ORIGINAL RESEARCH PAPER

Volume-7 | Issue-4 | April-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

CHILDREN AND ADRS : THE CORRECT USE OF DRUGS IN PEDIATRICS

Paediatrics

Ettore Napoleone

Cristiana Scasserra*

* Corresponding Author

ABSTRACT

The use of off label drugs increases the risk of adverse reactions in children. Pediatricians should pay more attention when they are recommented drugs. One of the problems of pharmacovigilance is the lack of knowledge due to absence of instructions. The problem of the incorrect use of drugs in pediatrics has become a public health concern.

In this context, the Family Pediatricians - Research Network on Medicines for Children (FP-MCRN) plays an important role in pediatric pharmacovigilance both through improved training and through a proper research methodology. There is a need for a cultural approach, implementing the culture of diseases related to adverse events. We must take into account the importance of post-authorization safety studies (PASS) according to GCP, GVP and

ENCePP Code of Conduct.

PASS can provide on one hand training and information regarding the proper use of drugs in children and, the other to constitute a territorial survey in the prescriptive appropriateness and safety of pediatric drugs aimed at assessing the risk ratio.

KEYWORDS

Children, Adverse drug reactions, Off-label, Post-marketing Clinical studies

Background

The use of off label drugs increases the risk of adverse reactions in children. Pediatricians should pay more attention when they are recommented drugs. (1-8).

Pharmacovigilance (PhV) knowledge has the outcome of being inadequate in particular due to the absence of instruction (1-4). There are differences such as the pharmacokinetics and pharmacodynamics of drugs in adults and children, as well as among children of different age groups; moreover, also the adverse events can be different in these two age classes (1-4).

To try to solve the problem of off-label and unlicensed prescribing in children, European regulations were realized with the purpose of obliging pharmaceutical companies willing to register new compounds, or indications and formulations for paediatric use, to submit "paediatric investigation plans" (9).

In Italy the regulatory authorities have tried in every way to improve the concept of the importance of ADR reporting by pediatricians to give a valuable and significant contribution to the process of Pediatric Pharmacovigilance (10-17).

In this context, the Family Pediatricians - Research Network on Medicines for Children (FP-MCRN) plays an important role in pediatric pharmacovigilance both through improved training and through a proper research methodology. There is a need for a cultural approach, implementing the culture of diseases related to adverse events. We must take into account the importance of post-authorization safety studies (PASS) according to GCP, GVP and ENCePP Code of Conduct to develop new methodological to recognise as early as possible issues of efficacy and safety reducing the health risks for such fragile populations as children (1-6)

In 15/2/2016 the REDS (REspiratory Drugs Survey) STUDY: Active surveillance of respiratory drugs, especially Inhaled Steroids (IS) in children (AIFA PhV CALL 2010-2011) conducted by Fp-MCRN had awarded with the ENCePP Study Seal according to principles of methodological standards,transparency and independence (18).

The REDS Study: Active surveillance of respiratory drugs, especially Inhaled Steroids (IS) in children was conducted in the territory by Family Paediatricians and had provide on one hand training and information regarding the proper use of Inhaled Steroids in children and, the other had constituted a territorial survey in the prescriptive appropriateness and safety of these drugs aimed at assessing the risk-benefit balance on usage.

Knowledge of Pharmacovigilance in pediatrics resulted to be poor, mainly due to the absence of adequate training in academy; despite this, the majority of Family Pediatricians affirmed to be interested to Pharmacovigilange and aware of its positive impact on their clinical practice (19). There will be a need for specific training courses to bridge this cultural gap in the next future.

Another important problem to consider is the reporting activity of the ADRs in children. In Italy, the activity of spontaneous reporting in children is very low: in recent years paediatric data- reporting has stood at around 1.6 to 1 percent, compared with 8% of total reporting.

Pediatricians case reports mainly involve vaccines followed by frequency reports of drugs used by children: antibiotics, antipyretics, inhaled corticosteroids, specific products for colds and drugs on the gastrointestinal tract andmetabolism.

Most of the ADRs, observed in children, mainly effect the skin (rash, urticaria) and the gastrointestinal system (diarrhea, nausea and vomiting), but we can also observe systemic reactions and reactions connected to the central nervous system (1-7).

