



Pharmacovigilance Bulletin of the Democratic Republic of the Congo

No. 2, January 2012

1. LEAD ARTICLE

Pharmacovigilance (PV) activities truly started in 2010 with 156 notifications entered in the Uppsala Monitoring Centre international database. During that year, we acquired experience and enhanced the reporting system, thereby improving our performance as the number of notifications entered climbed from 156 in 2010 to 1,027 in 2011. This is a major feat, but not enough in itself, because the goal is not to amass notifications, but rather to glean information from them that can help health care workers provide optimal treatment for diseases and therefore improve the health care system.

The importance of activities to train Focal Points and increase health care providers' awareness of PV has been demonstrated. In fact, it always substantially increases notifications.

2. NOTIFICATIONS RECEIVED IN 2010

Following the warm-up with the provisional PV program in late 2009, the National Pharmacovigilance Centre (Centre National de Pharmacovigilance; CNPV) effectively began operations in 2010.

An internal training enabled CNPV staff to become familiar with the various methods of causality, the international classification of diseases, and the World Health Organization Adverse Reaction Terminology (WHO-ART), a classification system for adverse drug reactions (ADRs). This was followed by training for Pharmacovigilance Focal Points and building awareness in some health care facilities in Kinshasa and specialized programs of the Ministry of Health. In two training waves (July–August 2010 and August–September 2010), 62 Focal Points were trained and nearly 600 health care providers gained increased awareness of PV. This enabled us to begin collecting notifications: 171 in total, 156 of which were entered fully in the Uppsala Monitoring Centre's international database.

Figure 1: Rate of receipt of notifications at the CNPV

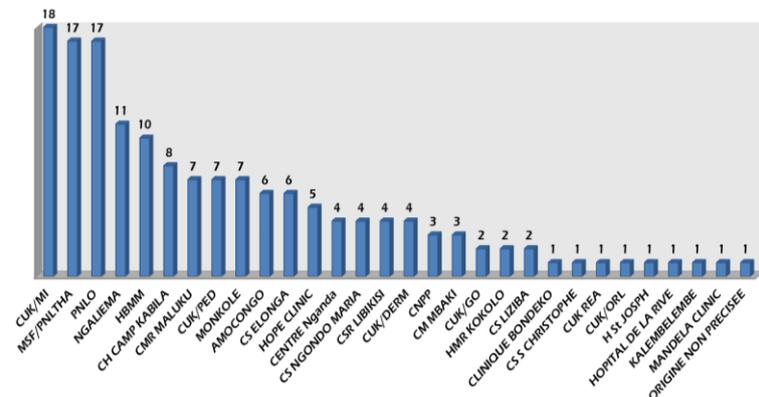


The immediate effect of the two trainings for Focal Points, with the consequent increase in notifications, should be noted.

Sources of the Notifications

We would like to thank all the Focal Points for their contribution to the notification efforts. Several health care facilities in Kinshasa sent notifications. A significant number of notifications came from the country's interior, notably Équateur (notifications from the National Onchocerciasis Control Program) and Oriental Province (notifications sent by the Doctors Without Borders/Switzerland team working in Doruma and Dingila). Figure 2 lists the various notification sources.

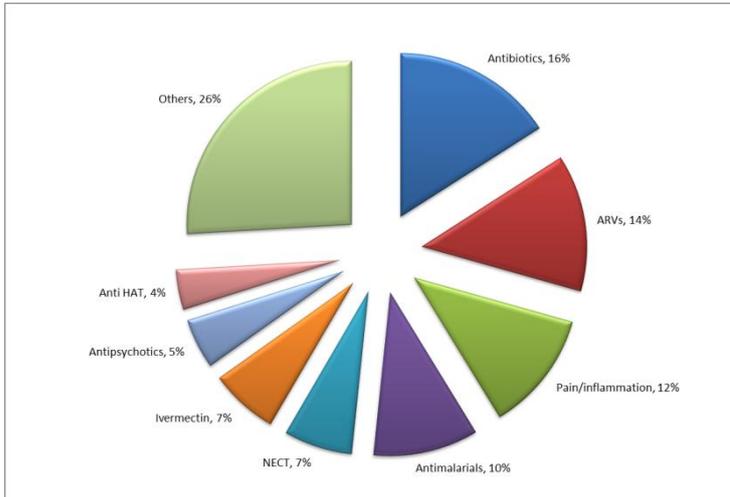
Figure 2: Distribution of health care facilities according to the number of notifications sent to the CNPV



Medicines Implicated

These notifications concerned adverse reactions caused by a total of 326 medicines. Following analysis and determination of causality, 251 medicines were considered responsible for adverse effects and 75 as concomitant medicines. (Note: Combination therapy such as HRZE is counted as a single medication.)

