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Some H2 Antihistaminics And Ppi-S Products Authorized In Albania And Their Availability For Pediatric Groups

Briseida Dosti, Msc.
Ledjan Malaj, Prof.
Medicine University of Tirana, Faculty of Pharmacy, Department of Pharmaceutical Technology and Biopharmacy, Tirana, Albania

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Abstract

The objective of this study was to evaluate the number of medicines and active ingredients for pediatric population that are authorized and marketed in Albania. For this purpose were selected two group's medicines: H_2 antihistaminics and Proton Pump Inhibitors. The availability of pediatric medicines and active ingredients was studied with the help of the database of the Albanian National Agency for Medicine and Medical Devices and SmPCs. Selected active ingredients were categorized based on their route of administration, type of pharmaceutical form, dosage, therapeutic indication, dose capability and suitability of the pharmaceutical form for use in children. From evaluation of SmPCs of selected products for the authorized age - group were found that 58 products are also authorized for use in children. Two of the active ingredients are authorized only for use in adults. The analyze of aspect if the recommended dose prescribed based on the classification of pediatric age stated give these data's: 35 products are authorized for use children and adolescents from 3–18 years and 23 products are authorized for use in children more than 1 year old. This study shows a lack of availability of pediatric medicines for selected products and shows that pediatric medicines may not be age-appropriate; even they are authorized for such use. It was shown that few medicinal products are specifically studied in children. Therefore, are needed more efforts to increase the number of drugs authorized for the pediatric groups. Even more, it is required by pharmaceutical companies to supply data on the effects of new drugs in children.

Keywords: Pharmaceutical form, pediatric medicines, H_2 antihistaminics, PPIs, authorized

Introduction

The lack of appropriate pediatric formulations is a worldwide problem (Giacoia et al. 2007). Pharmaceutical companies developed dedicated preparations for pediatric patients mainly if the products are likely to be marketable and will generate profit for the manufacturer (Pawaret al. 2002). Physicians often have prescribed unauthorized medicinal products due to lack of suitable and authorized medicine for children, in order to provide medical assistance to them (Chui J et al. 2004, Chui J et al. 2005, Cuzzolin L et al. 2006, Kairuz TE et al. 2006).This attitude seems to lead to an increased rate of adverse drug reactions and medical errors (Young L et al. 2009, EU Regulation no 19012006, Auby 2008).

Due to different strategies of Pediatric Regulation in the EU, approved on January 2007, the pharmaceutical industry is obliged to plan clinical trials in children at an early stage of the development of medicines containing a new active substance. The same requirement applies to the development of a new indication for existing medicinal drug products (Breitkreutz 2008, Ceci A et al. 2002). The design of currently authorized pediatric medicines is not always optimal (Cohen R et al. 2009). Sometimes tablets have been authorized for children below the age of 6 years, even though they may be not able to swallow tablets (Cohen R et al. 2009). Therefore, it is very important to study if authorized medicines are really adequate for use in children.

The first objective of this study was to evaluate the number of medicines and active ingredients for pediatric population that are authorized and marketed in Albania, for selected groups. Also, as an additional objective was to evaluate the age-appropriateness of the selected medicines based on their suitability of authorized dose and pharmaceutical form for use in children.

Methods

With the help of the database of medicines of the Albanian National Agency for Medicine, until 10 April 2015, was identifies authorized medicines for below stated active ingredients. In total was studied 84 medicinal products from selected active ingredients. For this study was selected and evaluated below mentions pharmaceutical groups: H_2 Antihistaminics: Ranitidine; Proton Pump Inhibitors: Omeprazole, Esomeprazole, Lansoprazole, Pantoprazole, Rabeprazole.

Database of medicines in Albanian is updated on a monthly level and contains all medicinal products authorized in Albania from National Agency for Medicine and Medical Devices and Ministry of Health. Authorized medical products refer to a single dosage or pharmaceutical form. For each

product were analyzed major characteristics as the route of administration, e.g. oral, intramuscular, approved dosage and pharmaceutical form.

