REVIEW

CME

Pisa Syndrome in Parkinson's Disease: An Integrated Approach From Pathophysiology to Management

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ABSTRACT: Pisa syndrome was first described in 1972 in patients treated with neuroleptics. Since 2003, when it was first reported in patients with Parkinson's disease (PD), Pisa syndrome has progressively drawn the attention of clinicians and researchers. Although emerging evidence has partially clarified its prevalence and pathophysiology, the current debate revolves around diagnostic criteria and assessment and the effectiveness of pharmacological, surgical, and rehabilitative approaches. Contrary to initial thought, Pisa syndrome is common among PD patients, with an estimated prevalence of 8.8% according to a large survey. Furthermore, it is associated with the following specific patient features: more severe motor phenotype, ongoing combined pharmacological treatment with levodopa and dopamine agonists, gait disorders, and such comorbidities as osteoporosis and arthrosis. The present literature on treatment outcomes is scant, and the uneven effectiveness of specific treatments has produced conflicting results. This might be because of the limited knowledge of Pisa syndrome pathophysiology and its variable clinical presentation, which further complicates designing randomized clinical trials on this condition. However, because some forms of Pisa syndrome are potentially reversible, there is growing consensus on the importance of its early recognition and the importance of pharmacological adjustment and rehabilitation. © 2016 International Parkinson and Movement Disorder Society.

Key Words: posture; drug therapy; rehabilitation; lateral trunk flexion; surgery

Pisa syndrome (PS) is a challenging clinical entity first described by Ekbom and colleagues in 1972.[1] This postural disorder has been progressively ascribed to patients with neurodegenerative disorders (eg, Alzheimer's disease, multiple system atrophy) other than those treated with neuroleptics and other drugs antagonizing dopamine receptors,[2-6] or with cholinesterase inhibitors and antidepressants.[2-7] In rare instances, idiopathic cases have been described in otherwise healthy patients not receiving any therapy.[8] Table 1 summarizes the etiologies of PS.

Postural abnormalities are hallmark symptoms of Parkinson's disease (PD).[48-50] Following the first descriptions of PD cases, the postural misalignment in PS has drawn increasing attention from clinicians and researchers.[21,36] One of the earliest representations of the postural disorders of PD patients is the combination of PS

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and forward flexion, as represented by the "statuette pathologique" by Richer in the 1895.[51] In more recent years, broad descriptors of PS (eg, scoliosis)[36] replaced its early identification as a specific postural abnormality.

This review summarizes the current knowledge on the epidemiology, pathophysiology, and different treatment options (pharmacological, surgical, and rehabilitative) for PS, particularly in PD. Indeed, most of the available data on the pathophysiology and treatment of PS are derived from studies in PD patients.

Search Strategy and Selection Criteria

We carried out a literature search of articles listed in MEDLINE, EMBASE, CINALH, PubMed, and Scopus electronic databases using the search terms "Pisa syndrome," "lateral trunk flexion," "trunk dystonia," and "Parkinson's disease." Articles published in English and French between March 1972 and March 2016 were included. The summary of the literature review is based on significant published articles on this topic.

Definition and Epidemiology

PS has been defined as a lateral trunk flexion that can be reduced by passive mobilization or supine positioning.[49] It presents as a postural deformity especially in the coronal plane, although some degree of forward trunk flexion and rotation can also be seen.

Bonanni and colleagues[25] first defined PS as an abnormal lateral flexion of the trunk of more than 15° as measured with a wall goniometer. The deformity increases during walking but resolves in the recumbent position; it may coexist with the absence of mechanical restriction to trunk movement (ie, ankylosis or clinical or radiological signs of degenerative vertebral or skeletal disease).[25]

Recently, Doherty and colleagues[49] suggested as a diagnostic criterion a lateral flexion of at least 10°, which can be completely alleviated by passive mobilization or supine positioning. PS can be classified by the angle of lateral trunk flexion as mild (<20°) or severe (≥20°).[52] Although these definitions are generally used in clinical practice, no consensus on the definition of PS or diagnostic criteria have been reached so far.

