST L (%)	14,71 (2,8)	13,47 (3,1)	.0333

B. Clinics parameters

In the clinical variables we observed a significant decrease in Total Score UPDRS Part III from 37.57 to 32.25 p = .0179; a significant decrease of ITEM 3.10 from 1.761 to 1.333 p = .025 and a significant decrease of ITEM 3.12 from 1.809 to 1.322 p = .0461. No other significant difference was observed at the end of active treatment (Table 3).

TABLE III: DIFFERENCES BETWEEN T0 AND T1 IN CLINICAL VARIABLES; WE USED WILKOXON SIGNED RANK TEST AND MC METHOD.

	Pre (dst)	Post (dst)	p value
UPDRS III	37,57 (16,4)	32,25 (12,0)	.0179
ITEM 3.10	1,761 (0.94)	1,333 (0,73)	.0250
ITEM 3.11	0,525 (0,94)	0,656 (0,92)	.1861
ITEM 3.12	1,809 (1,05)	1,322 (1,02)	.0461
ITEM 3.13	1,901 (1,17)	1,550 (1,03)	.0767

IV. CONCLUSION

It is already demonstrated that the vibration of the axial muscles, produces systematic change in the erect posture [15] and the in the orientation of the body [16], and it induces in an improvement of balance. The imperceptible vibration released from the Equistasi device, have already given a positive response in the rehabilitation of some neurodegenerative pathologies [2] [17] [18] and have also highlighted their capacity in the modulation of the spinal circuit [13]. Nevertheless, the data indicate a trend of improvement on all spatial-temporal parameters, as if the vibrations were acting even on different circuits from the dopaminergic. It is noted in literature how the rehabilitation of Parkinson's disease is centered on the stimulation of the vestibule spinal reflex (VSR), can modify those components of the ambulation more correlated with the rhythmicity and the equilibrium [19]. Furthermore precedent studies put in evidence how in PD there a compromise sense of timing [20] and of the discrimination of the proprioceptive input [21]. Therefore, the focal muscular vibration (FV) not only have an impact on the circuit on the spinal cord, but also provide a notable proprioceptive influx to different parts of the central nervous system, thus influencing the precision of the execution of the voluntary movements [14]. This open-label study has the limit of not being controlled and the number of patients must be calculated appropriately to have a power of at least 80%. Nevertheless, the results, in this group of patients, encourage to investigate the mechanical focal vibration as stimulation of proprioceptive system in Parkinson's disease patients, and open a new possibility for management of moderate PD patients. Moreover, this study confirms the importance of GA in the clinical approach of Parkinson's disease.

REFERENCES

[1] Peppe A, Chiavalon C, Pasqualetti P, Crovato D and Caltagirone C. "Does gait analysis quantify motor rehabilitation efficacy in Parkinson's disease patients?" Gait Posture. 2007 Sep;26(3):452-62.

[2] Volpe D, Giantin MG and Fasano A "A wearable proprioceptive stabilizer (Equistasi®) for rehabilitation of postural instability in Parkinson's disease: a phase II randomized double-blind, double-dummy, controlled study".PLoS One. 2014 Nov 17;9(11).

[3] Berardelli A, Wenning GK, Antonini A, Berg D, Bloem BR, Bonifati V, Brooks D, Burn DJ, Colosimo C, Fanciulli A, Ferreira J, Gasser T, Grandas F, Kanovsky P, Kostic V, Kulisevsky J, Oertel W, Poewe W, Reese JP, Relja M, Ruzicka E, Schrag A, Seppi K, Taba P and Vidailhet M. "EFNS/MDS-ES/ENS [corrected] Recommendations for the diagnosis of Parkinson's disease." Eur J Neurol 20: 16–3.

[4] Hoehn MM and Yahr MD (1967) "Parkinsonism: onset, progression and mortality. Neurology" 17: 427–442.

[5] Folstein MF, Folstein SE and McHugh PR (1975) ''Mini-mental state. A practical method for grading the cognitive state of patients for the clinician." J Psychiatr Res 12: 189–198.