This database doesn't allow extraction of marketed products and active ingredients classified based on age-appropriateness. For this reason were evaluated Summary of Product Characteristics (SmPC). Based on the Albanian regulation of approving products texts at the same time performed by the referent country of Marketing Authorization, the information of authorized SmPCs was checked in databases of Medicines Compendium, Irish Pharmaceutical Healthcare Association, Croatian Agency for Medicinal Products and Slovenian Agency of Medicinal Products. From published SmPCs were analyzed sections: pharmaceutical form, therapeutic indications, posology, and route of administration.

A special focus was dedicated to age-appropriateness of selected products. First investigated aspect was if recommended dose is prescribed to children based on the classification of pediatric age stated in Tablets 1 (ICH Topic E 11).

Table 1. Classification of pediatric population

Groups	**Age**
Preterm newborn infants	
Term newborn infants	0 – 27 days
Infants and toddlers	28 days – 23 months
Children	2 – 11 years
Adolescents	12 to 16-18 years (dependent on region)

Second investigated aspect was if approved pharmaceutical form, for selected products in this study, were suitable for use in children. If pharmaceutical form were considered as not suitable e.g., tablets 150 mg for children 3 years old), were verified the presence of an alternative form e.g. liquid pharmaceutical forms. For solid forms (such as tablets and capsules) were evaluated the presence of the score line and the possibility of opening or not contains capsules.

Based on all prescribed methodology use for this study were collected these data: authorized indications; authorized age-group; pharmaceutical form; authorized dosage; the presence of score line; information on the possibility for opening capsules contains.

Results and Discussions

The availability of selected medicines and active ingredients are described in Table 2.Were found 20 authorized products containing Ranitidine; 23 authorized products containing Omeprazole; 11 authorized products containing Esomeprazole; 4 authorized products containing Lansoprazole; 25 authorized products containing Pantoprazole; and 1 authorized products gastro-resistant tablets 20 mg containing Rabeprazole.

Table 2: Availability of selected medicines for the study

Active ingredient	Therapeutic class	Authorized indication	Authorized age-group	Authorized form and strength	Number of products
Ranitidine	H2 Antihistaminics	Reflux oesophagitis, benign gastric and duodenal ulceration, prophylaxis of duodenal ulceration	Adults, Children and adolescents from 3 – 18 years	Film-coated tablets 150 mg; Solution for injection 50 mg/ml	20
Omeprazole	Proton Pump Inhibitors	GER, duodenal and gastric ulcers, Zollinger-Ellison syndrome, Helicobacter eradication therapy	Adults, Capsules > 1 year, Powder for solution for injection > 1 year	Gastro-resistant capsules 20 mg; Powder for solution for injection 40 mg/vial	23
Esomeprazole	Proton Pump Inhibitors	Duodenal and gastric ulcers, GER	Adults, Adolescents >12years	Gastro-resistant tablets and capsules 20 mg and 40 mg; Powder for solution for injection 40 mg/vial	11
Lansoprazole	Proton Pump Inhibitors	Duodenal and gastric ulcers, GER, helicobacter pylori eradication, prophylaxis in reflux oesophagitis	Adults, Adolescents >12years	Capsules 15 mg and 30 mg	4
Pantoprazole	Proton Pump Inhibitors	GER, duodenal and gastric ulcers, Zollinger Ellison-syndrome, Helicobacter eradication therapy	Adults	Gastro-resistant tablets 20 mg and 40 mg; Powder for solution for injection 40 mg/vial	25
Rabeprazole	Proton Pump Inhibitors	Duodenal and gastric ulcers, GER, helicobacter pylori eradication	Adults	Gastro-resistant tablets 20 mg	1

From evaluation of the SmPCs of selected products for the authorized age - group were found that 58 products (69 %) are also authorized for use in children. Two of the active ingredients Pantoprazole and Rabeprazole are authorized only for use in adults. The analyze of aspect if recommended dose is prescribed to children based on classification of pediatric age stated give these data's: 35 products (60.34 %) are authorized for use children and adolescents from 3 – 18 years and 23 products (39.66 %) are authorized for use in children more than 1 year old (figure 1).

