Pharmacovigilance: Healthcare Professionals' Role in Benefits *Versus* Harm Analysis of Drugs Use

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ABSTRACT

Monitoring the negative effect of drugs is a concept that all healthcare professionals would be aware of as part of their professional responsibility. However, since 1968, it has evolved into a structured science called 'Pharmacovigilance'. This review aims to sensitize Caribbean healthcare professionals to the global pharmacovigilance network of the World Health Organization and how their active involvement at the national level is imperative to the benefit versus harm evaluation of drugs.

Keywords: Pharmacovigilance, adverse drug reactions, healthcare professionals, adverse drug events

La Vigilancia Farmacológica: el Papel de los Profesionales del Cuidado de la Salud en el Análisis de los Beneficios versus Riesgos de los Medicamentos

Análisis del uso de los Medicamentos

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RESUMEN

El monitoreo de los efectos negativos de los medicamentos es un concepto del cual todos los profesionales del cuidado de la salud debían tener conciencia como parte de su responsabilidad profesional. Desde 1968, este monitoreo se ha venido transformando en una ciencia estructurada conocida como "Vigilancia farmacológica", o "farmacovigilancia". El presente examen se dirige a sensibilizar a los profesionales del cuidado de la salud caribeños con la red de vigilancia farmacológica global de la Organización Mundial de la Salud, y a que tomen conciencia de cómo su participación activa a nivel nacional es indispensable para la evaluación de los beneficios y riesgos de los medicamentos.

Palabras claves: Vigilancia farmacológica, reacciones adversas del medicamento, profesionales del cuidado de la salud, resultados adversos del medicamento

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Healthcare professionals are challenged by concerns patients encounter related to their medication because anything foreign to the body may have effects beyond intended indication. If the effect is toxic, then it becomes characterized by words such as poison and overdose; however, the daily challenges are associated with the use of medicinal drugs at the standardized therapeutic doses.

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Adverse drug reaction versus side effect versus adverse drug event

An adverse drug reaction (ADR), as defined by the World Health Organization (1), is the response to a drug which is noxious, unintended and which occurs at doses normally used for prophylaxis, diagnosis or therapy of a disease or for the modification of physiological functions. An ADR may or may not be related to the pharmacological action of the drug. However, a "side effect", is an effect that is unintended and related to the pharmacological properties of the drug. Therefore allergic reactions are not side effects but ADRs.

During drug therapy, it may not be easy to determine whether a drug is truly the cause of an untoward reaction; then the term "adverse drug event" may be more appropriate; that is, although the event is occurring during drug use, it may not have a causal relationship with therapy (2, 3).

An overdose of diazepam with intention to commit suicide would not be an ADR but certainly an adverse drug event. All these terminologies form part of the global effort to keep a vigilant watch on the effects of pharmaceuticals, that is Pharmacovigilance.

Pharmacovigilance and the role of healthcare professionals

The accepted definition from the World Health Organization for pharmacovigilance is the science and activities relating to detection, assessment, understanding and prevention of adverse events or any other possible drug-related problems (1). In simple terms, it's the acceptance that all drugs will have adverse drug reactions while ensuring that the benefits significantly outweigh the harmful effects.

Pre-marketing clinical trials, in most cases, involve only a few thousand persons, most are generally healthy, unlikely to include children or the elderly and most certainly would not even include patients taking many drugs concurrently or using herbal/dietary supplementations. It is certainly impractical, unethical and possibly uneconomical to place a drug through all the possible matrices before making it available for general use. Pharmacovigilance is the post-marketing detection process that facilitates a rational approach to assessing whether there is more value to continue the use of a drug, despite the observed harms. It allows for a systematic evaluation of how to minimize the risk of an ADR occurrence through the identification of confounding factors such as patient compliance, drug-drug interactions, drug-food interactions, genetic differences and cultural practices. Therefore, participation in pharmacovigilance is not an option but an obligation of all persons involved in drug therapy.

