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Factors Related to Irrational Use of Medicines during Childhood

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ABSTRACT

This paper offers an analysis of some factors that lead to irrational use of medicines during childhood. Included among these factors are: the parents' limited knowledge about medicines, the insufficient testing of medicines on children, the limited knowledge of side effects, the problem of the prescription process for pediatric medicines, the inadequate follow-up of pharmacological treatment, and risks of accidental poisoning.

Rational medicine use by children is recommended. Achieving it requires the collaboration of the children, their parents, their doctors, their pharmacists, legislators, and drug manufacturers. The whole approach to medicine use in childhood should take account of cultural, social, and family environments.

Keywords: *Drug information; Drug prescribing; Drug use, inappropriate; Drugs, adverse reactions; Pediatrics; Review.*

Introduction

There is very little research regarding the use of medicines during childhood, especially if we consider not only those medicines prescribed by doctors, but also the ones that are self-prescribed by the children's guardians.

As in the case of adults, medicine use in childhood is often not very rational when compared with standards of clinical pharmacology [1]. Prescribed drugs are used in ways that are inappropriate, inefficient and even dangerous [2-8], and compliance to treatment is poor [3,9-14]. Frequently, parents acquire self-prescribed medicines [15-19] that can also be used inadequately to treat their children.

The purpose of this paper is to review the literature on pediatric drug use and to analyze some aspects related to medicine use during childhood, such as the characteristics and consequences of inappropriate use and recommendations for rational use of medicines.

Quantities and types of medicines prescribed to children

In a study of outpatients. Kennedy and Forbes [20] found that 12% of all prescriptions

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were for children of under 14 years (14% of the population).

A longitudinal study in the U.S. dealing with the quantities and types of prescribed medicines to children in ambulatory care during their first five years [21] confirmed what other studies had questioned: antibiotics, especially members of the penicillin family, are the most commonly prescribed medications. In this study it was demonstrated that antibiotics are prescribed by pediatricians for 95% of children before their fifth birthday. From birth to the age of four, children received an average of 8.5 courses of prescription medications and an average of 5.5 different medicines (87% was prescribed for two weeks or less). Within this group even higher quantities of medicines were prescribed for children aged between 7 and 12 months. These children are usually exposed – for the first time – to some infectious diseases, are very vulnerable to otitis media, and are building up an immunological arsenal. During the fifth year, only 42% of the cohort received prescribed medicines, but a greater percentage corresponded to the treatment of chronic conditions than when the cohort was younger. Subjects exposed to a high dose of medication had a tendency to use more medical services.

The authors of the above-mentioned study concluded that some children in their first five years of life received too much medication (up to 37 medicines). This, though, does not include non-prescription medicines which probably exceed those prescribed [22,23].

Nolan and O'Malley [24] examined the existing differences in patterns of prescription in relation to the patient's age. They observed a linear increase in the average of prescribed medicines in each prescription: from 1.5 in children of 0-9 years up to 2.8 in patients older than 80 years of age.

In Spain, studies of medicine use are very limited. In a study conducted at a family and community health center on the outskirts of one of the Canary Islands [25], it was shown that, in 1985, the average number of prescriptions issued per pediatric consultation was 1.2 per person compared to the national average of 2.5. 23% of the children did not receive any medication and 52% received only one prescription. In accordance with other pediatric studies, this study demonstrated that antibiotics topped the list of prescriptions emanating from pediatric visits, accounting for 33.5%. This last fact seems to be excessive, particularly if one considers that the predominant diagnosis is upper respiratory tract infection caused by virus which does not necessarily require antibiotics. Bronchodilators were the second most frequently used drugs in pediatrics (21.4%).

There are great differences between countries. For instance, a comparative study between Tenerife (Canary Islands) and Sweden [26] of medicine prescriptions for ambulatory children under 14 years of age showed a higher exposure to medicines in the Spanish population. For example, twice the number of Spanish children received antibiotic treatment in comparison to Swedish children. In both Tenerife and Sweden, the most common child illness was infection of the upper respiratory tract (28.2% in Tenerife and 28.8% in Sweden). Expectorants, cough and cold preparations, including vasoconstrictors and antihistamines, were common in both countries. Only half of the children in Sweden received medication as opposed to 90% of the children in Tenerife.