A further diagnostic criterion can be obtained by electromyographic (EMG) analysis of the pattern of activation of paraspinal (longissimus muscle) and non-paraspinal muscles (external oblique muscle) during different positions. It has been suggested that continuous EMG activity of the lumbar paraspinal muscles, ipsilateral to the bending side during standing or walking, may yield a further diagnostic information.[25-27]

Because of the lack of clear diagnostic criteria, along with the paucity of epidemiological large-scale studies, the real prevalence of PS is not well known.[53]

TABLE 1. Conditions associated with Pisa syndrome and proposed pathogenetic classification in Parkinson's disease

Category	Reference
Idiopathic (no underlying disease or exposure to medication)	8
Associated with medications	
Atypical antipsychotics (ie, sertindole, olanzapine clozapine)	3
Typical antipsychotics (ie, zotepine, chlorpromazine, haloperidol)	
Tricyclic antidepressants	
Selective serotonin reuptake inhibitors	
Cholinesterase inhibitors (ie, rivastigmine, donepezil)	
Antiemetic drugs	
Lithium carbonate	
Benzodiazepines	
Tiapride	
Associated with disorders of PNS	
Myasthenia gravis[b]	9
Associated with psychiatric diseases	
Schizophrenia[a] (exposed to antipsychotic drugs)	10,11
Associated with structural and other acquired disorders of CNS	
Postencephalitic parkinsonism[b]	12
Subacute sclerosing panencephalitis	13
Subdural haematoma[b]	14
Hashimoto's encephalopathy[a]	15
Associated with neurodegenerative diseases	
Multiple system atrophy[a]	5
Amyotrophic lateral sclerosis[a]	16
Dementia with Lewy bodies[a]	17
Presenile dementia[a]	1
Progressive supranuclear palsy[a,b]	18,19
Alzheimer's disease[a]	2,7,20-23
Huntington's disease[a]	24
Parkinson's disease	
Without apparent trigger	
Dystonic and/or myopathic mechanism and muscle atrophy	25-29
Impaired integration of vestibular and/or other sensory modalities	30-33
Scoliosis	34,35
Adverse effect of medication/surgery	
Dopaminergic therapy	36-42
Nondopaminergic therapies	21,43,44
Surgery (subthalamotomy, pallidotomy)	45-47

PNS, peripheral nervous system; CNS, central nervous system.
[a]Caused/triggered by medication.
[b]Present also in absence of medications known to cause/trigger Pisa syndrome.

Preliminary studies have reported a prevalence ranging from 2% to 90%. Recently, a large multicenter Italian study enrolling 1631 PD patients has estimated a more accurate prevalence of 8.8%.[52]

Clinical Presentation

PS can develop in a chronic fashion with subclinical onset and progressive worsening or it can appear

