

Pisa-Like Syndrome Under Baclofen in a Patient With Spastic Hemiparesis due to Ischemic Stroke

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Abstract: In its original description, Pisa syndrome was reported as an iatrogenic dystonia of the trunk caused by neuroleptic drugs. However, sometimes, not dystonic lateral flexion of the trunk is described as Pisa syndrome. These observations support the possibility of a drug-induced lateral flexion of the trunk with clinical presentation similar to Pisa syndrome, although with a different etiology and pathophysiology. Here, we describe the case of a male patient, with a previous ischemic stroke and residual spastic hemiparesis to the right side, who subacutely developed a dramatic lateral flexion of trunk (approximately 45° to the right) a few days after the introduction of Baclofen (5 mg 3 times per day). After the discontinuation of baclofen, a full recovery of the correct posture was obtained. In this respect, our case is paradigmatic: it is drug-induced but not clearly dystonic in its manifestation. Baclofen reduces the spasticity depressing the monosynaptic and polysynaptic reflex in the spinal cord by stimulating Gamma-aminobutyric acid B (GABA-B) receptors, which inhibit the release of excitatory amino acids, glutamate and aspartate. We believe that the definition of Pisa syndrome for these forms, not clearly dystonic, might be not completely appropriate, but they should be defined more correctly as Pisa-like syndromes.

Key Words: Pisa syndrome, spastic hypertonia, ischemic stroke, baclofen (*Clin Neuropharm* 2015;38: 217–219)

The term Pisa syndrome is used to indicate a particular postural deformity characterized by a marked lateral flexion of the trunk, which is typically mobile and resolves, for example, on lying down.¹ The first report on Pisa syndrome was about the onset of an acute truncal dystonia or pleurothotonus, occurring as a side effect in 3 elderly women affected by presenile dementia and treated with antipsychotic treatment.²

Subsequently, descriptions of patients affected by Pisa syndrome have also been reported in patients receiving other drugs, in those with neurodegenerative diseases, or in idiopathic cases.^{3–6}

More recently, Pisa syndrome has been described in patients affected by Parkinson disease (PD).^{7,8}

In PD patients, the onset of Pisa syndrome is often subacute, after a modification of antiparkinsonian therapy, such as the increase in dopaminergic treatment dosage or the introduction of a

novel treatment (ie, dopamine agonists, rasagiline, cholinesterase inhibitor, Catechol-O-methyl transferase [COMT]).^{7–13}

Although a cholinergic-dopaminergic imbalance in Pisa syndrome was initially supposed, the nature of the lateral truncal flexion is still controversial both regarding pathophysiology and its suggested dystonic features.^{1,14} In this scenario, the underlying pathophysiological mechanisms probably involved in the development of Pisa syndrome are probably much more complex than oversimplified models.

In this paper, we present a paradigmatic clinical case documenting as an iatrogenic lateral flexion of the trunk should not always be considered as a simple dystonic phenomenon, because dopaminergic-antidopaminergic drugs are not the only cause of postural disorders, and suggesting that other pathophysiological mechanisms should be investigated.

CASE REPORT

A 77-year-old male patient recently came for our observation of a subacute onset of a dramatic lateral truncal flexion of approximately 45° to the right (Fig. 1). This pathological lateral inclination of the trunk appeared a few days after the introduction of baclofen (5 mg 3 times per day). His medical history revealed that the patient suffered an ischemic stroke in left middle cerebral artery territory which resulted in right body spasticity observed 3 years before. With the aim to reduce spasticity, baclofen was prescribed, although the patient developed a lateral flexion of the trunk. The neurological examination showed mild weakness (Medical Research Council Scale for Muscle Strength was 4) and minimal spastic hypertonia of the right leg, homolateral hyperreflexia, and hypotonia of extensor trunk muscles, probably responsible of the lateral flexion. Neurological examination was negative with regard to any symptom or clinical sign of extrapyramidal disease, and any intake of other known drugs able to induce lateral flexion of the trunk was excluded. Also, his family history was negative for movement disorders. For this reason, baclofen was immediately suspended.