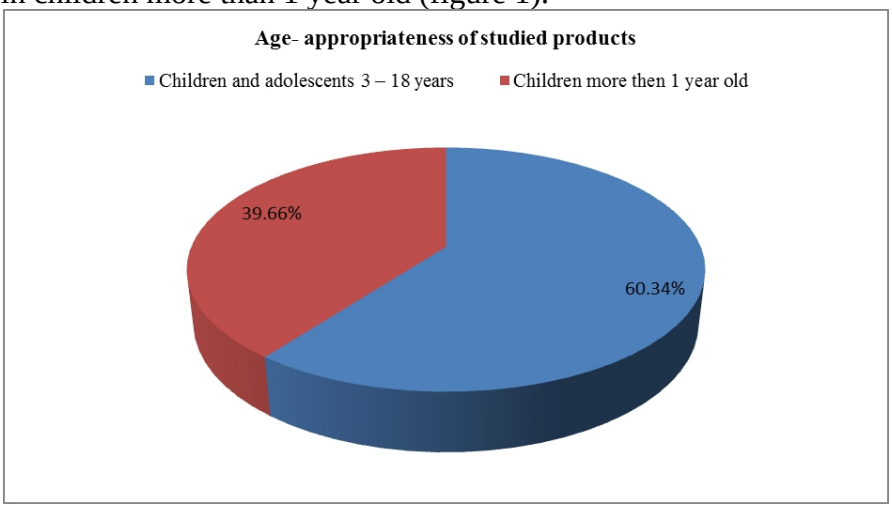

Figure 1: Authorized age-groups of products based on dose prescribed for children

Evaluation of SmPCs for age-appropriateness of these products on the suitability of pharmaceutical forms showed that all products are authorized as solid oral forms and as a solution for injections. All approved pharmaceutical forms are as follows: 14.3 % (n = 12) film coated tablets, 20.2 % (n = 17) solution for injection, 28.6 % (n = 24) gastro-resistant capsules and 36.9 % (n = 31) gastro-resistant tablets (figure 2). For any active ingredient wasn't found authorized liquid formulations, which are more appropriate for use in children.

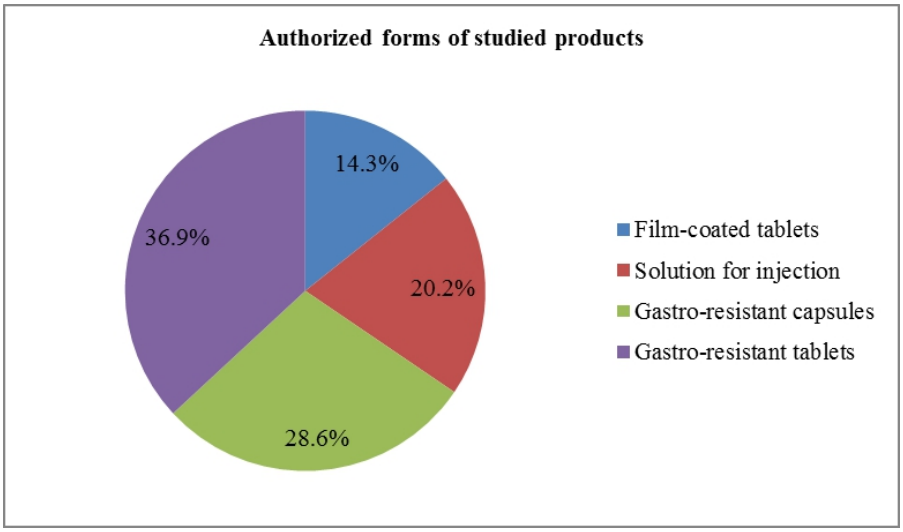

Figure 2: Authorized pharmaceutical forms for studied products

Results of investigation of solid approved form (tablets and capsules) for presence of score line in order to archives smaller dosages are as following: from 12 authorized products Ranitidine 150 mg film-coated tablets, 75 % (n = 9) of authorized products they were without score line, 16.7 % (n = 2) were with score line on one side of tablet and 8.3 % (n = 1) was with score line on both sides of tablets (figure 3).

