

Frequency of drug consumption and lack of pediatric formulations

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RESUMEN

Antecedentes: La falta de medicamentos pediátricos es un problema que ha limitado la prescripción en esta población a lo largo del tiempo, lo que conduce a errores en la administración del medicamento.

Objetivo: Determinar la frecuencia de consumo de medicamentos en el Instituto Nacional de Pediatría en un periodo de seis años, e identificar aquellos para los cuales no hay una formulación pediátrica adecuada.

Métodos: Se investigó la frecuencia de consumo de medicamentos, utilizando la base de datos de la Farmacia del Instituto Nacional de Pediatría, durante el periodo de enero del 2001 a junio del 2006. Los medicamentos se agruparon por la frecuencia que fueron recetados y se identificaron aquellos que no están disponibles para uso pediátrico y sin embargo se prescriben.

Resultados: Fueron utilizados cerca de 85 fármacos diferentes para atender las demandas del hospital; de ellos se prescribieron 7,514 veces durante el periodo de estudio. Los más utilizados fueron: ranitidina (4.7%), paracetamol (3.8%) y midazolam (3.7%). Los fármacos midazolam, furosemida, fenobarbital, omeprazol, prednisona y captopril, fueron más utilizados, de los cuales no hay formulaciones pediátricas comercialmente disponibles.

Conclusión: Se informa la frecuencia de consumo de medicamentos en un hospital pediátrico; el análisis se enfoca a la falta de formulaciones adecuadas para pacientes pediátricos en nuestro país.

Palabras clave: Consumo de fármacos, formulación extemporánea *, pediatría.

* hecha a partir de una fórmula conocida

ABSTRACT

Background: The lack of pediatric drug formulations is a problem that has limited the prescription in that population in the long term, resulting errors in drug administration by patients.

Objective: To determine the frequency of drug consumption at a National Pediatrics Institute in a six year-period, and identify those medications for which there is no available pediatric formulation.

Methods: The frequency of consumption of medications was investigated, using the data base at the Pharmacy of the National Pediatrics Institute during the period from January 2001 to June 2006. Drugs were grouped according to their frequency, identifying those not available for pediatric use which are nevertheless prescribed.

Results: About 85 different drugs were used to attend hospital demands, which were prescribed on 7514 occasions within the period of study. The most frequently used drugs were: ranitidine (4.7 %), paracetamol (3.8 %) and midazolam (3.7 %). Our results showed that midazolam, furosemide, phenobarbital, omeprazole, prednisone and captopril were the most prescribed drugs for which there are no pediatric formulations commercially available.

Conclusion: This article reports the frequency of drug consumption at a pediatric hospital and discusses it in view of the lack of adequate formulations for pediatric patients in our country.

Key words: Drug consumption, extemporaneous formulation, hospital pharmacy, pediatrics.

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Several reports on drug prescribing patterns have been published with the aim of identifying areas for practice improvement. Extensive deliberation on drug prescribing patterns is essential to improve prescribing standards and quality of care and it is vital for pharmacoepidemiological research.¹ Interest in studying drug utilization trends is increasing because drug costs show the fastest growth rate in all of the health care

system.² This information on pharmacoepidemiology is particularly important in developing countries where a rational drug policy has not been adopted yet.

It is important to emphasize the need for comprehensive measures, including information, training, legislation and education at all levels of the drug delivery system, in order to rationalize drug therapy by improving prescribing patterns and avoiding self-medication.³

Marketing may play an important role in the frequency of use of specific drugs, such as the recent use of sildenafil (vasodilator); their increased utilization cannot be explained by clinical trial evidence and/or practice guidelines. It is important to consider this when drugs are used in clinical trials on the pediatric population. Adequate trials to improve drug consumption in this population are seriously needed.