After the discontinuation of baclofen was carried out in about a week, the full recovery of the correct posture and the subsequent disappearance of lateral flexion attitude were obtained, proving a close relationship between drug and adverse effect (Fig. 2).

DISCUSSION

The fact that lateral trunk flexion is not synonymous of Pisa syndrome is actually an acquired concept. In fact, lateral deviations of the trunk include both Pisa syndrome and scoliosis.^{14,15} In this regard, whereas several forms of lateral truncal flexion are clearly associated with osteoarticular disorders, in our patient, there was a clear drug-related genesis, as in the case of classical Pisa syndrome.

However, the present case differs substantially from previous clinical findings, which support the role of an imbalance in basal ganglia functioning in the pathogenesis of Pisa syndrome. Indeed, according to previous observations, the contribution of

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dopaminergic pathways in the pathogenesis of Pisa syndrome is supported by the description of its occurrence after antidopaminergic drugs exposure,^{2,3} or in PD patients, by the introduction, increase, or reduction of dopaminergic medications, which can induce or reverse Pisa syndrome.^{7–13,16} These findings have been used to hypothesize that the asymmetry in the basal ganglia output might contribute to the appearance of the lateral flexion.¹⁶ Thus, according this hypothesis, the modification of the dopaminergic treatment might modify the striatal balance and lead directly to asymmetric regulation of postural muscle tone through the basal ganglia-brainstem system.¹⁴

Notwithstanding the present case, the sudden development of the lateral trunk flexion does not suggest a primitive asymmetrical imbalance in the basal ganglia output, but could be probably determined by an acute imbalance of pyramidal muscle tone (corticospinal pathway) provoked by the introduction of baclofen. It is useful to remember that spasticity is a very important compensation mechanism which follows the flaccidity of acute injury of cortical-spinal pathway (which represents the maximum functional disability). After a mild to moderate impairment of cortical-spinal pathway, the onset of spasticity often helps the recovery of erect posture and walking. In this context of compensation obtained with the increase of spasticity, the acute effect of baclofen could have modified the equilibrium. In fact, patients with hemiplegia do not usually develop Pisa syndrome, suggesting that baclofen's action should be considered as the key factor in its appearance in this patient. With this regard, baclofen reduces the spasticity depressing the monosynaptic and polysynaptic reflex in the spinal cord by stimulating GABA-B receptors, which inhibit the release of excitatory amino acids, glutamate, and aspartate. An antispasmodic effect in particular patients and in functionally injured districts can lead to functional damage, leading to an abnormal flexion posture of the trunk, clinically similar to the Pisa syndrome, but pathophysiologically different.



FIGURE 1. The patient with Pisa Syndrome during baclofen administration.



FIGURE 2. The same patient after baclofen discontinuation.

Interestingly, previous animal studies indicated that GABA-B receptors in the substantia nigra pars reticulata, but not the substantia nigra pars compacta, may play a major role in the control of nigrostriatal dopamine activity and the release of dopamine in the striatum.¹⁷

Nevertheless, baclofen administered orally has a poor ability to pass the blood-brain barrier, and thus this effect might be likely in human patients treated by intrathecal administration of baclofen. However, we cannot exclude that Pisa Syndrome could be partially dystonic in its origin because of the fact that clinical picture and the time course of the phenomenology might be compatible with a form of acute drug-induced dystonia and that the same baclofen could have played a secondary effect at this level. Unfortunately, a neurophysiological study on trunk muscles, probably helpful in the identification of electromyographic pattern, was not performed.

In conclusion, the lateral flexion of the trunk in our patient, which is only clinically similar to classic Pisa syndrome, supplements the knowledge concerning different physiopathological genesis of this disorder of posture. For a clearer nosological and pathophysiological distinction, we believe that these not clearly dystonic forms of lateral flexion of the trunk, with entirely different physiopathological bases from classical dystonic Pisa syndrome, might be called “Pisa-like syndrome.”

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