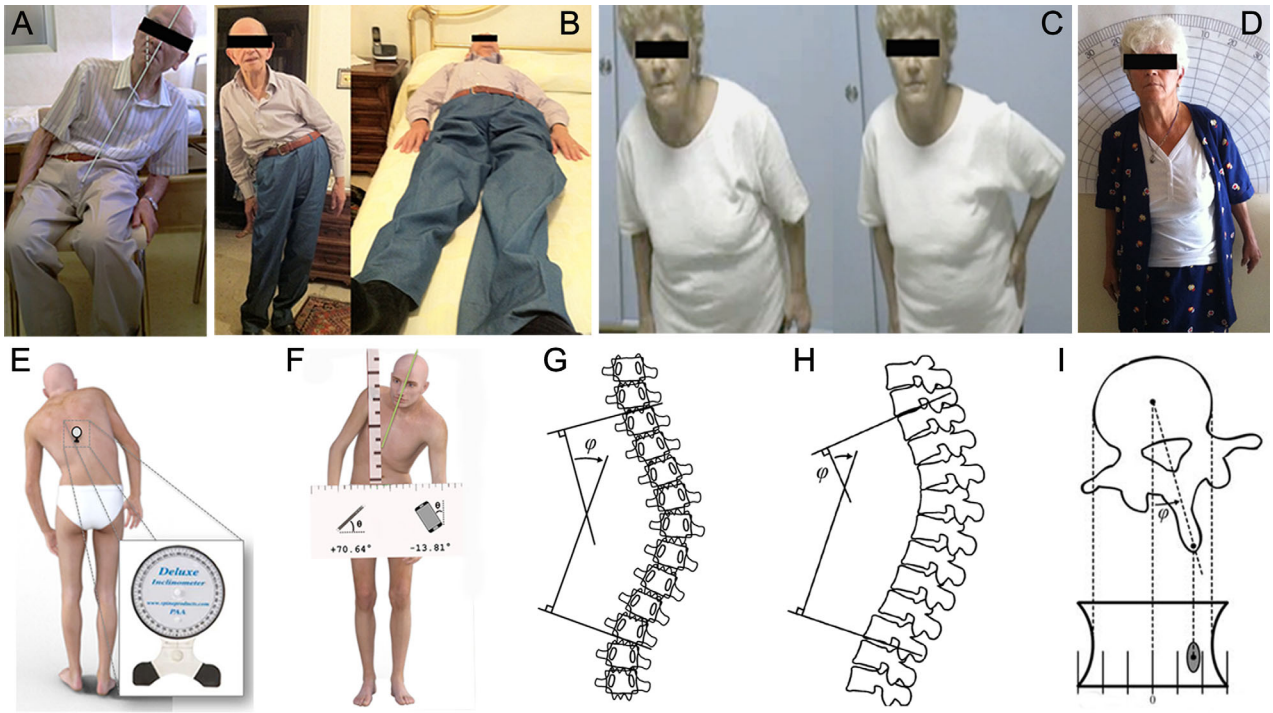

FIG. 1. A patient with Pisa syndrome (PS) without (A) and with (B) head realignment. Although PS is typically reverted by supine position, some patients present the combination of PS (reversible) and structural spine deformities (irreversible). Panel B shows a PD patient with a longstanding history of scoliosis preceding the onset of PS whose posture is only partially ameliorated during the supine position. PD with PS may have a sensory trick (touching one hip; C) feature supporting dystonic aetiology. (D) PS measured with a wall goniometer, (E) with an inclinometer, (F) with a smartphone app (Angle Meter©). (G) Two-dimensional (2D) coronal image according to Cobb's method, (H) 2D sagittal image according to modified Cobb's method, and (I) 2D axial image to evaluate axial rotation according to Cobb's method. [Color figure can be viewed at wileyonlinelibrary.com]

subacutely with rapid progression within days or weeks.[54] The latter has been mainly associated with medication adjustments (either dose reduction or increase). A typical example is the acute presentation after exposure to neuroleptics, which can be improved with anticholinergic treatment.

In both conditions, PS patients generally lean toward one side while sitting, standing, and walking.[49] They also can have impaired perception of their vertical position (awareness)[49] and sometimes do not adopt head compensation behavior to correct the alignment of visual input (Fig. 1A,B). Low back pain[55] and unsteadiness that leads to falls[30] can also occur.

Diagnosis

PS diagnosis is based on the clinical evaluation of trunk lateral displacement, which is the first sign of postural misalignment reported by patients and their caregivers. It can be easily tracked in clinical practice with the use of a wall goniometer (Fig. 1D), inclinometer (Fig. 1E), or even with smartphone applications (Fig. 1F). Theoretically, a radiograph of the patient's spine while standing is the most accurate method to assess the angle of curvature in the coronal and sagittal planes according to the Cobb angle (Fig. 1G) and its modified version (Fig. 1H). Although there is no consensus on the diagnostic criteria for PS, at least 10° in lateral flexion should be considered a criterion.[49,52]

Patients should be appropriately exposed and all body segments thoroughly examined. A radiograph (standing and supine positions) should be obtained to rule out structural bone changes and scoliosis and to evaluate vertebral rotation (Fig. 1I).[56,57] A distinguishing clinical clue is that scoliosis does not (or partially) resolve in the lying position; clinicians should be aware of the possible coexistence of both scoliosis and PS (Fig. 1B). Adult scoliosis is defined as a spinal deformity in a skeletally mature patient with a Cobb angle greater than 10°[58] and vertebral rotation. Although there are many known causes of spinal deformity in the adult, PS in PD may be concomitant with scoliosis deformities in some circumstances (Fig. 1B).

Pathophysiology of PS

The bulk of the literature on PS pathophysiology derives from animal model studies (reviewed in ref. [53]) and clinical data in PD patients. Although a detailed discussion of animal model studies is beyond the scope of this review, the animal evidence available so far

points toward the role of an asymmetric functioning of the nigrostriatal dopaminergic projections.[53] Overall, PS is the result of a multifactorial process involving both central and peripheral mechanisms,[49] as detailed below.

Central Mechanisms

Central mechanisms refer to basal ganglia dysfunction, abnormal sensorimotor integration, and cognitive dysfunctions affecting the body schema perception and postural control.[30,31,49] PS can be seen after neuroleptic exposure[1,2] or in PD after the introduction/withdrawal or modification (increase/decrease) of dopaminergic and nondopaminergic medications (Table 1).[37,39,54,59,60] Furthermore, numerous clinical observations support the role of basal ganglia loop imbalance in the development of PS in PD. It is not clear, however, whether patients lean toward to the more- or the less-affected side.[52,53] PD patients with PS show greater motor asymmetry than PD patients without PS.[26] Basal ganglia involvement is further supported by the occurrence of PS after basal ganglia surgery.[45,46,61]

Other underlying mechanisms might be involved. For instance, PS may occur as a side effect of cholinesterase inhibitors and can improve after contralateral[62] or ipsilateral[63] stimulation of the pedunculopontine (PPN), one of the principal cholinergic nuclei involved in regulating the postural tone,[64,65] which may also explain why PS diminishes in the supine position.[53] Nonetheless, no conclusive evidence has been provided thus far and the only pathology report of a PD patient with PS found no significant basal ganglia asymmetry or brain stem involvement.[29]