Various studies have associated cost savings with the use of pharmaceutical products in treating specific diseases. Evidence suggests that appropriate use of drugs can potentially lower total expenditures and improve the quality of care.⁴

In Mexico, there are some studies on patterns of drug consumption. This aspect in children from a rural community of the state of Morelos, Mexico, was studied. The study included 670 patients of ages from 0 to 14 years; the most frequent diagnosis were respiratory infections in 390 patients (58.2%), followed by gastrointestinal infections in 181 patients (27%) and dermatological illness in 62 cases (9.2%). The most frequently consumed drugs were: antitussives (29%) and antibiotics (23.5%). However, consumption of herbal products was very popular in this community. Thirty seven percent of the studied population consumed this kind of products and/or home remedies to cure the diseases. Since Mexico is a country of many traditions, herbal product consumption is a common practice. The patterns of consumption reported in this study are probably quite similar to those found in other Mexican rural communities.⁵

In another study describing consumption of antibiotics by children seen at the National Institute of Pediatrics, Juárez et al (1998) reported that in a period of 15 months, 406,773 medications were consumed, of which 130,627 (32.1%) were antibiotics. The highest

antibiotics consumption rate was registered in the Department of Surgery (63%) and Infectology (48.6%). The most frequently consumed antibiotics belonged to the penicillin group (30%), followed by aminoglycosides (27%), cephalosporins and macrolides (8%).⁶

At the Neonatal Infectology Department of the National Pediatrics Institute, antibiotics consumption patterns were described in 851 patients from 1993 to 2000. Of 93 drugs used, 34 were antibiotics. The antibiotics most frequently used were aminoglycosides, (30%), cephalosporins (18.4%) and aminopenicillins (16.4%). The five most commonly used antimicrobial drugs were: amikacin 23.8%; ampicillin, 16.28%; dicloxacillin, 14.13%; ceftriaxone, 7.4% and cefotaxime, 6.2%. A large number of patients received 4 different antibiotics, although not simultaneously. Physicians justified the wide use of antibiotics in order to fight against the increase in the number of resistant bacteria and to avoid the adverse reactions.⁷

The aim of the present study was to determine the pattern of drug consumption at the National Institute of Pediatrics in a six year-period, and identify medications for which there is no adequate pediatric formulation.

MATERIAL AND METHOD

A retrospective and descriptive study was performed to determine the pattern of drug consumption at the National Institute of Pediatrics. Information on the frequency of drug consumption was obtained from the database of the pharmacy at the Institute, from January 2001 to June 2006. Drugs were then ordered based on the frequency of consumption and their pharmacological group. The relevant literature was reviewed to determine the most frequently used drugs, for which only adult formulations are available in Mexico.

RESULTS

There were 85 different drugs used, which were prescribed on 7,514 occasions within the study period.

Antibiotics were the most frequently pharmacologic group, of prescribed drugs with a total of 2,840

consumptions (37.8%); dicloxacillin and amoxicillin were the most frequently prescribed drugs, both with a percentage above 3.5% (Table 1).

Other drugs were ordered according to the frequency of consumption: ranitidine (4.7%), followed by paracetamol (3.8%), midazolam (3.7%).

Based on the most frequently prescribed drugs and the review of the literature, drugs for which no adequate pediatric formulation is available in our country were identified (Table 2).

Midazolam (benzodiazepine), furosemide (diuretic) and phenobarbital (anticonvulsant) are available in tablets and as injection solution. Omeprazole (antiulcer medication) is available in capsules and as injection solution. Prednisone (corticosteroid) and captopril (antihypertensive) are only available in tablets.

All of these must be adjusted to the doses required by pediatric patients, since they are only available in adult formulations.

DISCUSSION

The present work determined the pattern of drug consumption at the National Institute of Pediatrics during a six year period, January 2001 to June 2006.

Antibiotics were the most commonly prescribed pharmacologic group (37.8%). The most frequently prescribed antibiotics were dicloxacillin (3.6%) and amoxicillin (3.5%), which are available in pediatric for-

mulations. However ranitidine is the most prescribed drug for children. Its wide use is for the treatment of gastroesophageal reflux and peptic ulcer, which are the most common diseases in this Institute.^{8,9}

Midazolam, furosemide, phenobarbital, omeprazole, prednisone and captopril were the most frequently prescribed drugs for which no adequate pediatric formulation is available in Mexico. Midazolam was the drug most used in the services of Emergency, Surgery and Intensive Care.

The most frequently prescribed medications for which there are no pediatric formulations implies that fractions of a tablet are usually administered, and therefore no certainty of the size of the administered dose is known. On the other hand, small children have difficulty in swallowing tablets.

In view of this concern, we have started a line of research and development of extemporaneous formulas requested by physicians at the Institute, as a temporary solution to the lack of pediatric drug formulations.

