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Editorial

CNPV's Vision for the Future: Involving Local Communities in Reporting Adverse Drug Reactions in the Democratic Republic of the Congo

Claudine Soubrié and Bénédicte Lebrun-Vignes have called worldwide adverse drug reactions (ADRs) a trickle-down disaster. This disaster can be assessed only if reporting is as comprehensive as possible so that decision makers are informed on the possible harmful effects of medicines. This assumes an efficient and modern information system has been sufficiently implemented in the relevant area.

Since 2009, the Democratic Republic of the Congo (DRC) has implemented a spontaneous reporting system that builds on the existing health system. Unfortunately, local communities have little access to this system, which limits the coverage of the pharmacovigilance system based on this model. To prevent ADRs and improve their management in our country, reporting hubs must be extended into local communities. For example, community health care sites can help provide information to people living far from health care facilities, while pharmacy and therapeutics committees at hospitals and clinics can be assigned tasks to support centralization of notifications at the health facility level. This information will be sent to the National Pharmacovigilance Centre (Centre National de Pharmacovigilance; CNPV), whose mandate is to inform and train institutional and community-based providers on the prevention and treatment of drug-related illnesses. The CNPV is expected to gradually set up regional centers that must become autonomous and take action in the areas under their authority. Missions to support the health system will be allocated to them in addition to facilitating their scientific empowerment.

Today, this vision has led the CNPV to promote the emergence of a new generation of health care providers and patients sufficiently experienced to play their parts. Implementation of various Drug and Therapeutics Committees (DTCs) experienced in pharmacovigilance throughout the country and integration of community-based pharmacovigilance in health areas supported by the Global Fund support this innovative vision currently promoted by new information technologies. SMS live, telephone hotlines, and teleconferences have now become essential tools to this significant progress. Everything must be tried in a vast country like ours with enormous geographic and financial constraints and barriers.

Nothing can stand in the way to stop progress if we want our country's future generations to live better than us. Therefore, let's act and truly get to work.

Célestin Nsibu Ndosimao

ACTION: Saved Lives, Thanks to Intervention from the CNPV and the General Referral Hospital DTCs

One afternoon on April 11, 2013, the CNPV received a call for help from a DTC in Katanga regarding a four-month-old infant in a coma who was admitted after taking a single-pill combination of paracetamol (500 mg) and codeine (60 mg) at home that the parents got at the local pharmacy. Specialists from the center were enlisted to solve the case and suggest measures to save this life threatened by a lethal overdose of codeine. First, the antidote, naloxone, was recommended, and then, routine resuscitation and stabilization measures were advised. This brought this innocent infant—whose only sin was to fall into a system where drug delivery in a "pharmacy" no longer meets the standards for proper dispensation—out of the coma. System error.

Imagine the joy of a woman from Boma in Bas-Congo whose 17-month-old infant who had been prescribed 30 medicines, one after another, for a fever lasting over six months. This courageous mother took methodical notes not only of the temperature curve tracing the changes in her baby's illness since the start of medication but also of all the various products administered to her baby. The CNPV's advice was crucial because stopping all medications put an end to the string of fevers.

These stories encourage our vision to step up networking and collaboration among the various DTCs set up in our country's general referral hospitals because these activities not only support increased notifications but also improve the treatment of medicine-related diseases.

Célestin Nsibu Ndosimao

Adverse Drug Reactions

1. Ciprofloxacin: Regularly used medicine is capable of causing serious ADRS.

The CNPV was enlisted to alleviate the excruciating pain that a young woman treated with intravenous ciprofloxacin for typhoid fever suffered for two months. This pain, combined with pruritus and photosensitivity, was followed by rashes appearing on the second day of a properly administered treatment.

Ciprofloxacin's regular use in our country led us to remind practitioners and the public that this medicine is not entirely risk free. Belonging to the fluoroquinolone group, ciprofloxacin is indicated for many bacterial infections. It is strictly contraindicated in pregnant women, breastfeeding women, and children under five years and in cases of a history of allergy to quinolone. This drug may cause adverse events, although they do not occur for everyone.

These adverse events can be serious and may require immediate medical treatment. They include (1) skin rash, itching, peeling of the skin, blisters or scabbing; (2) severe or painful redness or ulcerations of the skin or mucous membranes of the mouth; (3) swelling of the face or neck; (4) respiratory problems; (5) fever; and (6) jaundice (yellowing of the skin and integuments).

Skin rash occurs in fewer than 1 in 10 treated patients, and itching, peeling, blisters, or scabbing and swelling of the face and neck occur in 1 patient among 100 treated subjects.