PS may be seen as a form of trunk dystonia.[66] Dystonia may typically improve with sensory tricks (or geste antagoniste), a phenomenon seldom reported in PD patients with PS (Fig. 1C). Bonanni and colleagues[25] reported a pattern of continuous muscle activity compatible with dystonic contraction in the lower paraspinal muscles ipsilateral to the bending side. In contrast, Di Matteo and colleagues[28] observed continuous muscle activity contralateral to the bending side in the majority of their patients and dystonic contraction ipsilateral to the bending side in only a few. The same group distinguished 2 further subtypes in patients with hyperactivity of the lumbar paraspinal muscles ipsilateral to the leaning side: with thoracic paraspinal muscle hyperactivity ipsilateral to the trunk leaning side or with hyperactivity of the contralateral thoracic paraspinal muscles.[27] In addition, nonparaspinal muscles were found to be hyperactive, such as external oblique and rectus femoris.[27]

The variability of these findings might be a result of the implementation of different methodological approaches[26-28,67] and the lack of information on the level of EMG exploration.[25] Rigidity has been suggested as one of the common mechanisms leading to abnormal postures in PD patients.[68] Patients with PD were found to have a higher axial muscle tone than controls,[69] a remarkably reduced range of trunk movement around the axial axis,[70,71] and a reduction of intersegmental flexibility and ability to react against induced external perturbations.[72,73] Burleigh and colleagues[74] reported that dopamine depletion results in increased muscle tone in the stance condition, which can contribute to postural change.

Sensorimotor integration deficits have been suggested as a key factor in the pathophysiology of PS. Postural control is a complex function involving body orientation and stabilization[75] and requiring the integrity of sensory information coming from different sources such as proprioception, vision, and the vestibular system. In fact, PD patients are impaired not only in both postural orientation and postural stabilization[76,77] but also in the interaction between these 2 systems.

Although the classic stooped PD posture may itself produce postural instability,[78] it can also be seen as a part of a protection mechanism against backward-directed postural instability and falls.[78] By contrast, PS only increases postural instability in the static condition. In fact, static stabilometric assessment of patients with PD and PS showed a significantly greater velocity of center-of-pressure displacement in the anteroposterior and mediolateral directions when compared with PD patients without PS or age-matched controls.[30] Interestingly, PS does not seem to affect gait performance, suggesting that postural instability is quite preserved in dynamic conditions.[30] This probably reflects the presence of compensatory systems mainly relying on visual inputs. Accordingly, 1 study found that PS patients display a veering gait when asked to walk with eyes closed.[51] This observation is also in line with the notion that patients with PD make greater use of visual information for postural control than healthy participants.[30] When compared with healthy participants, postural sway velocity and frequency are increased in PD patients and in those with PS, with a worse performance in the eyes-closed condition.[30,76] The use of visual information improves the postural performance of PD patients in terms of both the orientation and stabilization of the upper body segments.[76,79]

Taken together, these findings suggest that although impairment of the proprioception system in patients with PD and PS may exist, a possible deficit in somatosensory integration processes may contribute to the development of further balance disorders.[80] Interestingly, PS patients are sometimes unaware of their posture and do not even correct the horizontal axis of the visual field by tilting their head (Fig. 1A).

Regarding the vestibular component, early studies did not enlist the notion of a dysfunction in the vestibular system to explain postural deficits in PD.[81] Although the otolithic system provides information about the vertical pull of gravity, the accurate perception of body orientation under quasi-static conditions depends largely on somatosensory rather than otolithic information. In contrast, vestibular feedback is thought to be more useful in dynamic situations.[82] Nevertheless, Vitale and colleagues[32] suggested that patients with PD and PS may have a vestibular impairment that they explained as a sort of peripheral unilateral vestibular hypofunction associated with damage of the vestibular pathways.

Other findings posited that an alteration of the subjective visual vertical (SVV) can, at least in part, explain the deficit in vestibular function with an alteration in somatosensory integration in PD.[33] It has been proposed that SVV results from the vectorial summation of the weighted influences of gravitational forces, which are perceived by the otolithic vestibular system, the perceived longitudinal body axis, and visual references to verticality cues.[83] PD patients with and without PS suffer from a SVV deviation when compared with healthy controls. This SVV deviation might be explained as a result of a primary perceptual dysfunction and as alterations of internal models of verticality involved in the reweighting of perceptual afferences.[33]

Finally, because a complex relationship exists between postural control and cognition in the elderly, postural control deficits have been variably associated with cognitive dysfunctions also in PD.[84] Recently, a significant association between PS and attentional and visuo-perceptual deficits was documented in patients with PD.[31] It has been suggested that the occurrence of PS may be associated with deficits in the fronto-striatal system and posterior cortical areas.[31]

Peripheral Mechanisms

Peripheral mechanisms refer to alterations of the musculoskeletal system such as myopathy and degenerative spinal and soft tissue changes.[49] Previous studies have suggested that muscle atrophy and fatty degeneration, investigated by computerized tomography (CT), can occur or be more prevalent in the bending side with a craniocaudal gradient.[26] Recently, it has been reported that atrophy and fatty degeneration, investigated by MRI, occur not only ipsilateral but also contralateral to the trunk-leaning side.[27] A possible explanation could be that atrophy with fatty degeneration might be caused by secondary mechanisms as a result of stretching stress on the muscle contralateral to the bending side. In contrast, muscle disuse or atrophy is mainly ipsilateral to the trunk-leaning side.[27] Fat involutions can also be observed in both sides.