The reasons for the low reports are maybe due to : 1) a poor diffusion of a culture of the disease caused by the misuse of drugs 2) a poor awareness of the benefits that the spontaneous reporting system can create for the community in terms of reducing patient risks and saving resources (1,2,19).

Often one of the main causes of ADR is determined by the families that cause adverse effects reactions due to non-rational use of drugs. A high percentage of emergency accesses for adverse reactions, after ingestion of an overdose of drugs, was recorded.

The main causes of overdose are: accidental ingestion of the drug due to lack of adult control, defective or inadequate packaging (eg lack of security locking systems), error in the preparation / dilution of a more concentrated drug (1-3).

When the drug is used in clinical practice in large unselected populations, PAS Studies, according to GCP,GVP and ENCePP Code of Conduct, are useful becouse they highlight all the events that occur during monitoring, with estimates of incidence of ADRs that cannot be obtained by spontaneous reports. In these studies a significant role can be played by the FP- MCRN with the participation to active pharmacovigilance projects (1-6).

Another study was conducted by FP-MCRN on the correct use of antibiotics in children in the age group from 0 to 2 years of age (21-23)

In this study , after a comparison of prescriptive data of 2013 and the

year 2015 and after the formation of Family Pediatricians and the 'information to families on the proper use of antibiotics and of any adverse events related to their misuse, we have achieved:

1) a significant decrease of 27%. of the prevalence of prescriptions from 83% (2013) to 56% (2015)
2) a reduction in the number of prescriptions (equal to 2938) and a reduction of the number of pieces prescribed (equal to 2975), maintaining almost unchanged the number of assisted of 0-2 years in the two years under review,.
3) a saving expenses of EUR 18,854.23
4) an improving prescriptive appropriateness according to guidelines: the most prescribed was Amoxicillin (38%), followed by Amoxicillin + clavulanic acid (29.3%), Macrolides (16.3%), and the Cephalosporins (15.2%).

The importance of proper pediatric drug training becomes crucial for the prescriptive appropriateness on drugs to be used in this vulnerable group of people. It is also essential to give correct information to families on the knowledge and experience of pediatric drugs and on the importance of always consulting the pediatrician before administering drugs to children.

A significant aspect is also the importance of the synergy of pediatricians and pharmacologists for the organization of both clinical research projects and training events aimed at the correct use of drugs in children.

The organization of specific training courses and research projects mast be aimed at:
1) develope the culture of iatrogenic disease in pediatrics;
2) promote prescriptive appropriateness and proper use of pediatric drugs;
3) encourage spontaneous reporting of ADRs in children;
4) involve Family Pediatricians in post-authorization safety studies according to GCP,GVP and ENCEPP Code of Conduct.

Therefore it is necessary to build pediatric clinical studies according to the methodological principles standard, transparency and independence (to eventually acquire an ENCePP Study Seal).

The FP-MCRN has acquired the skills and the experience to build high quality clinical studies, with methodology and scientific rigor.

The quality and ethics of research are becoming important key points of pediatrics, opportunities and the challenges of family pediatricians during their education and during health prevention in pediatric age groups.

The main objective of Family Paediatricians should be to take knowledge of pediatrics drugs through the training and construction of clinical trials and publishing of paper work about primary care in order to guarantee better decision-making (21-23).

Competing interests
The authors declare that they have no competing interests.

Acknowledgements
No sources of funding were used to assist in the preparation of this article.

Mrs Rosanna Rea provided assistance for preparing and editing the manuscrip t.