An example of this is the evaluation of an extemporaneous oral suspension of the (antiarrhythmic agent) propafenone in our laboratory, developed from commercial tablets, for the treatment of supraventricular tachycardia in children.^{10,11} All studies have been authorized by the Research and Ethics Committee of the National Pediatrics Institute. In addition, the development of these new formulations have been based on the guidelines for good manufacturing practice and

Table 1. The most frequently consumed drugs at the National Institute of Pediatrics. January 2001 to June 2006

<i>Drug</i>	<i>Pharmacologic group</i>	<i>Frequency of consumption</i>	<i>Percentage</i>
Ranitidine	Antihistaminics	350	4.7 %
Paracetamol	Analgesics	285	3.8 %
Midazolam	Ansiolitics	275	3.7 %
Dicloxacillin	Antimicrobians	267	3.6 %
Amoxicillin	Antimicrobians	262	3.5 %
Furosemide	Diuretics	258	3.4 %
Metamizol	Analgesics	245	3.3 %
Prednisone	Corticoesteroids	216	2.9 %
Phenytoin	Anticonvulsants	179	2.4 %
Phenobarbital	Anticonvulsants	167	2.2 %
Omeprazole	Antiulcers	126	1.7 %
Ondansetron	Antiemetic	111	1.5 %
Metoclopramide	Prokinetics	110	1.5 %
Captopril	Antihypertensives	101	1.3 %
Ambroxol	Mucolitic	93	1.2 %

Table 2. Drugs for which no adequate pediatric formulation is available in Mexico

<i>Drug</i>	<i>Pharmacologic group</i>	<i>Percentage of consumption</i>	<i>Formulation</i>
Midazolam	Ansiolitics	3.7 %	Tablets of 7.5 mg Injection solution of 15 mg/3mL and 5 mg/5mL
Furosemide	Diuretics	3.4 %	Tablets of 40 mg Injection solution of 20 mg/2mL
Prednisone	Corticoesteroids	2.9 %	Tablets of 5 mg, 20 mg and 50 mg
Phenobarbital	Anticonvulsants	2.2 %	Tablets of 100 mg Injection solution of 330 mg/ 2mL
Omeprazole	Antiulcers	1.7 %	Capsules of 20 mg Injection solution of 40 mg
Captopril	Antihypertensives	1.3 %	Tablets of 25 mg

the relevant Mexican Official Norm (NOM-073-SSA1-1993) which establishes the safety of medications in Mexico.¹²⁻¹⁴

The pattern of drug consumption found in this study are very similar to previously reported profiles; however, other studies do not consider if an adequate pediatric formulation is available.

The preparation of extemporaneous formulations has also been undertaken in other countries, such as the USA, Spain, Argentina and France.¹⁵⁻¹⁸

There are several reports on the stability and evaluation of pediatric extemporaneous formulations of those drugs for use in clinical trials.¹⁹⁻²³

In the present study, it is mentioned the pattern of drug consumption in our hospital but definitively not only those drugs detected are not formulated for children in our country but also there are other drugs that are only available in adult presentation; such is the case of sildenafil used in pediatric patients with pulmonary arterial hypertension (PAH).²⁴

The perspective of the present investigation is to work in the development and evaluation of extemporaneous formulas that can be adequate for use in children based on the pattern of drug consumption found in the present study specially those drugs that are not available as pediatric formulations.

Unfortunately, in our country there is no legislation regarding this type of preparations and this situation makes it difficult to propose new drug formulations.

This article reports the frequency of drug consumption at a pediatric hospital and discusses it in view of the lack of adequate formulations for pediatric patients in our country.