Whether muscle degeneration is a consequence of or 1 of possible concomitant causative factors for PS remains unclear.[26,27] It is interesting to note, however, that also in other postural deformities, such as camptocormia, paraspinal myopathy confirmed by muscle biopsy has been found in up to 64% of patients.[85] Moreover, it has been reported that many patients with PD and postural deformities may have a history of back surgery, trauma, degenerative spinal conditions, or associated medical conditions (osteoporosis and arthrosis). These associations have been reported especially in patients with camptocormia[49] and recently confirmed also in PS.[52] These concomitant factors of PS may potentially cause postural deformities by affecting the soft tissues and bones. Importantly, axial skeletal deformities occur in PD patients with long-standing, moderate-to-severe PS, and a large proportion of the scoliosis observed in PS patients is mainly related to a collapse or impaired postural tone rather than bony changes.[86]

Back pain is a frequent complaint of PS patients, found in 70.6% of the largest series published so far.[52] Pain affects up to 85% of PD patients, and most frequently involves the lower limbs.[87] To date, pain has received little attention with regard to its potential consequences on motor symptoms in PD[55] and little is known about its effects on postural stability and misalignment. The compensatory postures that patients adopt to temporarily relieve pain may negatively influence the proprioceptive and vestibular systems in the long term, leading to an abnormal body scheme.[49] In chronic conditions, moreover, pain can be associated with an adaptation in motor behavior that involves the redistribution of activity within and between muscle groups as well as changes in mechanical behavior. On one hand, this redistribution of muscle activity may protect against further pain (or injury) and may be complementary, additive, or competitive, with positive short-term benefits. On the other hand, the long-term consequences of these altered patterns include peripheral changes such as decreased range of movement and variability and increased load on the spine and/or lower limbs.[88]

Pharmacological and Nonpharmacological Approaches to the Management of PS

To date, the paucity of pharmacological and rehabilitative interventions for PS makes its management even more difficult in clinical practice. To improve the clinical management of PS (with a particular emphasis in PD patients), we propose an evidence-based

