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Oral dosage form administration practice in children under 6 years of age: A survey study of paediatric nurses

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ABSTRACT

The purpose of this study was to interview paediatric nurses on administration issues using extemporaneous capsules and marketed capsules and tablets in children younger than 6 years old, based on most frequently administered drugs in six participating wards. The 59 responding nurses estimated respectively at 7.7 ± 1.7 and 7.3 ± 1.8 years the age from which children would properly swallow extemporaneous capsules and marketed solids, with 33% and 37% of nurses considering that children under 6 would not get their prescribed treatment using these dosage forms. Refusal of the child to take the solid was the first reason to explain administration failure (85% of nurses for extemporaneous capsules, 89% for marketed solids). Although type of formulation and requirement of chewing were factors influencing the age at which children would take solid from nurses' experience, size of conventional tablets was not among these factors. All respondents use to crush tablets in children unable to swallow whole solids; 37% of nurses systematically split the tablets to ease the swallowing in children able to swallow. Only 11 nurses had an information tool at their disposal to guide manipulation of solids, with 7 of them using it in their daily practice. Providing specific-ward questionnaires, this study gives factual information on administration practices, perceptions and issues faced by paediatric nurses.

1. Introduction

The development of oral drug formulations that are suitable for children is one of the major issues for research in paediatric pharmacology and pharmaceutical industry (Standing and Tuleu, 2005; Cram et al., 2009; Salunke et al., 2011). There are numerous challenges for the formulation of medicines into appropriate dosage forms for the paediatric population; one of the most important relates to easy and accurate measurement of the dose. Liquid drug formulations are the most used oral dosage form among paediatrics as they allow accurate measurement of the dose per kg, and are considered the most appropriate for children unable to swallow tablets or capsules (European Medicines Agency, 2013). However, they present major disadvantages such as important volumes of liquids to be swallowed, low stability, poor taste and difficulties in taste masking (Arulanantham and Genel, 1978; Cram et al., 2009; Salunke et al., 2012, 2013). Oral liquid medicine multiple preparation steps as well as multi-dose packaging and various strengths are risk factors for administration errors in children (ANSM 2013; Lajoinie et al., 2015). More so, they are not convenient for children going to school, or that have chronic diseases that need long term treatments. The alternative to liquid formulations is the conventional solid oral dosage form, such as tablets or capsules. These present the advantages of greater stability, easy dose selection (single dose formulation), improved transportability and ease of storage with lesser use of preservative compared to liquids (Lajoinie et al., 2014). Solid forms also allow the development of modified-release formulations, minimizing administration frequency (Nunn et al., 2005; Buck and Health, 2013). Significant limitations may explain the low use of oral solid dosage forms in paediatrics, the most important being the swallowing difficulties in children (Buck and Health, 2013). The

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age at which children are able to safely swallow solids is highly controversial between healthcare professionals and caregivers, regulatory authorities and paediatric pharmacologists. While drug summary of products characteristics (SmCP) do not state the use of conventional solid oral dosage forms under the age of six, the European Medicines Agency (EMA) suggests that children with long-term illness should be encouraged to take their oral medicine as solid dosage forms from the young age of 3 years old (European Medicines Agency, 2006). Recently, randomized controlled trials increased evidence that appropriately sized solid dosage forms (*i.e.*, mini-tablets up to 4 mm in diameter) are well accepted by the children and the caregivers, and preferred to sweet liquid formulations (Spomer et al., 2012; Klingmann et al., 2013, 2015; Van Riet-Nales et al., 2013). Another presumed limit would be the lack of dosing flexibility compared to liquid formulations (Lajoinie et al., 2014). Indeed, in current practice, the lack of dosing flexibility of commercialized solid drugs leads to the manipulation of the dosage form to achieve the prescribed dose (Richey et al., 2013). Solid drugs are thus frequently administered off-license in paediatrics (Standing and Tuleu, 2005).

The purpose of this survey study was to interview paediatric nurses on administration issues using solid dosage forms in children younger than 6 years old. The survey focused on (i) extemporaneous capsules (*i.e.* drugs or combination of drugs prepared or compounded in hospital and community pharmacies, according to a prescription), (ii) marketed capsules and tablets and (iii) on information support available to assist nurses when manipulating solids. The questionnaire was adapted to each participating paediatric unit, based on the most administered oral drugs in children younger than 6 years old in each ward. Our aim was to provide relevant information on the administration issues faced by paediatric nurses for solid dosage forms actually administered in their daily practices. Our perspectives were to identify their concerns and difficulties to discuss ways to improve of their administration practices.