2. Late-stage hemoglobinuria following intravenous artesunate treatment: What about the DRC?

World Health Organization (WHO) recommendations on the gradual replacement of intravenous quinine by intravenous artesunate led various researchers involved in malaria control to collect data on the possible adverse events of this molecule destined for widespread use.

The US Centers for Disease Control and Prevention (CDC) published a review of 19 cases of late-stage hemoglobinuria reported worldwide since artesunate has been recommended as the first-line drug for treating severe malaria. Although this product has not yet been authorized in the United States, it is available through the CDC via an investigation protocol for new medicines. Intravenous artesunate used in this country is produced by the medical services of the US Army and given to soldiers posted in endemic areas. To date, no adverse event of this type has been reported by the US Army medical service.

However, late-stage hemoglobinuria has been described among patients who resided in endemic areas and who were treated for severe malaria with medicines produced elsewhere. The pathogenesis of malaria shows a closer relationship between the severity of the massive intravascular hemolysis and the severity of the malaria itself than with the malaria treatment.

Introduction of intravenous artesunate in our country summoned practitioners as well as donors to meetings where this aspect of the problem was addressed to prevent adverse events caused by intravenous artesunate.

Since then, practitioners have spoken out freely on the onset of late-stage hemoglobinuria among some patients treated with artemisinin-based combination therapies. Unfortunately, no supporting evidence is available because of the lack of studies. The CNPV has resolved to bridge this gap by developing the design for a cohort of more than 10,000 cases that will be monitored. In its pilot phase, 500 patients were followed over the last year. This study will be combined with other research that will investigate these new antimalarial molecules introduced in the DRC.

Célestin Nsibu Ndosimao

News from Around the World

What about pediatric domperidone?

A group of experts has formalized recommendations on the use of pediatric domperidone. **This medicine should no longer be used in children** (WHO Pharmaceuticals Newsletter No. 1, 2013).

Moreover, for adults this medicine is at the root of serious ventricular arrhythmias and sudden cardiac arrests. It should be used with caution in patients at risk, such as those presenting prolongation of the QT interval, congestive cardiac decompensation, and electrolyte abnormalities (hypokalemia, hypo-magnesemia) and in patients using CYP3A4 inhibitors such as itraconazole, verapamil, indinavir, atazanavir, amprenavir, fosamprenavir, nelfinavir, ritonavir, saquinavir, diltiazem, and aprepitant.

Aline Engo

Reminder on the interactions between grapefruit and drug treatments

The coming of the dry season with the citrus fruit harvest in our country is a good time to remind our fellow citizens about the dangers of grapefruit juice when combined with some products. Grapefruit is known to interact with certain drugs such as calcium blockers (felodipine), immunosuppressive drugs (cyclosporine, tacrolimus), antiarrhythmics (sertraline), an antidepressant (docetaxel), or some drugs targeting cholesterol (simvastatin, atorvastatin). Grapefruit increases the frequency and severity of their adverse effects.

Although the exact mechanisms are not yet fully understood, two hypotheses have been put forward to explain these abnormalities. They may involve the inhibition of drug metabolizing enzymes, causing increased risk of overdose, and a decrease in drug concentration in the blood, causing a risk of inefficacy.

However, no scientific publication has highlighted the risk of decreased efficacy for an antibiotic or cancer treatment or contraception in cases of grapefruit consumption.

Last, no interactions with other citrus fruits (oranges, lemons) or apples have been described.

Célestin Nsibu Ndosimao

CNPV Semi-Annual Activities

The CNPV is gradually expanding its partnerships by training providers (physicians and pharmacists) in pharmacovigilance in two of the country's provinces, Bas-Congo and Katanga. This activity was funded by the WHO country office, which plans to increase its support in Kasaï Occidental.

In addition, the CPNV participated in various reviews of malaria and tuberculosis programs organized in the country. Regarding malaria control, the CNPV is closely linked to the National Malaria Control Program's 2013–2016 strategic plan. The CNPV director has been co-opted as a member of the Central Africa Roll Back Malaria Network.

Several pharmacovigilance projects, including community-based pharmacovigilance, have been included in additional plans submitted to the Global Fund for malaria in DRC.

The CNPV participated on the steering committee for plans to include the future malaria vaccine in the national immunization calendar. One of its members participated in a large meeting on this vaccine in Nairobi that brought together experts from diverse backgrounds.

One of the CNPV members participates in the summer course organized each year by the Uppsala Monitoring Centre (UMC) in Sweden.

Jerry Liwono and David Pandi Belebinda Jr.