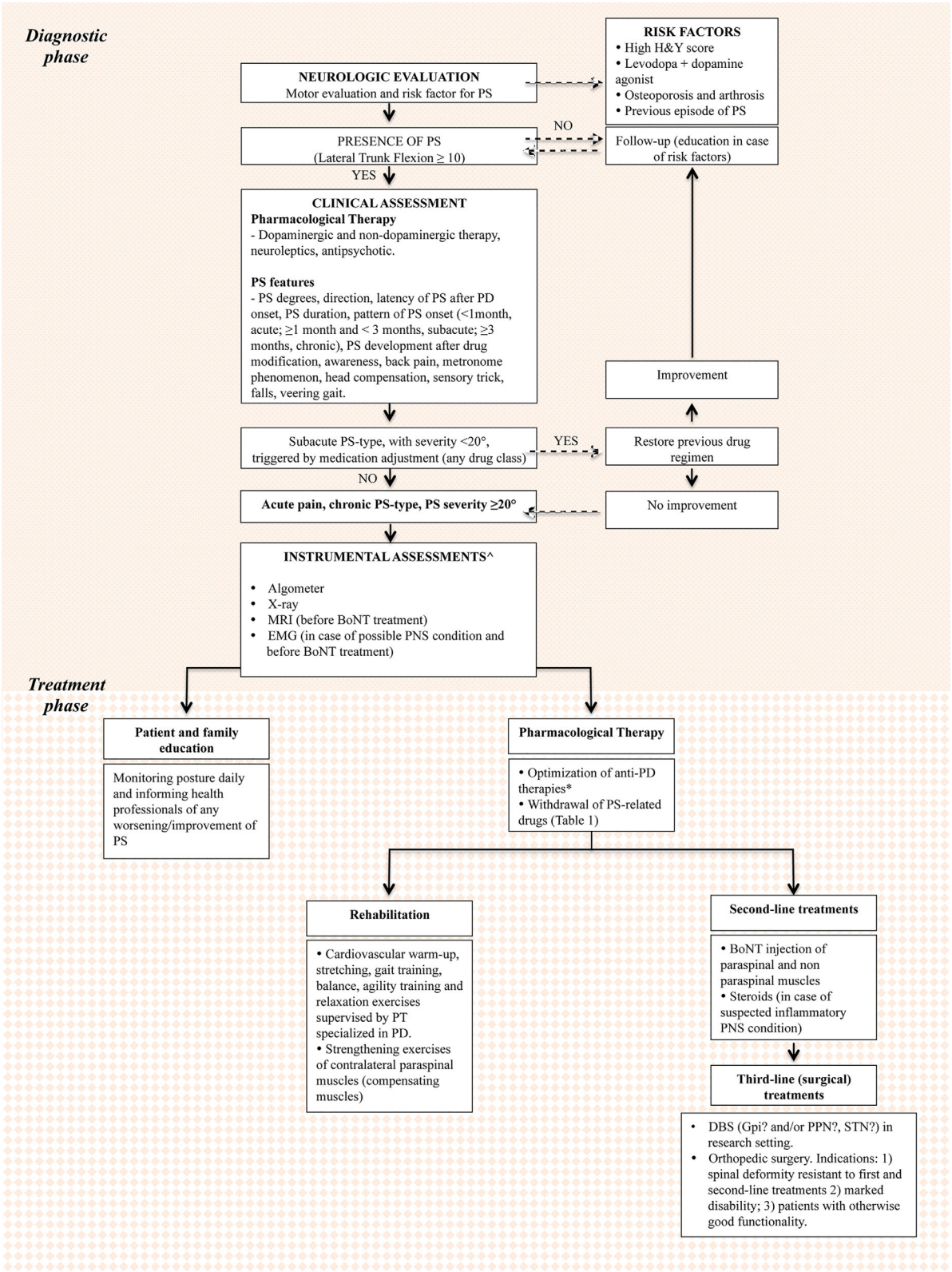

FIG. 2. Our proposed algorithm describing the various steps in managing Pisa syndrome (PS) in patients with PD. Abbreviations:^, to be considered in selected patients or in a research setting; *, both an increase and reduction of L-dopa might be considered because PS can be a result of either too little or too much dopaminergic stimulation. In keeping with what seen in antecollis, withdrawing dopamine agonists might be another option to consider; PS, Pisa syndrome; PD, Parkinson's disease; H&Y, Hoehn & Yahr Stage; MRI, magnetic resonance imaging; BoNT, botulinum toxin; EMG, electromyography; PNS, peripheral nervous system; PT, physical therapist; DBS, deep brain stimulation; STN, subthalamic nucleus; PPN, pedunculopontine nucleus; GPi, globus pallidus pars interna. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 2. Rehabilitation studies in patients with Parkinson's disease and Pisa Syndrome

Author	Capecci et al., 2014[94]	Tassorelli et al., 2014[91]	Bartolo et al., 2010[95]	Santamato et al., 2011[93]	Kataoka et al., 2013[96]
Study design	RCT	RCT	Open label	Case report	Case report
Sample size	n = 20 with anterior or lateral bending. Patients with lateral bending = 13 (PR = 4; PR + KT = 4; CG = 5)	n = 26. Rehab + placebo = 13; Rehab + BoNT = 13	n = 22	n = 1	n = 1
Age, y	PR = 66.8 ± 4.9 PR + KT = 73.4 ± 5.0 CG = 68.1 ± 5.6	Rehab + BoNT = 73.9 ± 4.3 Rehab + placebo = 74.2 ± 5.1	71.9 ± 6.6	68	80
Disease duration, y	PR = 9.5 ± 7.4 PR + KT = 11.0 ± 4.4 CG = 9.6 ± 4.9	Rehab + BoNT = 10.2 ± 8.2 Rehab + placebo = 10.4 ± 10.1	7.9 ± 3.0	NA	8
PS duration	NA	Rehab + BoNT = 3.1 ± 1.9 Rehab + placebo = 3.0 ± 1.5	3.6 ± 2.3	NA	1
Rehabilitation program	Four weeks (3 days/week, 40 minutes) of patient-tailored proprioceptive and tactile stimulation, combined with stretching and postural reeducation. PR + KT = KT strips on trunk muscles	Five days a week, 4 consecutive weeks. Individual 90-minute daily sessions (cardiovascular warm-up, stretching exercises, strengthening exercises, overground gait training, balance training, relaxation exercises)	Same rehabilitation program described in Tassorelli et al., 2014[91]	Two hours/day, 5 days/week for 15 days; then 1 hours for 3 days/week for 3 months. Agility exercises, stretching exercise, pilates exercises (in "On Med,'' 1 hour after the regular morning dose). Rehab combined with BoNT	Two weeks (5 days/week, 1 hour/day). "Bridge"exercises and straight leg raising in supine position, stretching exercises, balance exercises, resistance-training exercises
Follow-up duration	One month; 2 months	t1 = end of hospitalization; t2 = 3 months; t3 = 6 months	3 months; 6 months	15 days; 3 months	15 days
Outcome Measures	Degrees of trunk bending in the sagittal and coronal planes, Berg Balance Scale, TUG	Kinematic analysis trough an opto-electronic system; degree of anterior flexion of the trunk; range of motion of the trunk on the 4 plans; FIM score. VAS score for pain	Kinematic analysis trough an optoelectronic system	Degree of trunk inclination. Trunk Dystonia Disability Scale (TDDS). VAS score for pain	Angle of lateral bending; TUG; gait time, step number; VAS score for pain; CT of paraspinal muscles
Pain	NA	Reduced at t1 and t2; decrease more pronounced at t1in the Rehab + BoNT group	NA	VAS from 7/10 (baseline) to 3/10 (15 days after Rehab+BoNT)	VAS from 77 mm (baseline) to 8 mm (15 days after rehab)
Main results	Reduced lateral bending (degrees) in PR vs CG and PR+KT vs CG at 1 month but not 2 months	Kinematic measures of lateral and trunk flexion improved only in Rehab + BoNT at T1 and T2. Range of motion of the trunk improved in both study arms	↓ trunk flexion and ↓ trunk inclination in the static condition up to 6 months. Improved range of trunk flexion and inclination up to 3 months.	Lateral inclination from 35° (baseline) to 15° (15 days after Rehab + BoNT). TDSS ↓ by 5 points at 15 days. No specific details provided at 3 months	Lateral inclination from 27° (baseline) to 4°(15 days after Rehab. Improvement of TUG, gait time, ↑ step number. ↓ thickness of paraspinal muscles at L1 and L2 level

