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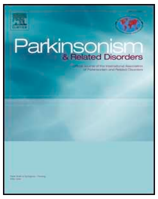

Setting in motion physiotherapy for MSAp[☆]

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Multiple system atrophy (MSA) is a highly debilitating neurodegenerative disease with few therapeutic options. It is considered an atypical parkinsonism since roughly half of cases feature predominant parkinsonism (the so-called parkinsonian variant or MSA-p as opposed to the cerebellar variant or MSA-c). These patients do not respond well to levodopa or dopamine agonists and other treatments are limited. Non-pharmacological treatments are recommended for management of parkinsonian and cerebellar symptoms, as well as for postural hypotension [1,2]; however evidence is scarce on the actual benefits these treatments may have. These non-pharmacological treatments include physiotherapy, occupational therapy, balance exercises, speech therapy and dietary recommendations for postural hypotension and dysphagia for example.

On the other hand, exercise [3], physiotherapy [4], speech therapies [5] and even singing [6] and dancing [7] have been evaluated and deemed beneficial for Parkinson's disease (PD). Evidence of such non-pharmacological strategies in MSA cases has mainly been reported in the form of case studies [8–11] or small and un-blinded studies with no placebo group [12]. The latter study for example, included 17 MSA patients (10 MSA-P cases, 2 MSA-C cases and 5 mixed variants), which were randomized to an intervention group vs. control group. The intervention group underwent an occupational therapy program that lasted for 8 weeks. Outcome measurements included the UPDRS scale, quality of life scales (PDQ-39) and anxiety and depression scales (HADS). Although there was no clear improvement on the UPDRS scale there was a clear difference between both groups since the control group significantly deteriorated in contrast to stable scores in the intervention group. Quality of life and ADL activities significantly improved in the intervention group as well, and there were no differences for depression and anxiety.

The paucity of this prior evidence and its limitations make of studies such as the one by Raccagni's et al. [13] an important step forward to evaluate the benefits of physiotherapy. Raccagni's et al. study is also a small pilot study that includes 10 MSA-P cases that underwent an in-patient supervised 60-min physiotherapy program for 5 days followed by a similar home-based program lasting two additional weeks. A strength of the study relative to previous research in this field is that besides the usual clinical scales (UMSARS, PDQ-39, MoCA and others), part of the outcome measurements were more objective as they resulted from an instrumented sensor-based gait analysis along.

The main conclusion of the trial, being a pilot and small-sized one, is that physiotherapy is feasible and safe for MSA-p patients and seems to be equally beneficial as in PD cases. Safety is a crucial issue as it is well known that MSA patients may suffer from exercise induced hypotension [14], which indeed may be an important contraindication for exercise-related therapies. This result is thus important as it stimulates further multicentric research in larger samples.

Issues to be considered in future trials include phenotypic heterogeneity in MSA (MSA-p vs. MSA-c) as well as the type of matching with comparator groups (as PD). Hence, in Raccagni's study only the MSA-p variant has been studied; however most MSA-c variants also have parkinsonian symptoms along with gait and postural instability that could benefit from tailored physical programs. Furthermore, most studies only include cases that are able to walk unassisted. MSA as mentioned is a highly debilitating disease and most cases quickly progress to assisted walking and become wheelchair-bound only a few years after onset. It is important to include advanced cases in these studies as these are the most vulnerable and have very limited therapeutic options. Yet, physiotherapy and other non-pharmacological strategies such as occupational, and speech therapies may still play a role in the palliative care of these cases, especially considering that small improvements in these patients may translate into substantial improvements in quality of life. In terms of matching in Raccagni et al.'s study since Hoehn & Yahr stage was chosen for matching, PD patients were older, and gait and postural stability are worse with aging both physiologically and due to co-morbidities. This might have driven partly the similar improvement in younger MSA-p participants relative to older PD ones and is to be taken into account in future research. A common handicap of most exercise studies also includes the lack of prospective information regarding the long term effects of the treatments. In Raccagni's study the home-based

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program was not as effective as the inpatient supervised program. It also remains to be seen whether or not these therapies could be beneficial for non-motor symptoms such as apathy, depression, cognition or sleep.

All these limitations notwithstanding, Raccagni et al.'s study is a relevant contribution to the field of physiotherapy in MSA. Remarkably, previous evidence about physiotherapy not only in MSA, but even in PD is scarce. It is even less for multidisciplinary programs combining physiotherapy with other non-pharmacological interventions. In PD, most of the studies of multidisciplinary education programs have mostly found differences in psychosocial outcomes [15], and there are few experiences combining sessions with the specialized nurse, physiotherapist, speech therapist and neuropsychologist [16]. Therefore, both PD and MSA are in need of more studies on the potential usefulness of comprehensive programs combining different interventions and health professionals to improve motor, non-motor symptoms and quality of life in these patients and caregivers.

In summary, many questions still arise when assessing non-pharmacological therapies for MSA. Future studies should ideally be multicenter, blinded and controlled designs as well as larger groups of MSA cases, including both the MSA-p and the MSA-c variants in different disease stages. Sensor-based analysis is a novel tool that should be taken into advantage and although UMSARS scores may not improve it is important to take note on the rate of deterioration as it may be reduced when compared to a control group indicating a possible effect on progression of disease. In this vein, controlled studies and longer follow-ups will also be crucial to rule out potential placebo effect. Raccagni et al.'s study is an important step in this endeavor of setting in motion physiotherapy for MSA.

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