

The Dark Side of Globalization: Lack of Universal Levodopa Availability

Marcelo Merello, MD, PhD* 

Based on initial reports, the prevalence of Parkinson's Disease (PD) was thought to be lower in Africa than in the rest of the world.¹ However, this remains unproven and reported ethnic differences might be due to under-diagnosis, the use of different diagnostic criteria or case-finding methods, and early mortality rather than real differences in disease prevalence.

In a way, the overwhelming disease burden of the “big three,” namely malaria, HIV, and TB,² as well of other infectious diseases in developing tropical and subtropical countries, has relegated healthcare for neurodegenerative disorders to a lower priority. Research papers from Sub-Saharan Africa, including Okubadejo et al.,³ published in the current issue, are an important step towards shedding more light on noncommunicable degenerative disorders in the region like PD, and in developing initiatives to improve patient access to treatment.

Almost 50 years have passed since the introduction of levodopa (L-DOPA) for the treatment of PD. Since then, it has proven to be the most effective antiparkinsonian agent available with no other medication or surgical procedure offering better results.⁴ Despite this fact, worldwide L-DOPA availability for individuals affected with PD is far from 100 percent and greatly varies between countries. Africa is probably one of the best examples of this disparity.

The first report on L-DOPA use in Africa dates from 1972, not long after it was first introduced, and referred to a five-year experience of 30 PD cases treated at an outpatient clinic in Nairobi, Kenya.⁵ With the exception of South Africa, current reports from similar geographic areas show little progress in L-DOPA availability and utilization in the continent since that time.^{6–8} At this pace, the target set by the WHO of 80% worldwide availability of affordable essential medicines, including generics to treat major noncommunicable diseases for both the public and private sector by 2025,² will not be reached in the case of PD unless urgent actions are taken.

Regrettably, not only in Sub-Saharan Africa, but also in South American Amazonia, L-DOPA is mostly unavailable or unaffordable. Reports from Bolivia indicate that, due to the unaffordability and unavailability of pharmaceuticals, patients frequently use powdered seeds from *Mucuna pruriens*, a traditional Ayurvedic Indian medicine, as a replacement or supplement for the pharmacological preparations of L-DOPA/DDI to treat Parkinsonism.⁹

Okubadejo et al. surveyed more than 100 pharmacies in the public and private sector in Nigeria to evaluate the availability of antiparkinsonian medications and found that in all categories private pharmacy stocks exceeded those of public sector establishments. The medications mostly available for PD treatment were: dopamine receptor agonists (DAS; 68.3%; predominantly ergot-derived bromocriptine), anticholinergics (56.1%; mostly trihexyphenidyl), and L-DOPA formulations (48%; mainly 250/25 L-DOPA/DDI). However, only two medications (trihexyphenidyl tablets and biperiden injection) were affordable according to the WHO definition, by which the lowest paid unskilled government worker (LPGW) should not have to spend more than one days' wages to purchase a 30-day supply of any standard treatment regimen.²

The results of Okubadejo et al. merit discussion on several levels, including (1) the only affordable medications for PD they found were anticholinergics; (2) the availability of L-DOPA was low both in the public and private sector; and, probably the most surprising and controversial, (3) even DAs were as unaffordable as L-DOPA and their availability was better in both the public or private sectors.

So the question is why are DAs, which are inferior to L-DOPA, offered at the same or higher cost, and why are they more frequently available? Also, why are six different types of DAs of comparable efficacy offered when no single L-DOPA generic is marketed? Whatever policies and interventions are used nationally, price transparency is vital, as it empowers

Movement Disorders Section, Neuroscience Department Fleni, Universidad Catolica Argentina (UCA). Consejo Nacional de Investigaciones Cientificas y Técnicas (CONICET)

***Correspondence to:** Prof Marcelo Merello, Institute of Neurological Research, Fleni, Montaneses 2325, 1428 CABA, ARGENTINA; mmerello@fleni.org.ar.

Keywords: Africa, dopamine receptor agonists, levodopa, Parkinson's disease. Relevant disclosures and conflicts of interest are listed at the end of this article.

Received 14 September 2018; accepted 22 October 2018.

Published online 16 November 2018 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mdc3.12704

governments when conducting medication procuring bidding and healthcare providers when prescribing antiparkinsonian medication. In this case, priority must be given to original formulations of L-DOPA and its lower-priced high-quality generics, as they represent indubitably the gold standard for treating PD.