KT, Kinesio Taping; NA, not applicable; BoNT, treatment with Botulinum toxin; PR, postural rehabilitation; CG, control group; CT, computed tomography; TUG, timed up ang go test; VAS, visuo-analogue scale.

algorithm of the various steps in managing PS in people with PD (Fig. 2). An updated summary of therapeutic procedures is reported next.

Pharmacological Approaches

PS may subacutely develop after any type of medication change,[3] sometimes also of anti-PD medications.[54] Therefore, the first step would be reverting whatever change has been associated to the onset of PS. When no change is associable, both an increase and reduction of L-dopa might be considered, because PS can be a result of either too little or too much dopaminergic stimulation.[39] In keeping with what seen in antecollis,[49] the slow withdraw of dopamine agonists might be another option. Particular attention should be paid to antipsychotic and cognitive enhancing treatments, because PS in non-PD patients has been frequently related to the use of dopamine receptor blockers or cholinesterase inhibitors.[2,50,59,89] Drug-induced PS predominantly develops in women and older patients with organic brain changes.[3] Sometimes it appears after the introduction of an antipsychotic or arises insidiously in antipsychotic-treated patients for no clear reason. This condition commonly disappears after the antipsychotic drugs are withdrawn. Although pharmacological therapy for drug-induced PS has not been established, it has been reported that anticholinergic drugs are effective in about 40% of patients who have episodes of drug-induced PS, with the remaining patients responding to withdrawal or reduction in daily doses of antipsychotic drugs.[3]

Botulinum Toxin

Treatment with botulinum toxin (BoNT) has been proposed in patients with PS based on its efficacy in those conditions characterized by excessive muscular hyperactivity.[90] Two Randomized clinical trials (RCTs) (n = 4 placebo/5 BoNT, crossover study[25]; n = 13 placebo + rehabilitation/13 BoNT + rehabilitation, parallel groups study[91]) and 2 case reports[92,93] suggest that BoNT may be a therapeutic option for PS, able to enhance the effect of rehabilitation treatment[91,93] (see also the following sections).

AbobotulinumtoxinA (100[93]-125[25] U per site; total dose 500[25]-600[93] U) and incobotulinum toxin (50 U per site; total dose 100 U[92]; 50-200 U[91]) were employed after preliminary EMG evaluation (except for 1 study[92] and with different injection strategies (fixed a priori vs individually selected). Bonanni et al.[25] injected the paraspinal muscles ipsilateral to the bending side at the L2-L5 level, previously found to be hyperactive at EMG in those patients in whom bending was only lateral and fulcrum was at the L2-L5 level. Yet, Tassorelli and colleagues[91] used preliminary EMG of the paraspinal, abdominal, and iliopsoas muscles, injecting those muscles in which involuntary tonic activity longer than 500 ms was detected; accordingly, the most frequent hyperactive and injected muscles were the iliopsoas and the rectus abdominis, which often required bilateral injections.[91]

Overall, although BoNT seems to be a valid option in some patients with PD, definite conclusions should be drawn with caution given the small number of patients reported, the unclearness on predictive factors of response, and the heterogeneity in muscle selection and injection technique.

