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Serious Adverse Drug Reactions in Older Adults Notified to Pharmacovigilance

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Abstract – Purpose. To report the serious adverse drug reactions (ADRs) in older adults notified to pharmacovigilance, to identify the incriminated drugs and to search for risk factors of occurrence. **Methods.** A retrospective study including 106 serious adverse drug reactions notified to pharmacovigilance in patients aged of 65 years and more, over a period of 16 years. Imputation was established according to the French method and seriousness according to the World Health Organisation (WHO) criteria. **Results.** Adverse drug reactions were essentially systemic. Incriminated drugs were mainly antibiotics, allopurinol and cardio-vascular drugs. Gender, age and number of administered drugs did not seem to be risk factors of serious ADRs occurrence. Among older adults, 4% died further to a serious ADRs. **Conclusion.** Systemic notification to pharmacovigilance will allow a better analysis of risk factors of serious ADRs occurrence and to insure safety and health to the older adults.

Mots clés :
effet indésirable grave ;
médicament ;
sujet âgé ;
pharmacovigilance

Résumé – Effets indésirables médicamenteux graves chez les sujets âgés notifiés en pharmacovigilance. Objectifs. Rapporter les effets indésirables graves survenus chez les sujets âgés notifiés en pharmacovigilance, identifier les médicaments incriminés et rechercher les facteurs de risque de leur survenue. **Méthodes.** Étude rétrospective incluant 106 cas d'effets indésirables graves notifiés en pharmacovigilance sur 16 ans chez des sujets âgés de 65 ans et plus. L'imputabilité a été établie selon la méthode française et la gravité définie selon les critères de l'Organisation mondiale de la santé (OMS). Résultats. Les effets indésirables graves étaient essentiellement systémiques. Les médicaments incriminés étaient surtout les antibiotiques, l'allopurinol et les médicaments à visée cardio-vasculaire. Le sexe, l'âge et le nombre de médicaments administrés ne semblent pas représenter des facteurs de risque de survenue des effets indésirables graves. Les décès étaient notés dans 4 % des cas. **Conclusion.** Une notification systématique, en pharmacovigilance, chez les sujets âgés, permettrait une meilleure analyse des facteurs de risque de survenue des effets indésirables graves dans cette population particulière.

1. Introduction

Worldwide, the proportion of older adults, aged of 65 years or more, is growing faster than any other age group. Between 1970 and 2025, a growth in older adults of 223% is expected. As populations age, the triangular population pyramid of 2002 will be replaced with a more cylinder-like structure in 2025. If ageing, longer life must be accompanied by continuing opportunities for health and security.

The aims of pharmacovigilance are to enhance patient care and safety in relation to the use of drugs and to provide reliable and balanced information for the effective assessment of the risk-benefit profile of drugs, especially in older adults.[1] As they are exposed to drug overconsumption due to polypathology, a special attention is focused on adverse drug reactions (ADRs) and mainly on serious ones occurring in this particular category of people. These ADRs are frequent in older adults and are serious in 10 to 20% of cases.[2]

Table I. Gender, age and average number of administered drugs distribution according to the adverse drug reactions seriousness.

	Gender		Age		Number of administered drugs										
	Men (n=186)	Women (n=219)	[65, 75] (n=306)	≥75 (n=99)	1	2	3	4	5	6	7	8	9	10	12
Group S	27.4%	25%	27.4%	25%	30	16	10	17	20	5	4	0	1	0	1
Group NS	72.6%	75%	72.6%	75%	87	88	49	45	35	17	10	6	5	1	0

Many studies concerned epidemiology of ADRs in older adults. Published studies concerned some specialized departments, they were limited to a particular therapeutic class or a certain type of ADRs.

The aim of this study was to search for risk factors of serious ADRs occurrence, to report the serious ADRs notified in older adults, and to identify incriminated drugs.

2. Material and methods

We performed a retrospective study concerning 1 235 observations of adverse events notified to the Tunisian national Centre of Pharmacovigilance in persons aged of 65 years or more over a period of 16 years (from december 1990 to december 2006). Patients were addressed by medical doctors from public and private institutions to the Tunisian National Centre of Pharmacovigilance. In this study, data collection was made from medical files of the Tunisian National Centre of Pharmacovigilance then reproduced on an Excel file.

The studied parameters comprised:

- the epidemiological informations of the older adults and their histories;
- the events classified according to the affected organ and their evolution in time: improvement, worsening or total disappearance;
- the diverse drugs taken: date of introduction, doses, the drug's ruling or continuation, the delay of ADRs occurrence and the intrinsic and extrinsic scores of imputation. So the incriminated drug(s) had the highest score of imputation.

We included all the cases of ADRs notified in older adults where the responsibility of only one drug was retained after a pharmacovigilance investigation. The drug's responsibility in the occurrence of the event was estimated by the french method of imputation of Bégaud *et al*.[3] We individualized the group M where the responsibility of a single drug was retained after investigation.

The ADRs were classified according to the affected organ. The ADRs with a multisystemic injury were classified according to their delay of occurrence and semiology. They were anaphylactic reactions or drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome. In anaphylactic reactions, delay of occurrence should be of few hours and can be an anaphylactic shock, a cutaneous and mucosal edema, an immediate loss of consciousness or a generalized erythema with convulsion. The DRESS syndrome is the association of a drug rash, an eosinophilia and systemic symptoms. Seriousness of an ADRs was defined according to the World Health Organisation (WHO) criteria.[4,5] An ADR is considered serious in case of a hospitalization, a prolonged hospitalization, an organ failure, a fatal achievement or an occurrence of sequelaes. Hepatic ADRs were considered serious according to Zimmerman criteria: [6] in case of associated icterus, hepatic encephalopathy or a prothrombin factor less than 50%. According to these criteria, we defined in the group M, 2 subgroups: group S comprising 106 older adults presenting a serious ADR and group NS comprising 299 older adults presenting an ADR without any sign of seriousness. In order to avoid the use of inappropriate drugs and to limit the occurrence of serious ADR, "Beers criteria" were established.[7] A total of 66 drugs were considered at high risk of serious ADR occurrence. In this study, we picked out drugs at high risk of serious ADR occurrence according to Beers criteria. In the statistical analysis, the used Software was the version 2.0 of Pythagore biostat.

3. Results

In this study, we respectively searched for risk factors of serious ADRs occurrence by comparing gender, age and number of administered in the groups S and NS, then we reported serious ADRs notified in older adults and identified incriminated drugs in the group S.

3.1. Risk factors of serious ADRs occurrence

In the group M, we defined the group S comprising 106 (26%) older adults presenting a serious ADRs and the group NS comprising 299 (74%) older adults. In the group S, there was 55 women and 51 men (sex-ratio Women/Men [W/M]=1.08). In order to search for risk factors of serious ADRs occurrence, we compared gender, age and number of administered drugs in the groups S and the group NS (table I). We found that there was no significant difference in gender distribution according to the seriousness (p=0.59) [table I].

In the group S, mean age was 71 years [65, 90]. No significant difference was found in age distribution according to the seriousness (p=0.98) [table I].