Figure 3: Distribution of the medicines implicated

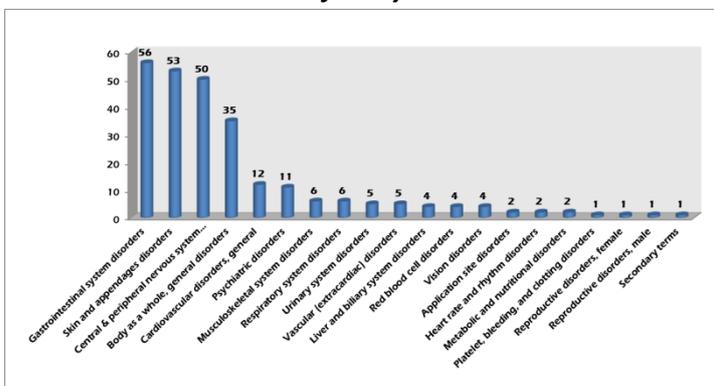


Among the medicines implicated, anti-infectious medicines predominate, including antibiotics, antimalarials, ivermectin (to treat onchocerciasis), and NECT (Niurtimox-Eflornithine Combination Therapy), the current treatment for Human African trypanosomiasis (HAT, or sleeping sickness).

Reported Adverse Reactions

The adverse reactions reported were classified according to WHO-ART. Figure 4 classifies them according to their System-Organ Class (SOC).

Figure 4: ADRs reported to the CNPV in 2010 classified by SOC

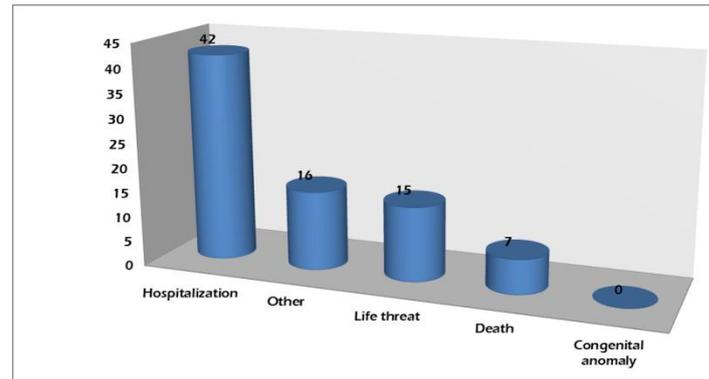


The predominance of three systems should be noted: the digestive system, skin and appendages, and the nervous system; but general symptoms were noted as well. For

example, vomiting (32%), nausea (20%), abdominal pain (16%), and digestive hemorrhaging (7%) were among the digestive system disorders. Rash (30%), itching (17%), and hives (13%) were noted for the skin and appendages, with Lyell and Stevens-Johnson Syndromes accounting for a total of 10%.

Of all these adverse reactions, 49% were severe. The severity rates are presented in figure 5.

Figure 5: Severe ADRs distributed according to severity



It should be noted that 42 hospitalizations and seven deaths were caused by medicines. Remember that medicines are responsible for 3% to 17% of hospitalizations globally.

3. A FEW SPECIFIC CASES

It is important to note a few specific cases:

Extrapyramidal Syndrome with Metoclopramide:

Five cases of extrapyramidal syndrome following intravenous (IV) administration of metoclopramide were reported in children. This involved a major failure to heed an important warning. The injectable form is reserved for adults; the IV route increases the risk of extrapyramidal syndrome in children.

→**CNPV Recommendation:** In children, **enteral** administration (oral or rectal) **of metoclopramide** is preferable.

Lyell's Syndrome: We are astounded by the high mortality rate (100%), since the literature refers to a ±30% death rate. A study is under way in collaboration with dermatologists to propose strategies for early diagnosis

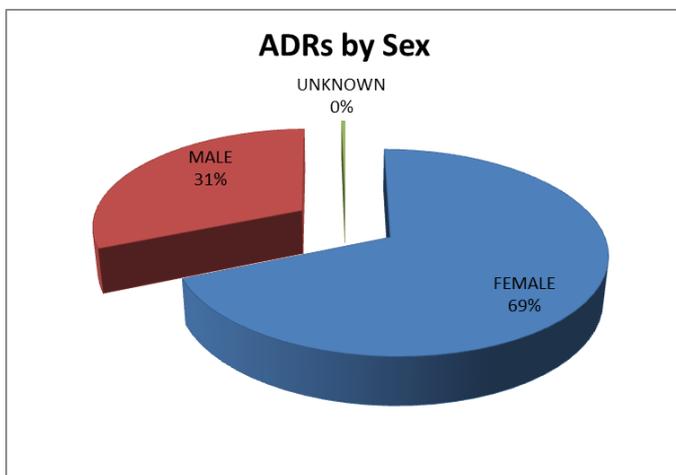
and effective (and necessarily multidisciplinary) treatment of this severe syndrome.

Naphthalene Poisoning: One case of severe naphthalene poisoning was reported. It involved a newborn who presented dyspnea and agitation just after being placed in an incubator. While preparing the layette, the mother placed naphthalene balls in her suitcase as a moth repellent. A memorandum about naphthalene has been written and will appear in the next pharmacovigilance bulletin.