Rehabilitation

Rehabilitation programs should be preferred to surgical approaches, which might also lead to additional peripheral complications.[86] Two randomized controlled studies,[91,94] 1 open-label study[95] and 2 case reports,[93,96] have provided evidence that motor rehabilitation is an effective tool for PD patients with PS. Details on sample size, rehabilitation program, outcome measures, and the main results are reported in Table 2.

Rehabilitation programs reported are heterogeneous, but they share the concept of high intensity with 4 to 5 days a week for 2 or 4 weeks. Moreover, in 2 studies rehabilitation was combined to BoNT[91,93] and in 1 to Kinesio Taping[94] (KT). In the RCT by Tassorelli et al.,[91] the effect on kinematic trunk measures were more pronounced for both lateral and anterior bending when rehabilitation was associated to BoNT (Table 2). In another study, the add on of KT to rehabilitation did not further improve the positive outcome produced by rehabilitation alone.[94] Regarding the type of rehabilitative program, stretching exercises were included in all of the studies,[91,93,95,96] whereas proprioceptive and tactile stimulation, postural re-education through active movement execution,[94] or strengthening exercises and concomitant balance and gait training[95] were included in a few studies. The duration of the benefit of the rehabilitation program was assessed during a maximal period of 6 months, with most of the outcome measures improving up to 3 months and waning at 6 months.[91,94,95] Finally, only 2 case reports[93,96] and 1 RCT[91] evaluated the effect on pain and demonstrated a significant improvement by visuoanalog scales.

In conclusion, in carefully selected patients under the care of expert hands, rehabilitation is a valid procedure to restore mobility in PS patients. Still open is what specific intervention has the greatest chance to improve postural realignment and for how long the program should last. In our opinion, a structured exercise program to strengthen of contralateral paraspinal muscles, which has been supposed to play a compensative role, may represent a promising strategy.[27]

Surgical Treatment

Most of the existing studies investigating the effects of deep brain stimulation (DBS) on postural deformity are related to camptocormia,[97-101] whereas a few have addressed PS. Preliminary data suggest that postural abnormality in patients with PD may be ameliorated by subthalamic nucleus (STN) deep brain stimulation (DBS).[101] The clinical course of 18 patients with significant postural abnormality (score ≥ 2 on item 28 of the UPDRS III) that underwent bilateral STN DBS was reviewed. A total of 8 patients suffered from camptocormia and the remaining 10 patients were considered to have PS. Most patients had significant motor fluctuations as a result of L-dopa therapy. Of 13 patients with moderate postural abnormality (score of 2 on item 28 UPDRS III), 9 improved soon after surgery. One patient relapsed, and 2 patients improved gradually over time, whereas 2 patients showed no improvement. Of 5 patients with severe postural abnormality (score of 3 or 4 on item 28 of the UPDRS III), 2 improved slightly in the long-term follow-up period, whereas the remaining patients did not improve at all.[101]

Recently, Shih and colleagues[62] described a progressive improvement of PS and asymmetric bradykinetic gait in a 62-year-old woman with right PS and postural instability after left PPN DBS. Ricciardi and colleagues[63] showed that unilateral PPN stimulation provides short-term benefits in PS. A patient with PD developed subacute PS toward the right side. After several pharmacological attempts, ipsilateral PPN DBS was offered. The motor condition was videotaped before surgery and then 6 months after surgery and

assessed by a blinded examiner by means of the motor part of the UPDRS. A wall goniometer was used to assess posture in the sagittal and frontal planes. At postsurgical assessment, except for improvement in PS, no other relevant changes in the UPDRS III scores were noted. During the following years, the patient's posture progressively worsened, as did his motor and cognitive functions.

Spinal surgery might represent a further option for complex spinal deformities that are not responsive to conservative management. However, no high level of evidence is available, and surgery might be associated to high rates of mechanical complications necessitating subsequent revision surgery. Therefore, only very well-selected patients might be candidates for this type of surgery.[102]

Conclusions

The literature is conspicuous for the scarcity of reports on multidisciplinary approaches to PS. Multiprofessional management involving medical specialists (eg, neurologists, physiatrists, psychiatrists) and rehabilitation experts (eg, physical therapists, psychologists) might allow for the development of a comprehensive strategy to address PS, beginning with diagnosis and continuing through to treatment.[103] Furthermore, both pharmacological and nonpharmacological interventions (ie, rehabilitation) should be considered as integral parts of a comprehensive and integrated management plan to improve a patient's quality of life.[91,103,104] Despite evidence supporting the importance of optimizing drug therapy as the first level of intervention, many issues on diagnosis and the best treatment option for managing PS remain open. ■

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