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Pharmacovigilance knowledge in family paediatricians. A survey study in Italy

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ABSTRACT

Drugs prescription in children correlates with a high risk of developing unknown or rare adverse drug reactions (ADRs). In the absence of appropriate clinical trials in the paediatric population, the spontaneous reporting of suspected ADRs is an important means to promote reasonable warning signals. In this context, family paediatricians (FPs) play a crucial role although a general poor compliance in their ability of reporting of ADR is widely described. To understand the reasons beyond this situation we performed a survey, the first of its kind in Italy, to evaluate FPs knowledge, feeling and compliance in ADR reporting. A total of 552 FPs evenly distributed throughout the Italian territory provided a feedback to the survey. Knowledge of pharmacovigilance (PV) resulted to be poor, mainly due to the absence of adequate training in academy; despite this, the majority of FPs declared to be interested to PV and aware of its positive impact on their clinical practice. Yet, FPs reported a poor compliance to the reporting of ADRs. A very high variability in ADRs reporting however, was observed among the regions, possibly because of variability of regional educational programmes dedicated to PV.

1. Introduction

Post-marketing surveillance plays a crucial role in drug safety, through the spontaneous reporting of adverse drug reactions (ADRs). Such surveillance is of paramount importance in the paediatric setting because of the relative paucity of pre-registration studies. One of the main weakness of the paediatric PV system is the lack of compliance in reporting ADRs [1] resulting in underestimation of ADRs frequency, with negative impact on the ability of the surveillance system to detect appropriate warning signals and thus the safety vs efficacy profile of the marketed drugs. Moreover, the selective reporting of ADRs by FPs introduces a bias in the surveillance system [2,3]. Non-serious ADRs being not life-threatening and of no immediate danger to the patient's health are generally not reported and quantified with the same diligence as serious and unknown ADRs.

Several studies [4–7] explain the underreporting phenomenon with a lack of time, different care priority,

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uncertainty about drug causing ADR, difficulty in accessing/compiling of the reporting forms and a lack of knowledge of the aim and clinical utility of PV [5]. In a systemic review, Hazell et al. observed a median underreporting rate (UR) of 94% (interquartile range 82–98%) for all severity of ADRs [8]. A lower UR for serious ADRs was also reported [6].

In order to manage and overcome the bias introduced by underreporting, Biagi et al. [1] recently proposed for General Practitioners a three stages intervention aimed at improving reporting rate, consisting in an initial survey, followed by a periodically e-mail update on PV and a final survey detecting the improvement in PV knowledge. This study while showing that such an approach increases the number of reports, also highlights the necessity of understanding why underreporting/selective reporting does occur.

Underreporting is an even more serious problem in the paediatric population. Pharmacokinetic and pharmacodynamics profiles and the effects of drug interactions differ significantly between children and adults as well as between children of different age groups, with significant differences in term of type/level of the observed ADRs. Finally, most genetic and rare diseases have a paediatric onset, which adds to the diversity of this population from the adult one [9]. These limitations, compounded with the lack of clinical trials, lead to a frequent off label treatment of children, with increased risk of drug toxicity [4]. The exact frequency of paediatric ADRs is difficult to assess, although it has been estimated to be of 1 ADR every 10 hospitalised patients and 1 ADR every 500 out patients [10].

An analysis of the Italian surveillance system between the years 2004 and 2008 revealed that less than 5% of the overall Italian ADRs reports was provided by FPs, indicating a diffuse lack of compliance [9]. Another study demonstrated that the activity of spontaneous reporting on children in Italy is still very low: in recent years paediatric data-reporting has stood at around 1.6%, compared with 8% of total reporting on adult patients [11].

We decided to evaluate the status of knowledge and attitude of FPs towards PV in order to programme appropriate interventions. We performed a survey using a fast and cost-effective method consisting of a multiple-question web survey on the FPs knowledge about PVs, their compliance in ADR reporting and their feeling about PV, using an already tested methodology [12]. The results obtained indicate viable and cost effective ways to improve the paediatric PV system.

2. Materials and methods

2.1. Questionnaire formulations and survey

A team of experts consisting of two pharmacists, a clinical pharmacologist, two paediatricians and a statistician formulated the questionnaire to be addressed to FPs by a web survey accessible at the website homepage of the Federazione Italiana Medici Pediatri (FIMP), an association of FP widely and evenly distributed across the Italian territory, for one month. All questionnaires were numbered and validated by a linguistic and a clinical psychologist.

Table 1
Main characteristic of enrolled paediatricians.

		N	%
Sex	Male	276	50%
	Female	276	50%
Age	35–45	32	5.8%
	46–55	340	61.59%
	55–65	177	32.07%
	>65	3	0.54%
Years in practices	<5	5	0.91%
	6–9	5	0.91%
	10–15	46	8.33%
	16–20	133	24.09%
	>20	363	65.76%
No. of patients	<600	25	4.53%
	601–700	23	4.17%
	701–800	72	13.04%
	801–900	137	24.82%
	901–1000	136	24.64%
	>1000	159	28.8%

The web survey was opened to all FP on a voluntary basis and designed in such a way that FPs could answer to questionnaire only once. The questionnaire evaluated overall knowledge of PV, the compliance in ADRs reporting and the perceptions about the necessity of information in PV. Some questions to record basic demographic characteristics of FPs were also included. The questionnaire had 25 multiple choice questions with one correct answer. The questionnaire was based on the Regulation (CE) N° 1901/2006 because the newer regulation (1235/2010) was introduced in Italy in July 2012.

2.2. Data records and statistical analysis

Data from the received questionnaires were analysed in terms of number and proportions of submitted answers. Statistical analysis was performed considering the difference between proportions among the various Italian regions using a chi-square test. All analyses were performed by using R (v 2.15.2).

3. Results

3.1. Demographic characteristics of family paediatricians

Of the 6391 Italian FPs, 552 (response rate 8.64%) participated into the survey. The majority of participants had between 46 and 65 years of age, with more than 15 years of experience, and more than 700 patients in care (Table 1). The age group between 45 and 55 years of age provided the largest feedback. There was a considerable variability in the response rate between different regions (Table 2) ranging from 4.42% of Lazio to 20.8% of Abruzzo, compared to the total number of FPs.

3.2. Family paediatricians knowledge of pharmacovigilance

The level of FPs knowledge on PV was assessed through 11 questions focused on definition of ADR, the differences between ADR in children and adults and phytovigilance (Table 3).