P84

Sex differences in levodopa pharmacokinetics in levodopa-naïve patients with Parkinson's disease

Maria Claudia Russillo[1], V. Conti[2], V. Izzo[2], M. Picillo[1], M. Amboni[3], C.L. Scaglione[4], A. Nicoletti[5], I. Cani[4], C.E. Cicero[4], E. De Bellis[2], B. Charlier[2], V. Giudice[2], G. Somma[1], G. Corbi[6], P. Barone[1], A. Filippelli[1], M.T. Pellecchia[1]

[1]Center for Neurodegenerative Diseases (CEMAND), Department of Medicine, Surgery and Odontology "Scuola Medica Salernitana", University of Salerno, Salerno, Italy
[2]Clinical Pharmacology Unit, Department of Medicine, Surgery and Odontology "Scuola Medica Salernitana", University of Salerno, Salerno, Italy
[3]Movement Disorders Centre, Hermitage-Capodimonte, Naples, Italy
[4]IRCCS "Istituto delle Scienze neurologiche di Bologna", UOC Neurological Clinic, Bellaria Hospital, Bologna, Italy
[5]Department of Medical, Surgical Sciences and Advanced Technologies, GF Ingrassia, Neurologic Unit, AOU "Policlinico-San Marco", University of Catania, Catania, Italy
[6]Department of Medicine and Health Sciences, University of Molise, Campobasso, Italy

Introduction: Levodopa (LD) is the most effective drug in the treatment of Parkinson's disease (PD) [1]. Women seem more prone to develop LD prolonged use related complications, such as motor/non motor fluctuations (MNMF) and dyskinesias (DYS) [2]. Nonetheless, there is a paucity of prospective studies examining gender-related predictors of MNMF and DYS. Among several factors, which concur with a very complex scenario, changes in LD pharmacokinetics influence the drug effectiveness.

Objective: To assess gender-related differences in LD pharmacokinetics in PD patients at their first ever intake of LD.

Methods: This multicentric study enrolled LD-naïve PD patients who received a single dose of LD/benserazide (100/25 mg) formulation. To measure plasma LD concentrations and pharmacokinetic parameters (AUC, Cmax, Tmax, t1/2), fasting blood samples were collected before drug intake and then at 8 time points until 260 minutes. LD concentrations were measured by ultra-high performance liquid chromatography coupled with mass spectrometry. Multiple linear regression analyses were performed to identify the predictors of the parameters.

Results: 35 patients (16 women and 19 men) were consecutively enrolled. AUC and Cmax were significantly higher in women than men ($p=0.0006$ and $p=0.0014$, respectively). No statistically significant difference was found regarding Tmax and t1/2. Multiple linear regression analyses revealed that female sex ($p<0.0001$) and BMI ($p= 0.014$) significantly predicted AUC. Only female sex significantly predicted Cmax ($p =0.001$). Moreover, only BMI significantly predicted t1/2 ($p =0.017$). Stratifying by gender, BMI was confirmed to significantly predict t1/2 in women ($p =0.027$), but not in men.

Conclusions: This study provides novel insights on gender differences in LD pharmacokinetics, possibly contributing to the later development of motor complications and dyskinesia in PD.

References:

[1] Abbott A. Levodopa: the story so far. Nature (2010) Aug 26;466(7310): S6-7.

[2] Zappia M, Crescibene L, Arabia G, Nicoletti G, Bagalà A, Bastone L, Caracciolo M, Bonavita S, Di Costanzo A, Scornaienchi M, Gambardella A, Quattrone A. Body weight influences pharmacokinetics of levodopa in Parkinson's disease. Clin Neuropharmacol. 2002 Mar-Apr;25(2):79-82.