Reckoned per consultation, the children who received a prescription received an average of 1.4 medicines in Sweden and 2.3 in Spain. Furthermore, doctors in Spain chose a wider variety of medicines and more frequently used fixed combinations of products. The ten most commonly prescribed products in Sweden contained 11 active drugs altogether, as compared to 25 in Spain. These most frequently used products represented two-thirds of all the prescriptions for Swedish children but only one-third for Spanish children. The observed differences may be due to a variety of factors such as therapeutic traditions and drug promotion that need to be further explored. The outcomes of the therapy in relation to the differences in medication were not included in this study.

Some studies have analyzed the adverse drug reactions in children leading to hospitalization. Mitchell, Lacouture and Sheehan [27] studied a group of 10,297 hospitalized children, and found that 2% of admissions were due to adverse reactions to medicines. McKenzie et al. [28] also described 2% of 3,556 admissions of children into hospital as the result of adverse drug reactions. Even though doctors and parents are careful

about medicines given to children and keep a careful watch for the reactions, the aforementioned figures could be explained by pharmacological and psychosocial factors, including knowledge and attitudes regarding medicines.

Factors related to the irrational use of medicines in childhood

There are many factors that influence inadequate use of drugs during childhood. Such factors are not only related to children and parents, but also to legislators, pharmaceutical companies, doctors, and pharmacists. We should also bear in mind that the cultural, social, and family environment affects the use of medicines. As an example, what parents know about medicines from listening to the media and promotional campaigns, and having observed how their own parents had used medicines, will affect the actual use of drugs in childhood. There are nevertheless very few qualitative studies that focus on these aspects [29-31]. Among these non-medical factors are: setting and rituals of use, expectations, symbolic meanings attached to medicines and perceptions about them, sources of drug information, social learning phenomena, and use of medicines in the family context. But we will only consider some of the most relevant factors.

1. Parents' inadequate knowledge of medicines

At present, non-compliance to treatment is considered a serious problem. Some studies have found a relationship between parents' inadequate knowledge of medicines and non-compliance to treatment [3,11-13].

Donnelly, Donnelly and Thong [11] evaluated the knowledge of parents of asthmatic children regarding medicines that were used. Results indicate that between 0 and 42.2% of the parents had a very simple and elemental knowledge about the effects of these medicines, depending on the different drug compositions. Regarding the information on when to use the medicines, the percentages varied between 0 and 50% for different products; in relation to secondary effects, the extent of knowledge varied between 5.9% and 51.6%. Lack of knowledge about pharmacology for asthma was made evident by the fact that parents used antibiotics, antihistaminics, and decongestants for treatment. According to the authors, poor parental knowledge may account for the high prevalence of non-compliance in childhood asthma.

This study becomes especially relevant since asthma is one of the most common diseases in children, and it requires a continuous use of medication for long periods of time.

The need for a patient-parent educational approach if we wish to enhance compliance, is also highlighted by Finney et al. [12]. According to these authors, compliance with short-term antibiotic regimens for otitis media is improved by providing parents with an educational hand-out, a self-monitoring calendar, and a brief telephone reminder.

Simon [13] recommends that pediatricians give parents written information on non-prescription, OTC medication, and to take note of the parents' degree of distraction while the information regarding treatment is being discussed. According to this author, physicians should not assume that older, more experienced, or more educated mothers are less apt to mistake what they hear.

In Spain, Avila Guerrero [3] points out the lack of knowledge that families have in the use of medicines. This researcher indicates that there is a significant absence of health education, which leads to the assumption that remediation of symptoms and cure of illness are equivalent. He also observes the disproportionate fear of medicines; patients distrust doctors and they do not comply with their prescriptions.

Avila Guerrero's study also makes reference to the fact that families with high cultural and socio-economical levels, and those with a large number of members, are those most interested in reading the instructions for use. These households are also the ones that pay the greatest attention to expiration dates and preserving measures for drugs.

However, other studies such as the one by Zahr et al. [14] failed to support the hypothesis that patient education or written instructions help increase client compliance. The authors suggest that teaching methods aimed at increasing pediatric compliance should be made more attractive and tailored to the individual needs of clients.

According to the World Health Organization (WHO) European Regional Office

(EMRO) [32a], to achieve a safe and effective use of medication, children and parents must be informed. The doctor is responsible for providing such information. This should be accomplished through an open conversation with both parents and child regarding the treatment that is proposed. In most cases, the conversation should cover other themes, such as the possibility of choosing non-pharmacological therapies, including changes in diet, behaviour therapy, and physiotherapy, instead of, or as a complement to medicines.