Advances of the global pharmacovigilance network

The global pharmacovigilance programme had its genesis in 1968 and was a World Health Organization (WHO) initiative to ensure that there is never a repeat of the phocomelia tragedies of thalidomide (14). The strength of the global pharmacovigilance network is dependent totally on the active participation of healthcare professionals submitting ADRs through national pharmacovigilance centres (or division of national health systems). This global network is managed by the WHO-Drug Monitoring Centre in Uppsala, Sweden, which holds a database of over 4.6 million ADRs and grows at more than one hundred thousand ADRs monthly contributed by over ninety participating countries (Tables 1 and 2). Potential problems, referred to as "signals", are generated by the WHO-Drug Monitoring Centre through a systematic evaluation of the ADR reports in its database balanced with all the arguments for and against the drug *versus* ADR association (5). There have been many signals detected through this global network that have significantly influenced drug information both at the international and national level (6–17). Additionally, all participating countries have free access to the global database.

Table 1: Official member countries of the WHO-Drug Monitoring Centre network and their year of entering the Programme (as of June 2009)

Andorra (2008)	Republic of Korea (1992)
Argentina (1994)	Kyrgyzstan (2003)
Armenia (2001)	Latvia (2002)
Australia (1968)	Lithuania (2005)
Austria (1991)	The former Yugoslavia Republic of Macedonia (2000)
Barbados (2008)	Madagascar (2009)
Belarus (2006)	Malaysia (1990)
Belgium (1977)	Malta (2004)
Botswana (2009)	Mexico (1999)
Brazil (2001)	Republic of Moldova (2003)
Brunei Darussalam (2005)	Morocco (1992)
Bulgaria (1975)	Mozambique (2005)
Canada (1968)	Namibia (2008)
Chile (1996)	Nepal (2006)
China (1998)	Netherlands (1968)
Columbia (2004)	New Zealand (1968)
Costa Rica (1991)	Nigeria (2004)
Croatia (1992)	Norway (1971)
Cuba (1994)	Oman (1995)
Cyprus (2000)	Peru (2002)
Czech Republic (1992)	Philippines (1995)
Denmark (1968)	Poland (1972)
Egypt (2001)	Portugal (1993)
Estonia (1998)	Romania (1976)
Ethiopia (2008)	Russian Federation (1998)
Fiji (1999)	Saudi Arabia (2009)
Finland (1974)	Serbia (2000)
France (1986)	Sierra Leone (2008)
Germany (1968)	Singapore (1993)
Ghana (2001)	Spain (1984)
Greece 1990)	Slovakia (1993)
Guatemala (2002)	South Africa (1992)
Hungary (1990)	Sri Lanka (2000)
Iceland (1990)	Sudan (2008)
India (1998)	Suriname (2007)
Indonesia (1990)	Sweden (1968)
Islamic Republic of Iran (1998)	Switzerland (1991)
Ireland (1968)	Thailand (1984)
Israel (1973)	Togo (2007)
Italy (1975)	Tunisia (1993)
Japan (1972)	Turkey (1987)
Jordan (2002)	Uganda (2007)
Kazakhstan (2008)	Ukraine (2002)

Promoting national pharmacovigilance

The impact of factors specific to the Caribbean remains an area to explore. Some very obvious factors to consider are:

* reasons for failure of drug therapy; for example, influence of resistance and genetic variability
* prevalence of allergic reactions in the population
* implications of the drug-drug interactions
* implications of drug-herb/plant interactions

These are only a few of the burning issues facing healthcare professionals in daily practice; yet knowledge of benefit *versus* harm of drugs used in the Caribbean relies to a great extent on data from countries outside of the region and is likely to have significant population differences. It therefore means that there is a need to build national and ultimately

Table 2: Associate member countries of WHO-Drug monitoring centre. Countries can join initially as associates to receive some of the benefits of the global network until they are able to change status to member.

Algeria	Georgia
Anguilla	Grenada
Antigua and Barbuda	Iraq
Bahrain	Jamaica
Benin	Kenya
Bhutan	Mongolia
British Virgin Islands	Montserrat
Burkina Faso	Pakistan
Cambodia	Panama
Cameroon	St Kitts and Nevis
Côte d'ivoire	St Lucia
Dem Rep of Congo	St Vincent and The Grenadines
Dominica	Senegal
Eritrea	Zambia
	Zanzibar

regional databases of ADRs and with time, many of these concerns can be more prudently addressed.

It is unlikely that ADRs would not be of concern for the Caribbean region, as it is well documented that ADRs are among the top leading causes of mortality and morbidity (18–21). Therefore, all countries in the region would benefit from promoting ADR reporting. Participation in the global effort should be the ultimate goal joining Cuba, Barbados, Jamaica and the Eastern Caribbean Islands which are already making their contributions.

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