REFERENCES
1) Napoleone E. Children and ADRs (Adverse Drug Reactions). Ital J Pediatr 2010 Jan 15, 36:4
2) Napoleone E, Radice S. From pharmacovigilance to therapy amelioration in paediatric patients: The role of the clinical pharmacologists and family paediatricians Part of a series on Paediatric Pharmacology, guest edited by Gianvincenzo Zuccotti, Emilio Clementi, and Massimo Molteni. Pharmacol Res.65 (2012)168-170
3) Napoleone E. Medicines for children ADRs: from spontaneous reporting to active souveillance.Child :care, health and development , 2009. 36 (Suppl.1); 106-107.
4) Blake KV, Zaccaria C, Domergue F, La Mache E, Saint-Raymond A, Hidalgo-Simon A.Comparison between paediatric and adult suspected adverse drug reactions reported to the European medicines agency: implications for pharmacovigilance.Paediatr Drugs. 2014 Aug;16(4):309-19.
5) Clavenna A., Bonati M.. ADR Epidemiology in Paediatrics. M&B,2009,28:503-504.
6) Venegoni M. The importance of case reports in Pharmacovigilance. M&B,2009,28:501-503..
7) Napoleone E. Adverse drug reactions and Family Paediatricians. M&B,2009,28:505-506.
8) Palmaro A, Bissuel R, Renaud N, Durrieu G, Escourrou B, Oustric S, Montastruc JL, Lapeyre-Mestre M. Off-label prescribing in pediatric outpatients. Pediatrics. 2015 Jan;135(1):49-58.
9) Regulation (EC) No 1901f2006 of Ihc European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use [online]. Available from URL: http: //ec. europa. eu/enterprise/ pharmaceuticals/ eudralex/ vol/reg 2006 1901/reg 2006 l901_en.pdf
10) Bellis JR, Kirkham JJ, Nunn AJ, Pirmohamed M.Adverse drug reactions and off-label and unlicensed medicines in children: a prospective cohort study of unplanned admissions to a paediatric hospital..Br J Clin Pharmacol. 2014 Mar;77(3):545-53.
11) Thiesen S, Conroy EJ, Bellis JR, Bracken LE, et all. Incidence, characteristics and risk factors of adverse drug reactions in hospitalized children - a prospective observational cohort study of 6,601 admissions.BMC Med. 2013 Nov 7;11:237.
12) Aagaard L, Hansen EH. Adverse drug reactions associated with asthma medications in children: systematic review of clinical trials. Int J Clin Pharm. 2014 Apr;36(2):243-52.
13) Aagaard L, Hansen EH. Adverse drug reactions in children reported by European consumers from 2007 to 2011.Int J Clin Pharm. 2014 Apr;36(2):295-302.
14) Choonara I. Educational paper: aspects of clinical pharmacology in children pharmacovigilance and safety. European Journal of Pediatrics 2012:31.
15) D'Amore C.,Menniti-Ippolto F, Traversa G. La Farmacovigilanza in età pediatrica. Prospettive in Pediatria, 2014, Vol.44.N.175.203-207.
16) Ferrajolo C, Capuano A, Trifirò G, et all. Pediatric drug safety surveillance in Italian pharmacovigilance network: an overview of adverse drug reactions in the years 2001 - 2012.Expert Opin Drug Saf. 2014 Sep;13 Suppl 1:S9-20.
17) Fabiano V, Mameli C, Cattaneo D, Delle Fave A, Preziosa A, Mele G,Clementi E, et al. Perceptions and patterns of use of generic drugs among Italian family pediatricians: first round results of a web survey. Health Policy 2012;104:247–52.
18) http://www.encepp.eu/encepp/viewResource.htm?id=17452
19) Pellegrino P.; Carnovale C, Cattaneo D, Perrone V ,Antoniazzi S, Pozzi M, Napoleone E, Filograna MR,Clementi E, Radice S. Pharmacovigilance knowledge in family paediatricians. A survey study in Italy.Health Policy 2013 Nov 27;113(1-2):216-20. Epub 2013 Aug 27 Journal of Clinical Pharmacology 1996;41:434–5.
20) Napoleone E., Scasserra C. Pharmacovigilance in Pediatric Age: The Role of Family Pediatricians- Medicines for Children Research Network (FP-MCRN). J Pharmacovigilance 2015, 3: 168
21) Napoleone E., Lavalle A., Scasserra C., Ricci M. Active Surveillance on the Use of Antibiotics in Children, Particularly in the Age Group from 0 to 2 Years. J Pharmacovigil 2016, 4: 205
22) Napoleone E. The appropriate use of antibiotics in early children: the FP-MCRN study J Develop Drugs, 2016, 5:2 (Suppl), 87
23) Napoleone E., Lavalle A., Scasserra C., Gentile S., Ricci M."Improper Use of Antibiotics in Early Children Increases the risk of ADRs and Drug Resistance : the FP-MCRN Study" Cogent Medicine (2016), 3: 1265203, pgg 3-4