Our Impact around the World

Documentation grading and report completeness

For over two years, the CNPV has continually received praise from the WHO pharmacovigilance collaboration center, an institution based in Uppsala, for the quality and completeness of its notification sheets. For two consecutive years, UMC gave the CNPV a grade bordering on the maximum 100 percent. This quality is attained through the supportive interaction between the notifiers and the CNPV staff, thus confirming the validity of medical collaboration.

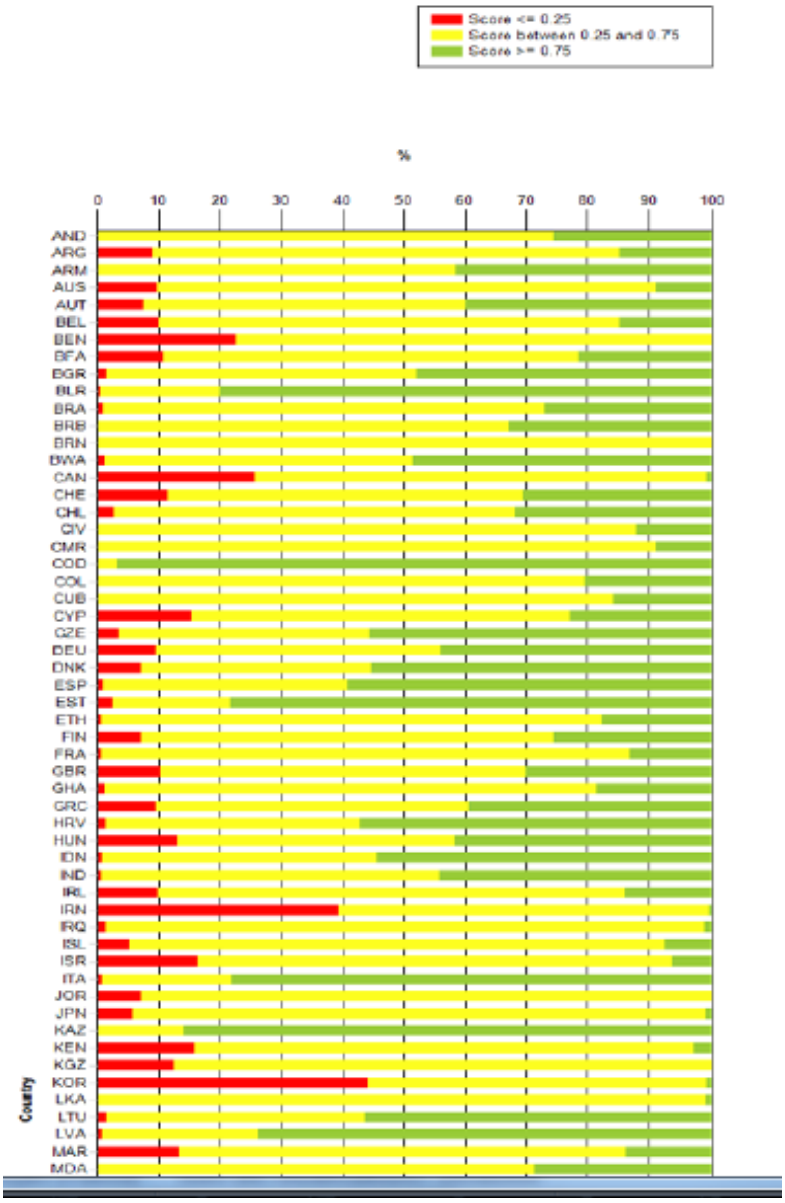
However, this ongoing research to explain cases also has its pitfalls, notably the excessive time lapse between analyzing each case and inputting information in the UMC database via Vigiflow and, moreover, the low number of forms that are introduced and validated for all reported cases. From 2010 to 2012, 3,421 forms were added to the database, of which 2,651 were validated. At least 22.5 percent (or 770) of the forms were still being processed at the CNPV. During the same period, 2,500 other notifications still had not been entered in the database. The harvest appears plentiful, but the hands to reap it are beginning to fail. The CNPV risks becoming a victim of its own completeness.

Could a discussion ensue on the possible reorientation of our priorities to unite the other pharmacovigilance referral centers based on the three virtues: **quality, quantity, and promptness**? The CNPV excels in quality, but the two other indicators are still in the red. Must quality be compromised in the name of quantity and promptness for a center that has only just been established and whose agencies have only been partially implemented? Or must we focus on quality first to set a precedent and then have the solid foundations that will support future development? Isn't it possible to combine these two options to create a center that hopes to be an innovator in sub-Saharan Africa? **Who will decide?**

We need worthy and committed arms for this cause.

PS: Graph representing the performance of each country reporting to the UMC. Note that our country [COD] has performed below 75 percent.

Célestin Nsibu Ndosimao



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