4. NOTIFICATIONS IN 2011

The experience gained in 2010 facilitated increased notifications in 2011. The poliomyelitis vaccination campaign was an opportunity to collect a large number of notifications on this vaccine. Also, notifications continued to be made from sentinel sites for malaria, as well as those about NECT, notably from Doctors Without Borders. In addition notifications continued from trained Focal Points. Thus, a total of 1,027 notifications were collected, analyzed, and entered in the international database; with 1,651 adverse reactions listed, we have an average of 1.6 ADRs per patient.

Figure 6: Distribution by sex

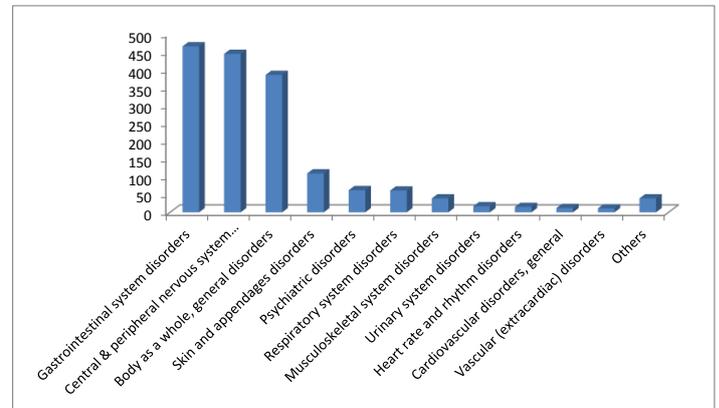


The predominance of females is becoming apparent. Various studies show that ADRs are more frequent among female patients. The reasons for this phenomenon are not fully understood, but it should be analyzed and health care providers should keep it in mind.

Adverse Reactions Reported

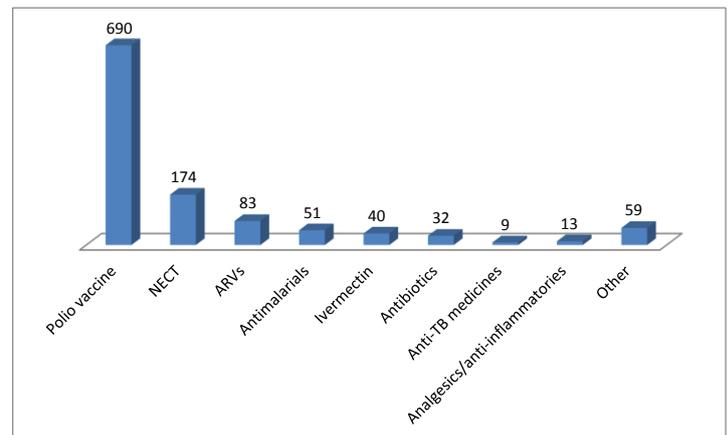
They are classified by SOC category according to the WHO-ART.

Figure 7: ADRs reported to the CNPV in 2011, classified by SOC



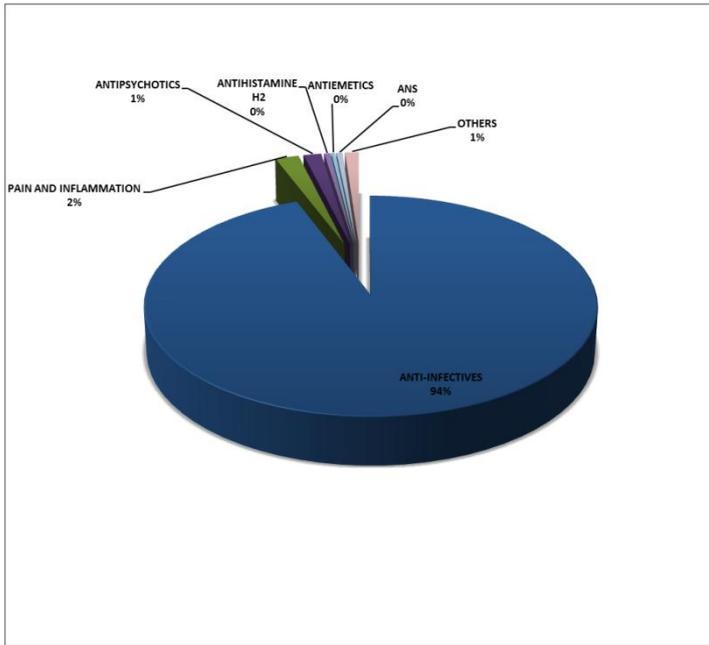
A strong predominance of symptoms related to the digestive system, the nervous system, and general symptoms were followed by cutaneous ADRs. This distribution is probably influenced by selection bias inherent in passive PV; those who report more are better represented in the sampling. In our case, the major polio vaccination campaign and numerous notifications on NECT dominate the data set.

Figure 8: Medicines implicated in ADRs reported in 2011



The polio vaccination campaign made itself felt in the data with a wide predominance of the polio vaccine. Next came NECT (reports from the National Sleeping Sickness Control Program by Doctors Without Borders/Switzerland). Other medicines emerged from standard reports of health care facilities and sentinel sites of the National Malaria Control Program. The clear dominance of anti-infectious medicines is striking.

Figure 9: Group of medicines implicated in ADRs reported in 2011



Anti-infectious medicines are prescribed most. Therefore, they are subject to particularly close oversight.