Farm Hosp. 2012;36(4):180–186

Farmacia HOSPITALARIA

www.elsevier.es/farmhosp

ORIGINAL

Drug utilization study in pediatric prescriptions of a university hospital in southern brazil: off-label, unlicensed and high-alert medications

L. Dos Santos[a,*], I. Heineck[b]

[a] *Paediatric Unit of Hospital de Clínicas de Porto Alegre (HCPA), Porto Alegre/RS, Brazil*
[b] *Department of Medication Production and Control, in the Pharmacy Faculty, Porto Alegre/RS, Brazil*

Received 6 September 2010; accepted 29 December 2010
Available online 24 October 2011

KEYWORDS
Children;
Hospitalized children;
Unlicensed drugs;
Off-label;
Drug prescriptions

Abstract
Objective: To describe and determine the extent of use of unlicensed, off-label and high-alert drugs in the general pediatric units of a university hospital in southern Brazil.
Methods: A cross-sectional study conducted from November 2007 to January 2008 involving patients up to 14 years of age. Intensive care and pediatric oncology unit patients were excluded. Classification according to the Food and Drug Administration approval criteria was performed using the DrugDex-Micromedex® and high-alert medications were classified according to the Institute for Safe Medication Practices.
Results: During the study period, 342 prescriptions were analyzed. Analgesic drugs were the most frequently prescribed therapeutic class of drugs (26.9%) and antispasmodic drugs (31.5%) were the most frequently issued off-label drugs. About 12% of the prescriptions analyzed presented unlicensed drugs and 39% presented at least one off-label drug, especially in relation to its therapeutic indication (38.4%) and age (21.9%). Approximately 6% of the total (2026) were classified as high-alert medications, such as opioid analgesic drugs (35%). No association was observed between off-label use and high-alert drugs.
Conclusion: Frequency of unlicensed and off-label drug prescriptions showed in the study is according to the literature and may be considered high. High-alert drugs, although low in frequency, can present risks due to the harmful effects they can produce in patients. Thus, the highlighted drugs in this study constitute a constant concern in hospitals.

* Corresponding author.
E-mail address: lusantos@hcpa.ufrgs.br (L. Dos Santos).

1130-6343/$ - see front matter © 2010 SEFH. Published by Elsevier España, S.L. All rights reserved.
doi:10.1016/j.farma.2010.12.008

PALABRAS CLAVE
Infancia;
Niños hospitalizados;
Fármacos no aprobados;
Indicaciones no aprobadas;
Prescripciones de medicamentos

Estudio sobre el uso de fármacos en prescripciones pediátricas en un hospital universitario del sur de brasil: medicamentos de alto riesgo, no aprobados y en indicaciones no aprobadas

Resumen
Objetivo: Describir y determinar el alcance del uso de medicamentos de alto riesgo, no aprobados y en indicaciones no aprobadas en las unidades generales de pediatría de un hospital universitario del sur de Brasil.
Métodos: Estudio transversal realizado entre noviembre de 2007 y enero de 2008 en el que participaron pacientes de hasta 14 años. Se excluyó a los pacientes de las unidades de oncología pediátrica y cuidados intensivos. La clasificación, según los criterios de aprobación de la Agencia de Alimentos y Medicamentos de EE. UU., se realizó usando DrugDex de Micromedex,® y los medicamentos de alto riesgo se clasificaron de acuerdo con el Instituto para las Prácticas de Medicación Seguras.
Resultados: Durante el periodo de estudio se analizaron 342 prescripciones. Los analgésicos fueron la categoría terapéutica más prescrita, con un 26,9%, y los antiespasmódicos, con un 31,5%, fueron los medicamentos más usados en indicaciones no aprobadas. Alrededor del 12% de las prescripciones correspondían a medicamentos no aprobados, y el 39% contenían al menos un medicamento para una indicación no aprobada, especialmente en relación con su indicación terapéutica (38,4%) y la edad (21,9%). Aproximadamente el 6% del total (2.026) de los fármacos se clasificaron como medicamentos de alto riesgo, y entre ellos destacaron los analgésicos opiáceos (35%). No se observó ninguna relación entre el uso de fármacos en indicaciones no aprobadas y los medicamentos de alto riesgo.
Conclusión: La frecuencia de la prescripción de fármacos no aprobados y de medicamentos en indicaciones no aprobadas coincide con la hallada en la literatura, y puede considerarse alta. A pesar de su baja frecuencia, los medicamentos de alto riesgo pueden ser peligrosos, por los efectos perjudiciales que pueden causar en los pacientes. Por lo tanto, el uso de los fármacos en los que se centra este estudio constituye una alerta constante en los hospitales.

Introduction

More than 35 years ago, the term *therapeutic orphans* was created in order to highlight the fact that children were not frequently included in clinical trials for the development of new drugs.[1] Examples such as congenital malformations associated with thalidomide, in the 1960s, development of kernicterus (severe brain damage related to neonatal hyperbilirubinemia) with the use of sulfonamides in neonates, gray baby syndrome associated with the use of chloramphenicol in the neonatal period, and, more recently, cardiac arrhythmia with the use of cisapride in the treatment of gastroesophageal reflux, brought attention to the need to set norms in order to regulate the experimentation and trade of new drugs for children, ensuring safety, effectiveness and quality.[1–3]

Based on new research regulations, the European Medicines Agency (EMA) and the Food and Drug Administration (FDA) have encouraged the development of studies involving individuals of less than 18 years of age, searching for improved safety in drug use through the creation of adequate formulations and pharmacokinetic assays for this population.[4–9] In Europe, only 35% of all commercially available drugs are estimated to be licensed for use on children. Likewise, in the United States, until 2003, only 20–30% of the drugs were approved for use on children.[4,10]

The high prevalence of prescriptions with unlicensed (11%) and off-label drugs (30–50%) in hospitalized children has been described in several studies and is considered common practice in hospitals.[11–15] In general pediatric units, 16 to 62% of the drugs are estimated to be off-label or unlicensed.[16] Likewise, the prescription of off-label and/or unlicensed drugs to children outside the hospital is high, ranging from 11 to 37%.[12]

In addition, some drugs are classified as high-alert medications, since they present reduced safety and, thus, higher susceptibility to inflict harm, such as mild-to-severe adverse reactions caused by medication misuse.[17,18] Several of these drugs are also classified as unlicensed or off-label, which increase the risks when used in children. The study aimed to describe and determine the extent of use of unlicensed, off-label and high-alert drugs in the general pediatric inpatient unit of a university hospital in southern Brazil.

Methods

A descriptive prospective cross-sectional study was conducted in the pediatric inpatient unit of Hospital de Clínicas de Porto Alegre (HCPA), a tertiary general public university hospital in southern Brazil. The pediatric inpatient unit is equipped with 71 beds for patients from 0-14 years of age assisted in clinical and surgical conditions. The study was based on the collection of variables related to the patients and the prescribed drugs available on clinical records and from information provided by the health care team.