WHO/EMRO proposes ten issues on which children and parents should be informed before using prescribed drugs.

- The name of the medicine,
- The reason for using it,
- When and how to take it,
- How to know if it is efficient and what to do if it is not,
- What to do when one or two doses are not taken,
- Possible risk involved in not taking it,
- How long you have to continue taking the medicine,
- Most common side-effects and what to do if these effects become manifested,
- The possibility of taking or not taking other medicines simultaneously,
- Other possible alternatives to the pharmacological therapy.

It seems obvious that most doctors and parents are not informed about these issues.

2. Lack of verification regarding efficacy and innocuousness of medicines in children

From a scientific, ethical, and legal point of view, it is a general rule that before introducing a medicine on the market, clinical trials should be conducted in order to evaluate its safety and its efficacy. At present, these trials are considered the most efficient tool available to determine whether a drug can be used [33]. Special caution should be taken before a new drug is used in the pediatric population, and there must be a long-term follow-up for adverse effects. Drugs can interfere in the process of development and growth, and some adverse effects may not appear until long after the medicine has been administered [34,35].

It is well recognized that it is very difficult to apply drug data from an adult population to a pediatric population. We have to consider, among other things, that there is a specific pathology in children, differences in pharmacokinetic and/or pharmacodynamic behaviour between children and adults (for example, absorption through the skin, degree of maturation of the metabolic systems, etc.), which provoke significant variations in the quantity of medicine that is available, and other specific difficulties in drug administration, depending on age [33,36,37]. However, this practice continues, although pediatric clinical trials – many of them directed to treatment of specific childhood pathologies – are becoming more common [33, 56]

There are also ethical and legal issues that affect the studies at verifying the efficacy of drugs used by children [7,34,38]. Even though freedom of research is a basic principle in society, certain restrictions should apply to protect the research subject himself. Both the need for parental informed consent and the evaluation of the risk-benefit ratio are of essential importance. Furthermore, the child should be informed in a manner appropriate to his age and understanding.

The control of the efficacy of both OTC and prescription drugs used by the children can only be established when their use has been indicated in the pediatric population. In some cases, doctors prescribe medicines for therapeutic indications that are not included in the product's labelling, which makes it even more difficult to probe its efficacy. According to Thompson and Heflin [7], the prescribing for unlabelled uses in pediatric patients is low and there is sufficient evidence in the medical literature to support at least some of these uses.

Another identified problem is the difficulty of adapting adult forms and dosages for the pediatric use without loss of efficacy and safety [39,40]. Liquids, for example, are more easily administered to the children than pills. Drug adjustment for pediatric use is, however, a complex process that involves many risks and limitations that can only be overcome through the dialogue between physicians and the pharmaceutical companies.

3. Lack of knowledge by doctors and parents regarding other effects of medicines upon development and nutrition

Adverse effects – such as those related to nutrition – that are due to medication in children are not always mentioned in the in-

structions accompanying pediatric medicines.

Some drugs have specific adverse effects on growth and development. For example, tetracyclines stain the teeth, cytotoxics cause fertility and growth problems, and systemic corticosteroids retard growth [32b]. Some adverse effects may be prevented by measurement of drug levels but the most important factors are rational prescribing and continued vigilance by the prescribing physician.

Pediatric drugs may also have significant nutritional consequences via their effects on appetite, nutrient absorption, nutrient metabolism, and nutrient excretion. Examples of common drugs and effects on nutrition include the inhibition of vitamin C storage by aspirin [41], and metabolism and utilization of folic acid impaired by phenobarbital and phenytoin [42]. These consequences have more clinical significance in malnourished children and in those who take medicines over very long periods of time [5]. As pediatric literature on this issue is very limited, parents cannot be informed about the possible effects of the medicines on nutrition [5]. And as instructions for use do not always specify the effects of pediatric medicines upon nutrition, growth and development, it is very important for doctors and parents to be cautious about such possible effects. This caution will allow them to recognize the effects and spread information about them [32b].

4. The problem with prescriptions for children

Many visits to the pediatrician conclude with pharmaceutical treatment. As a consequence, the basis for prescribing of medicines is very important [43]. Nevertheless, medication management in the pediatric setting is not always appropriate or rational, and it can even be dangerous due to the adverse reactions that it can cause [2,44-47].