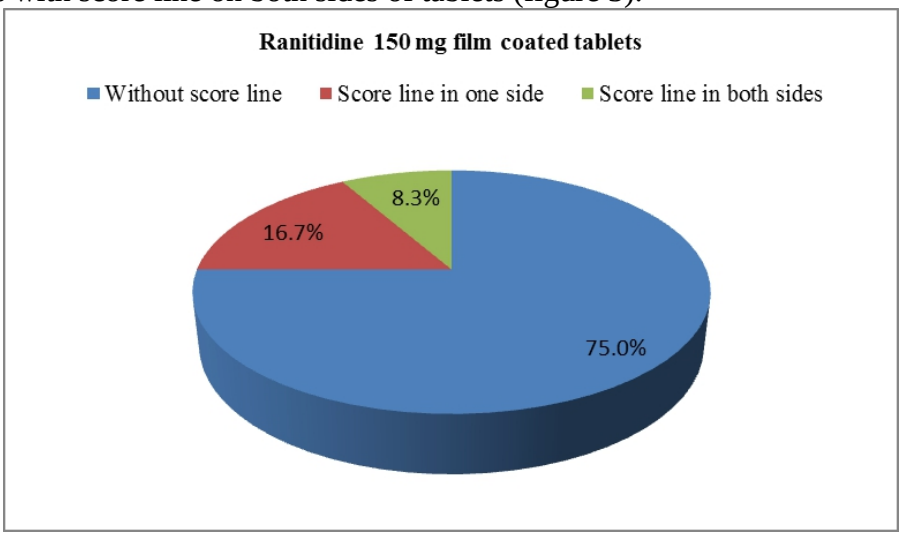

Figure 3: Presence of score line in Ranitidine 150 mg film coated tablets

This shows that only a few products in solid forms are suitable for archives smaller dosages than those for adults, in order to have an exact dosage needed for children treatment.

As it is known that children below the age of 6 years may be not able to swallow tablets (Cohen R et al. 2009), we evaluate the possibility of opening capsules and use it contains orally. Information studied from SmPCs of products available in capsules shows that only for Omeprazole authorized products is stated that patients can open the capsule and swallow the contents with half a glass of water or after mixing the contents in a slightly acidic fluid and that the dispersion should be taken immediately (or within 30 minutes).

Conclusion

This study shows a lack of availability of dosage forms for selected products and shows that pediatric medicines may not be age-appropriate; even they are authorized for such use. It was shown that few medicinal products are specifically studied in children. Also, it is shown that medicines authorized for children may differ with respect to their ability to provide the recommended dose and suitability of pharmaceutical form. Therefore, are needed more efforts to increase the number of drugs authorized for the pediatric groups. Even more, it is required by pharmaceutical companies to supply data on the effects of new drugs in children. The dose capability was considered important criteria. A medicine is either dose capable or it is not. However, the suitability of pharmaceutical forms is not as absolute. According to EU reflection paper tablets and capsules are only suitable for the age of 6 years. However, recent studies have shown that small tablets can be swallowed by young children (Thomson SA et al. 2009, Sturkenboom MC et al. 2008). Also, some capsules can be opened and can be ready for use if contains is mixed with water or liquids.

Physicians and pharmacists should consider that by using formulation not appropriate for children may cause administration errors, lack of therapeutic income and unexpected side effects. In order to reduce the risk of any of below problems, they are encouraged to search for marketed products the most appropriate medicine for treating groups of the pediatric population.

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