[6] Fahn S and Elton R Members of the UPDRS Development Committee (1987) "Recent developments in Parkinson's disease." Fahn S, Marsden C, Calne D, Goldstein M, editors. Folorham Park, NJ: Macmillan Health Care Information. 153–163, 293–304.

[7] Tomlinson CL, Stowe R, Patel S, Rick C, Gray R, et al. (2010) "Systematic review of levodopa dose equivalency reporting in Parkinson's disease." Mov Disord 25: 2649–2653.

[8] Fay MP, Kim HJ and Hachey M. "On Using Truncated Sequential Probability Ratio Test Boundaries for Monte Carlo Implementation of Hypothesis Tests". J Comput Graph Stat. 2007;16(4):946-967.

[9] Hozo I, Tsalatsanis A and Djulbegovic B. "Monte Carlo decision curve analysis using aggregate data." Eur J Clin Invest. 2017 Feb;47(2):176-183.

[10] Benatru I, Vaugoyeau M and Azulay JP. (2008) "Postural disorders in Parkinson's disease." Neurophysiol Clin 38: 459–465

[11] Smulders K, Dale ML, Carlson-Kuhta P, Nutt JG and Horak FB. "Pharmacological treatment in Parkinson's disease: Effects on gait." Parkinsonism Relat Disord. 2016 Oct;31:3-13

[12] Schlenstedt C, Mancini M, Horak F and Peterson D. “Anticipatory Postural Adjustment During Self-Initiated, Cued, and Compensatory Stepping in Healthy Older Adults and Patients With Parkinson Disease.” Arch Phys Med Rehabil. 2017 Jul;98(7):1316-1324

[13] Alfonsi E, Paone P, Tassorelli C, De Icco R, Moglia A, Alvisi E, Marchetta L, Fresia M, Montini A, Calabrese M, Versiglia V and Sandrini G. “Acute effects of high-frequency microfocal vibratory stimulation on the H reflex of the soleus muscle. A double-blind study in healthy subjects.” Funct Neurol. 2015 Oct-Dec;30(4):269-74.

[14] Kording KP and Wolpert DM (2006) “Bayesian decision theory in sensorimotor control.” Trends Cogn Sci 10: 319–326.

[15] Courtine G, De Nunzio AM, Schmid M, Beretta MV and Schieppati M (2007) “Stance- and locomotion-dependent processing of vibration-induced proprioceptive inflow from multiple muscles in humans.” J Neurophysiol 97: 772–779.

[16] Lackner JR and Levine MS (1979) “Changes in apparent body orientation and sensory localization induced by vibration of postural muscles: vibratory myesthetic illusions.” Aviat Space Environ Med 50: 346–354.

[17] Spina E, Carotenuto A, Aceto MG, Cerillo I, Silvestre F, Arace F, Paone P, Orefice G and Iodice R. “The effects of mechanical focal vibration on walking impairment in multiple sclerosis patients: A randomized, double-blinded vs placebo study.” Restor Neurol Neurosci. 2016 Sep 21;34(5):869-76.

[18] Leonardi L, Aceto MG, Marcotulli C, Arcuria G, Serrao M, Pierelli F, Paone P, Filla A, Roca A and Casali C. “A wearable proprioceptive stabilizer for rehabilitation of limb and gait ataxia in hereditary cerebellar ataxias: a pilot open-labeled study.” Neurol Sci. 2017 Mar;38(3):459-463.

[19] Tramontano M, Bonnì S, Martino Cinnera A, Marchetti F, Caltagirone C, Koch G and Peppe A. “Blindfolded Balance Training in Patients with Parkinson's Disease: A Sensory-Motor Strategy to Improve the Gait.” Parkinsons Dis. Hindawi Publishing Corporation Parkinson’s Disease Vol 2016, Article ID 7536862, 6 pages.

[20] Fiorio M, Stanzani C, Rothwell JC, Bhatia KP, Moretto G, et al. (2007) “Defective temporal discrimination of passive movements in Parkinson’s disease.” Neurosci Lett 417: 312–315.

[21] Jacobs JV and Horak FB (2006) “Abnormal proprioceptive-motor integration contributes to hypometric postural responses of subjects with Parkinson’s disease.” Neuroscience 141:999–1009.

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