The report underlined in particular how increased commitment is needed both from governments and others, to improve public access to essential antiparkinsonian medication. Policies designed to tackle prerequisites for new medication approval as well as promoting the use of first-line treatment are lacking in developing countries, as is a formal regulatory framework for negotiations between medication purchasers and medication manufacturers and pricing of new prescription medications within the context of particular local healthcare scenarios.

One example of an extremely well organized model from a developed country is the one put forward by The Drug Commission of the German Medical Association (DCGMA). This committee of scientific experts advises the German Medical Association on fundamental questions related to pharmaceutical policies. If a new medication offers no additional value over a previously available one, it is either not approved or, payers will reimburse for it only at prices currently paid for older existing medications or therapies, optimizing the use of available resources and guaranteeing patients both from private and public sectors receive the best and most cost-effective treatment.¹⁰

In 2012, the IP-MDS created a Task Force on Africa to address training, as well raise awareness and advocacy for better medication treatment in Sub-Saharan Africa. So far, in terms of medical education, the task force has made important advances. However, education will always clash with reality if policymakers are not included in the conversation; and if the relationship between private/public sector stakeholders and scientific societies and non-government organizations (NGOs) is not strengthened.

GAVI (Global Alliance for Vaccines and Immunization), the vaccine alliance, is a great example of the power of coordinated efforts to increase the availability of healthcare worldwide. In 1999, a coalition of UN member states, vaccine manufacturers, researchers, NGOs, and philanthropists was launched. It later received the name GAVI during the 2000 World Economic Forum at Davos.² Its main goals included increasing vaccination rates in poorer countries and maintaining predictable financing for global immunization. Perhaps, after 50 years of use in PD, and having proved its indubitable contribution to improving quality of life in individuals affected with the disease, the time has come to replicate the GAVI initiative for L-DOPA use in Africa and undeveloped countries of the world.

Author Roles

Research project: A. Conception, B. Organization, C. Execution; 2. Statistical Analysis: A. Design, B. Execution, C. Review and Critique; 3. Manuscript Preparation: A. Writing of the first draft, B. Review and Critique;

M.M.: 1A, 1B, 1C, 2A, 2B, 2C, 3A, 3B.

Disclosures

Ethical Compliance Statement: IRB approval and patient consent was not necessary for this work. The author has read the Journal's position on issues involved in ethical publication and affirms that this work is consistent with those guidelines.

Funding Sources and Conflicts of Interest: No specific funding was received for this work. The author serves as Co-Editor-in-Chief of Movement Disorders Clinical Practice.

Financial Disclosures for previous 12 months: MM discloses the following: Consultant for St. Jude/Abbott; Honoraria from Glaxo; Research grants from Glaxo, Allergan, TEVA, and CONICET; Royalties from Springer, Random House, Cambridge University Press, and Humana Press; Editor Honoraria from Wiley, and the Movement Disorder Society.

References

- Lombard A, Gelfand M. Parkinson's disease in the African. *Cent Afr J Med.* 1978; 24:5–8.
- Farmer P, Kleinman A, Kim J, Basilio M, editors. *Reimagining Global Health: An Introduction.* Oakland, CA: University of California Press; 2013.
- Okubadejo NU, Ojo O, Wahab K *et al.* A Nationwide Survey of Parkinson's disease medicines availability and affordability in Nigeria. *Mov Disord Clin Prac.* 2018; doi: 10.1002/mdc3.12682.
- Olanow CW, Stocchi F. Levodopa: A new look at an old friend. *Mov Disord.* 2018; 33:859–66.
- Harries J. L-dopa in the treatment of Parkinsonism in Africans. *East Afr Med J.* 1972; 49:112–5.
- Cubo E, Doumbe J, Martinez-Martin P, Rodriguez-Blazquez C. *Kuete C². J Neurol Sci.* 2014; 15(336):122–6.
- Cilia R, Akpalu A, Sarfo FS *et al.* The modern pre-levodopa era of Parkinson's disease: insights into motor complications from sub-Saharan Africa. *Brain.* 2014; 137:2731–42.
- Dotchin CL, Msuya O, Walker RW. The challenge of Parkinson's disease management in Africa. *Age Ageing.* 2007; 36:122–7.
- Cilia R, Laguna J, Cassani E *et al.* Daily intake of *Mucuna pruriens* in advanced Parkinson's disease: a 16-week, noninferiority, randomized, crossover, pilot study. *Parkinsonism Relat Disord.* 2018; 49:60–6.
- Drug Commission of the German Medical Association. (Arzneimittelkommission der deutschen Ärzteschaft Wissenschaftlicher Fachausschuss der Bundesärztekammer) <https://www.akdae.de/en/>. Accessed June 2018.