

## Letter to the Editor

# Hemodiafiltration for Intoxication with Lithium Unmasking Its Anti-Parkinsonian Effect

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From lithium it is known that it exhibits an anti-Parkinson effect [1]. Accordingly, smokers develop less frequently Parkinson's Disease (PD) than the non-smoking population [2]. This is because tobacco contains a significant amount of lithium [3]. The anti-PD effect of lithium is explained by increased autophagy and reduction of intracellular  $\alpha$ -synuclein [3]. Lithium inhibits GSK-3 $\beta$  and consequently increases the  $\beta$ -catenin activity [4]. Development of a Parkinson crisis due to flushing out of lithium by Hemodiafiltration (HDF), as in the following case, has not been reported.

The patient is a 63 years male (height 180cm, weight 75kg) who was living with his mother in a retirement home and developed fever since 4 days prior to admission. His previous history was positive for psychosis, bipolar disorder, arterial hypertension, chronic renal failure, chronic obstructive pulmonary disease, diabetes, bilateral hydrocele, prostate hypertrophy, polyneuropathy, lithium intoxication, and hyperlipidemia. He had the diagnosis of a questionable extra-pyramidal syndrome but no anti-Parkinson medication. His home medication included aripiprazole (400 mg/once every 30 d), biperiden (8 mg/d), midazolam (0.25 mg/d), lithium (900 mg/d), quetiapine (50 mg/d), trazodone (75 mg/d), nebivolol (2.5 mg/d), metformin (850 mg/d), simvastatin (20 mg/d), tamsulosin (0.4 mg/d), fenoterol with ipratropium-bromid, and tiotropium plus olodaterol.

On admission (hospital day-1 (hd1)) he was comatose, had spontaneous resting tremor, and arterial hypotension (80/40 mmHg). Blood tests revealed hypokaliemia, hypernatremia, and renal insufficiency (Table 1). The swab test for SARS-CoV2 was negative. ECG showed AV-block-I, right bundle-branch-block, and QT-prolongation (501 ms). X-ray of the lung was normal. Clinical neurologic exam on hd2 revealed somnolence, pain upon maximal passive anteflexion of head, nuchal rigidity, ptosis, ophthalmoparesis, spontaneous myocloni all over the body, mild rigidity of all extremities, reduced tendon reflexes on the lower limbs, and clonus of the left lower leg (Table 1). Cerebral CT-scan was non-informative. He was treated with fluid substitution, cefuroxime, levetiracetam (LEV) (1000 mg/d), and discontinuation of all psychiatric medication.

Since EEG on hd3 showed a myoclonic state, valproic acid (VPA) was added to LEV. Myocloni resolved but occasionally, generalized tonic-clonic seizures occurred, which responded to lorazepam. Since the lithium serum level was increased to 1.57 mmol/L (n, 0.6 mmol/L to 1.0 mmol/L) on hd3, lithium intoxication was diagnosed and HDF was begun. Under this regimen serum lithium levels successively became normal on from hd4 (Table 1). Clinical neurologic exam on hd4 surprisingly revealed an akinetic Parkinson crisis with massive, generalized rigidity, inability to voluntarily move head or limbs or open the mouth despite discontinuation of all neuroleptic drugs (Table 1). L-DOPA had a beneficial effect. The patient could be discharged without seizures, PD manifestations, or electrolyte disturbances on hd36. Lithium remained discontinued.

The presented patient is educative for several aspects. First, lithium had obviously an anti-Parkinson effect, as lowering the serum lithium level by HDF induced a massive PD crisis. Second, lithium intoxication manifested with coma, resting tremor, hyperthermia, lower-leg clonus, generalized myocloni, and generalized tonic-clonic seizures. Third, discontinuation of psychiatric medication and application of L-DOPA resulted in complete resolution of the Parkinson crisis. Whether ptosis and ophthalmoparesis were due to myopathy or myasthenia, triggered by the lithium intoxication, as

**Table 1:** Findings on clinical neurologic examination and laboratory investigations before and after HDF.

	Before HDF (hd2)	After HDF (hd4)
Consciousness	comatose	somnolence
Myocloni	generalized	none
GTCS	yes	none
Clonus	left lower leg	none
PD	mild	severe
Opening of mouth	possible	impossible
Neck rigidity	mild	severe (inability to move head)
Rigidity of limbs	mild	severe
Hypokinesia	mild	severe
Resting tremor	yes	yes
Reduced DTR	yes	yes
Ptosis	yes	yes
Ophthalmoparesis	yes	yes
EEG	myoclonic state	no paroxysmal activity
Potassium (3.4-4.5mmol/l)	4.9mmol/l	3.8mmol/l
Sodium (136-145mmol/l)	150mmol/l	145mmol/l
Creatinine (0.7-1.2mg/dL)	1.8mg/dL	0.68mg/dL
Lithium (0.6-1.0mmol/L)	1.57mmol/L	0.74mmol/L

GTCS: Generalized Tonic-Clonic Seizures; PD: Parkinson's Disease; DTR: Deep Tendon Reflexes

previously reported [5], remains speculative.

**Keywords:** Lithium; Hemodiafiltration; Parkinsonism; Psychosis; Extra-pyramidal symptoms

### Author Contribution

JF: design, literature search, discussion, first draft, critical comments: literature search, critical comments, revision.

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