2. Material and methods

2.1. Step 1: designing of the questionnaire

Six paediatric wards participated to the study: Endocrinology & General Paediatrics, Neurology & Epileptology, Cardiology, Nephrology & Rheumatology, Pulmonology and Hepatogastro-enterology. Data on the drugs' administration in children hospitalized in the Mother & Child Hospital (HFME, Lyon, France) were provided by the EREMI study (French Medicine Agency funding; Clinical Centre of Paediatric Investigations of HFME) (Lajoinie et al., 2016). This study included patients aged under 15 years old, hospitalised at the Hospices Civils de Lyon for at least 3days.

For the present study, we targeted oral drugs administered in children under 6 years old over the 6-month period preceding the dissemination of the questionnaire (September 1st, 2013–March 1st, 2014). A total of 3983 oral medicine courses – including liquids and solids – were administered in 811 children under 6 years old during this period. Finally, 186 medicine courses of extemporaneous capsules and 406 medicine courses of marketed capsules and tablets (Table 1) were administered in 256 children, corresponding to a total of 2394 and 3032 administrations. Twenty-two children (8.6%) were newborn infants [0–27 days], 136 (53.1%) were infants [28 days-23 months], and 98 (38.3%) were preschool-age children [2–5 years] (European Medicines Agency, 2001). They received a mean number of 2.3 ± 2.1 medicine courses per child, corresponding to 9.2 ± 20.3 administrations, for a mean duration of 5.4 ± 10.3 days; there was no statistical differences between age groups for these variables.

The questionnaire was divided into 3 parts (Appendix A). The first two parts concerned the administration practices of solid oral dosage forms: (1)-*Administration of extemporaneous capsules*, and (2)-*Administration of marketed capsules and tablets*. Part (1) contained a set of generic questions (*i.e.,* common to all participating wards) on the acceptability and the administration practices of extemporaneous capsules, while citing ward-specific examples of the most frequently administered medicines in this form. Acceptability was explained to nurses as the overall ability and willingness of the patient to use a medicine as intended (European Medicines Agency, 2013). Part (2) contained a first set of ward-specific questions regarding the acceptability of marketed capsules and tablets. It provided the same clusters of items for every marketed capsule or tablet that reached at least 2% of the total number of oral marketed solid courses administered in a given ward (Appendix A: questions 2.1–2.3). These marketed solids, listed in Appendix B, were presented in the questionnaire with their name (INN and commercial name), size (mm), formulation (*e.g.,* orodispersible tablet, divisible tablet) and a scaled photo of the solid on a graph paper. The second set of Part (2)'s items were generic questions regarding administration issues and manipulations of drugs required to administer marketed tablets. Part (3)- *Information support for the manipulation of oral solid dosage forms* focused on nurses' knowledge and opinion on support tools available to assist them when manipulating solid drugs (extemporaneous capsules as well as marketed tablets or capsules).

The survey consisted of closed-ended questions (dichotomous or multiple choice). Numeric variables (children's age) were measured using numeric scales. The questionnaire was pre-tested amongst seven paediatric nurses from another hospital before being distributed in our paediatric hospital.

2.2. Step 2: conduct of the survey study

We presented our study and survey to the paediatric nurse managers in every participating wards. They were responsible for organizing 15–20 min sessions dedicated to the completion of the questionnaire by their nurses, which had to be filled independently and anonymously. We aimed to collect 10 questionnaires per ward, or a total of 60 questionnaires.

Table 1
Number of oral medicine courses (N) in each participating paediatric ward for the 3 studied orally administered formulations (*i.e.*, extemporaneous capsules, marketed tablets and capsules and solution for injection *via* the oral route), also given as the percentage (%) of the total number of oral medicine courses in the ward (total for oral medicine courses).

	Extemporaneous capsules		Marketed tablets and capsules		Others oral dosage forms		Total
	N	%	N	%	N	%	**N**
Cardiology	131	8.3	65	4.1	1386	87.6	**1582**
Endocrinology & General Paediatrics	13	1.8	66	9.2	641	89.0	**720**
Pulmonology	18	3.0	100	16.8	477	80.2	**595**
Neurology & Epileptology	2	0.5	68	14.8	377	84.3	**447**
Nephrology & Rheumatology	18	4.2	81	19.0	328	76.8	**427**
Hepatogastro-enterology	4	1.9	26	12.3	182	85.8	**212**
Total	186	4.7	406	10.2	3391	85.1	**3983**