Sources of problems

The WHO/EMRO [32c] points out some possible sources of problems in pediatric prescriptions. They are the following:

- Some prescribers are poorly educated in the basic principles of prescribing for children,
- Parents often exert inappropriate pressure on physicians to prescribe for their children even for mild, self-limiting conditions,
- An excessive emphasis on the role of drug therapy in relation to other therapeutic approaches,
- Doctors are under considerable pressure from drug companies to prescribe their products,
- Limited time for consultation may increase the pressure to prescribe.

First, we have to question whether medicine is necessary. This is difficult to answer, since we must consider if medicine is to be prescribed for a specific treatment or just to relieve a symptom. Many medicines used by children are frequently used for symptoms for which there is no established knowledge of efficacy. In a study conducted in a pediatric hospital [7] a total of 62 (7%) of the 951 drug orders were unlabelled pediatric indications. A consensus of appropriate use was achieved in 24 (39%) cases, and a consensus of inappropriate use was achieved in 10 (16%) instances. No consensus was reached in 45% of cases. Among the most common non-approved indications were mannitol for diuresis, and cimetidine for gastric acid hypersecretion.

Problem areas

The WHO/EMRO [32d] elaborated a list of specially problematic areas relating to medicine prescription during childhood. Among the most common are, for example, prescription of antibacterial medicines for upper respiratory tract infections that are usually viral, the use of medicines for diarrhoea, and the use of medicines to increase appetite. These areas of medicine correspond to 70% of all medicines taken by children. As a consequence, about two-thirds of the medicines prescribed to children may have little or no value. This fact could have significant consequences regarding future prescriptions, especially in terms of the parents' demand for and expectation of drug therapy. The social and psychological consequences that could be induced in the child by the way medicines are administered are still unknown. Children might grow up believing that medicines are a solution for many of life's problems [32e].

In a study conducted at a pediatric teaching hospital [2], an extensive use of antibiotics was observed. It was indicated that antibiotic management was inappropriate in 66 % of surgical patients and in 21 % of medical patients because of not conducting appropriate studies, lack of indication,

wrong drug, dose or timing. This situation leads us to conclude that appropriate studies – including culturing prior to initiating therapeutic courses of antibiotics, the timing of prophylaxis, and the duration of administration – prior to and during therapy seem to be necessary to avoid rising medical costs and the emergence of antibiotic-resistant bacterial strains.

Another study at two pediatric hospitals revealed a frequency of 1.35 and 1.77 mistakes, respectively, per 100 days of hospitalization for each patient [6]. The most common error was with dose, overdose being the most frequent. Children two years old or less received the highest proportion of prescriptions with errors. Newborns received, however, the fewest prescriptions with errors. The more experienced doctors, and those with more training, were less liable to commit errors with prescriptions than those doctors with a lower level of training and experience.

The increasing complexity of pharmaceutical formulas will probably increase the risk of errors in pediatric prescriptions [6].

Choosing medicines

The WHO/EMRO [32e] suggests the following seven considerations for choosing medicines: efficacy, low toxicity, clinical use and kinetic data availability, cost, availability of appropriate administration method, risk of poisoning, and combination products.

Children differ from adults in the way they respond to medicines. There is also a significant variation in response among children of different ages. These differences may persist even when dosage is adjusted for body weight or surface area [32g, 36].

Theoretically, a prescription based on research in age groups and for a specific disease should result in a safe and effective pediatric therapy. However, each child is different and the doctor should anticipate the possible variations in the use and responses to medicines. These inter- and intra-individual differences make rational medicine use difficult in children. Sanz [48] suggests the need to analyze the differences in children's medicine use from a multidisciplinary approach that will take into consideration psychosocial factors affecting drug use in children. According to this author, attitudes and beliefs regarding medication play a key role to the point that some drugs — such as vitamins and appetite stimulants — are kept on the market because they are regarded as "good for health" substances, even though their efficacy in most cases cannot be proved.

In order to establish criteria to prevent errors in medicine dosaging, certain countries, like France, issue tables of medicine doses for pediatric use; these tables serve as official documents. In this matter, Lechat [49] points out that there are certain problems in determining the official dose. Some of these problems have to do with the choice of age groups, medicine selection, how to express the dose, the usefulness or lack of usefulness of indicating maximum dose, and the disseminating of this data among doctors and pharmacists.