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REFERENCES

1. Antonakis N, Xylouri I, Alexandrakis M, Cavoura C, Lionis C. Seeking prescribing patterns in rural Crete: a pharmacoepidemiological study from a primary care area. *Rural Remote Health* 2006; 6(1): 488.
2. Jackevicious CA, Tu K, Filate WA, Brien SE, Tu JV. Trends in cardiovascular drug utilization and drug expenditures, in Canada between 1996-2001. *Can. J. Cardiol.* 2003; 19(12):1359-66.
3. Dineshkumar B, Raghuram TC, Radhaiah G, Krishnaswamy K. Profile of drug use in urban and rural India. *Pharmacoecconomics* 1995; 7(4):332-46.
4. Copeland C. Consumption drugs: issues of cost, coverage and quality. *EBRI Issue Brief* 1999; 208: 1-21.
5. Chico AP, Hidalgo FJ, Pérez GG, Camacho VA, Guillé PA, De la Roca J, Lares AI, Juárez OH, . Prescribing patterns and consumption of medication in a rural community in Mexico. *Journal of Pharmacy Practice and Research* 2003; 33(4): 330.
6. Juárez OH, Flores PJ, Lares AI, Montes OI. Perfil de consumo de antibióticos en un hospital pediátrico de la ciudad de México. *Perinatol. Reprod. Hum.* 1998; 12: 157-62.
7. Juárez OH, Camacho VA, Guillé PA, Hernández AG, Pérez GG, Saltigeral SP. Uso de antibióticos en las enfermedades infecciosas de recién nacidos. *Acta Pediatr. Mex.* 2004; 25(3): 175-9.

8. Ramírez MJ, Garrido GL, Villalobos CC y cols. Ranitidina y alteraciones electrocardiograficas en niños. *Alerg. Asma Inmunol. Pediatr.* 2001; 10(2): 40-2.
9. Ramírez MJ, Cervantes BR, Mata RN y cols. Determinación de pH intraesofágico por 24 horas en niños con reflujo gastroesofágico y asma de reciente diagnóstico tratados con ranitidina. *Rev. Alerg. Asma Inmunol. Pediatr.* 2000; 9(6): 188-90.
10. Flores PC, Juárez OH, Flores PJ, Ramírez MB, Bobadilla C.J. A simple method to measure plasma levels of propafenone with fluorescence detection. *Chromatographia* 2005; 62: 373-7.
11. Juárez OH, Flores PC, Flores PJ, Ramírez MB, Carrasco PM, Bobadilla C.J. Bioavailability of an extemporaneous suspension of propafenone made from tablets. *Biopharm. Drug Dispos.* 2006; 27: 241-5.
12. Norma Oficial Mexicana NOM-073-SSA1-1993. Estabilidad de medicamentos. In: *Diario Oficial de la Federación, México.*
13. *Farmacopea de los Estados Unidos Mexicanos FEUM*, vol. I and II, 8th edn. México, 2004; 39, 1351-61.
14. Alfonso RG. Remington. *Farmacía*, 19th edn. Medica Panamericana: Buenos Aires, Argentina, 1998; 1735-1748, 2291-2308.
15. Johnson CE, Streetman DD. Stability of oral suspensions of ursodiol made from tablets. *Am. J. Health Syst. Pharm.* 2002; 59: 361-3.
16. Vandenbussche HL, Johnson CE, Fontana EM, Meram JM. Stability of levofloxacin in an extemporaneously compounded oral liquid. *Am. J. Health Syst. Pharm.* 1999; 56: 2316-8.
17. Real Decreto Español 175/2001. Normas de correcta elaboración y control de calidad de formulas magistrales y preparados oficinales.
18. Normas de recomendación, Argentina, 2002. Buenas practicas de elaboración profesional de medicamentos magistrales y preparados oficinales.
19. Mishra LD, Sinha GK, Bhaskar Rao P, Sharma V, Satga K, Gairola R. Injectable midazolam as oral premedicant in pediatric neurosurgery. *J. Neurosurg. Anesthesiol.* 2005; 17(4): 193-8.
20. Burnett JE and Balkin ER. Stability and viscosity of a flavored omeprazole oral suspension for pediatric use. *Am. J. Health Syst. Pharm.* 2006; 63: 2240-7.
21. Glass BD, Haywood A. Stability considerations in liquid dosage form extemporaneously prepared from commercially available products. *J. Phar. Pharm. Sci.* 2006; 9(3): 398-426.
22. Brion F, Nunn AJ, Rieutord A. Extemporaneous (magistral) preparation of oral medicines for children in European hospitals. *Acta Paediatr.* 2003; 92(4): 408-10.
23. Ghulam A, Keen K, Tuleu C, Wrong IC, Long PF. Poor preservation efficacy versus quality and safety of pediatric extemporaneous liquids. *Ann. Pharmacother.* 2007; 41(5): 857-60.
24. Nahata MC, Morosco RS, Brady MT. Extemporaneous sildenafil citrate oral suspensions for the treatment of pulmonary hypertension in children. *Am. J. Health Syst. Pharm.* 2006; 63: 254-7.