These problems make it necessary to set out specific criteria for doctors to be taken as guidelines for prescribing, and, even more important, to let parents know the dose determined for medicines that their children are going to take. Berlin [50] recommends giving parents careful instructions about appropriate dose and the instruments to measure them with accuracy, so we can avoid such words as "small spoon" or "big spoon"[1].

5. Supervision of pharmacological treatment

Due to variations in children in the use and responses to medicines, as well as the narrow margin of safety that medicines might have in this population, the WHO/EMRO [32g] recommends that physicians anticipate a variation in drug responses from patient to patient and supervise drug handling and response. This practise is common and traditional in clinics. However, most physicians practising outside hospitals do not have the facilities for the monitoring of the pharmacological treatment.

Therapeutic drug monitoring provides many advantages. It helps to determine the dose capable of producing safe and effective concentrations. It also allows the evaluation of compliance with treatment and the interpretation and understanding of medication interactions. Blood analysis is the most recommended evaluation [32g,34]. The use-

[1] In some countries, e.g. Sweden, the dose for liquid medicines must be accurately prescribed in ml and dosage cups are delivered from the pharmacy together with the medicine. [Editor's comment].

fulness of routine monitoring of drug concentrations during the treatment of some common clinical conditions has, however, been questioned by Spector et al. [51]. These authors claim that no prospective, randomized, controlled trials exist demonstrating that a strategy of monitoring target concentration is superior to experienced clinical observation. This suggests that drug assays might be overused, which would have significant implications in cost containment.

The efficacy control of medicine that is on the market should not be limited to the follow-up of the patient, the child in this case. It should also include post-marketing studies in order to obtain the necessary information for its very best use [52].

6. Poisoning risk due to medicine use

Poisoning due to the use of medicine in preschool children is one of the main reasons motivating visits to acute departments at in hospitals [8,32h]. We have to recognize, nevertheless, that this is no longer an important cause of mortality [32h].

According to the WHO/EMRO [32h], accidents by poisoning could occur for some of the following causes:

- The child's exploratory behaviour, particularly in children aged 18-36 months,
- Doctor's prescription for excessive doses of medicines or mistakes by pharmacies,
- The child mistaking medicine for sweets,
- Inadequate storage or supervision,
- Adolescent suicide attempt or cries for help,
- (Rarely) Inappropriate administration of medicines by parents.

In case of poisoning, it is very important that parents know the immediate measures which must be taken.

Avila Guerrero [3] made a qualitative and quantitative analysis of medicines in some homes in the city of Córdoba (Spain). He concluded that these medicines become a potential risk for the health of house members. The risk is a consequence of medicines that are used without any previous medical diagnosis, and the possibility of inducing accidental/undesirable effects, e.g. intoxication, especially in children.

King and Palmisano [8] point out that medicines tend to be too accessible to children and that the containers are easy to open. These are the two main factors that cause poisoning. To avoid this, they recommend the use of child-resistant packaging of many hazardous household products and prescription drugs.

Three of the seven medicines that cause most cases of poisoning in children in the United States were also among the five medicines most prescribed in that country [8]. This suggests the obvious conclusion that the simple fact of availability of medicine is a risk factor. As a matter of fact, in the King and Palmisano's study [8], 60% of such medicines belonged to mothers and grandmothers.

It is equally important that all medicines be identified by name on the container, since with such a precaution many deplorable problems could be avoided. Prevention represents the most effective approach [53]. Health education programmes for parents and children will also help in identifying risks and consequently adopting preventive measures.

Conclusion

Some of the factors leading to irrational medicine use during childhood can be controlled if there is collaboration between children, parents, doctors, pharmacists, legislators, and drug manufacturers. In particular, health education is necessary in order to enable parents and children to improve their knowledge of medicines. The effects of medicines on development and nutrition should also be taken into consideration by both parents and doctors. In addition, it is important that doctors supervise drug use and response.

The implications of early exposure to medicines need to be further explored. For example, it would be necessary to conduct research regarding to what level exposure to medications in early life is related to subsequent excess in consumption or a dependency pattern from a pleasure effect of medication.

Studies of the determinants of similarities and differences in pediatric prescribing among countries will help to identify major therapeutic problems and to develop a more rational pharmacotherapy, e.g. by educational programmes for the prescribers, as well as for the children and their parents.

Finally, pharmaceutical companies should perform clinical trials to evaluate safety and efficacy, and they should use safe containers for children.

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