Paediatric and Perinatal Drug Therapy, 2008; 8 (4)

How long does it take to administer oral medicines to children?

Claire Skwierczynski, Sharon Conroy

Academic Division of Child Health, University of Nottingham, Derbyshire Children's Hospital, Derby UK

Corresponding author

Sharon Conroy, Lecturer in Paediatric Clinical Pharmacy, Academic Division of Child Health, University of Nottingham, The Medical School, Derbyshire Children's Hospital, Uttoxeter Road, Derby, DE22 3DT, UK.
Email: sharon.conroy@nottingham.ac.uk

Background: **Many children require liquid medicines, however many drugs are not available in a licensed liquid formulation. Nurses therefore need to manipulate solid dose forms to produce a preparation that the child can take. This study aimed to quantify and describe the number of episodes, time taken and drugs involved when nurses need to manipulate medicines in order to administer them to a child.**

Method: **Drug administrations were observed on paediatric wards in Queens Medical Centre, Nottingham and the Derbyshire Children's Hospital, Derby, UK. The time taken and any manipulations made to the drugs before administration were recorded.**

Results: **One hundred and ninety eight drug administrations to 100 children were observed. Nineteen (9.6%) of drugs administered required manipulation and ten (10%) children received a manipulated drug. The administration of a manipulated drug took twice as long as a non-manipulated drug, median time 4 and 2 minutes respectively (Mann–Whitney test, $P<0.001$). The most frequent manipulation was crushing and dissolving tablets in water prior to administration. Manipulations of medicines were required across all age groups. Liquid medicines were required by two-thirds of children and took significantly longer to administer than tablet forms, median time 2.3 and 1.5 minutes respectively (Mann–Whitney test, $P<0.001$). Children with a feeding tube required manipulated medicines four times more often than those without.**

Conclusion: **The need to manipulate drugs in order to be able to administer them to children is common on paediatric wards. It increases the time taken to administer drugs with a likely significant impact on nursing staff resources. Such manipulations can lead to inaccurate dosing and little is known on the impact of such manipulations on the drug's effects.**

Paed Perinat Drug Ther 2008; 8: 145–149

Keywords: children – medicines – formulations – administration

Introduction

Licensing of drugs is important to ensure that they are safe, effective and of high quality[1]. Most drugs prescribed for adults are licensed. In contrast, children are commonly prescribed drugs that are either not licensed at all (unlicensed) or used outside the terms of the license (off label)[2-4]. Examples of unlicensed drugs include modifications to a licensed medicine, use of chemicals as

medicines, medicines used prior to granting of a license and imported medicines[5]. Off label drugs may include use in a different indication, dose, age, route or contraindication to that recommended by the manufacturer's license. Such use is common and has been extensively documented[3,4].

There are many consequences of the need to treat children with unlicensed and off label medicines. These include the possibility that they miss out on potential drug benefits; concerns about safety due to lack of testing in appropriate populations; lack of suitable formulations to provide the child's dose in a product that they are able and willing to take and variation in the quality and bioavailability of unlicensed products. If an appropriate formulation is unavailable, manipulations of drugs by paediatric nursing staff may be needed, e.g. cutting tablets or dissolving soluble tablets in a measured quantity of water and taking an appropriate portion to obtain the desired dosage[6]. Such manipulations may be time consuming and can also be inaccurate, potentially leading to the administration of toxic or sub-therapeutic doses. It is also not always clear what the effects of such manipulations are on the bioavailability and effects of the drug. The issue has not been studied in detail and the aim of this study was to quantify and describe the number and nature of episodes, time taken and drugs involved when nurses need to manipulate medicines in order to administer them to a child.

Methods

The study was conducted on the paediatric wards in the Queen's Medical Centre, Nottingham and the Derbyshire Children's Hospital, Derby, UK. Surgical, medical, oncology and neurology wards and an ambulatory day case unit were studied. On the morning of each study day the researcher (a third year medical student) asked each ward sister how many patients were receiving drugs and at what times. She subsequently spent most of the day on the wards where most drugs were prescribed in order to observe the maximum number of administrations in the time available.

The researcher asked for nurses' verbal consent to observe them when administering drugs to children. Posters were displayed in all study areas to inform carers, patients and nurses of the study and to enable them to opt out of being observed during drug administration rounds if they so desired. The poster included a summary of the study aims and methods and contact details for the researcher and supervisor.

The patient's ward, age and sex and the names and formulation of all drugs administered were recorded. Any manipulations of medicines, e.g. crushing or cutting tablets, opening capsules etc were also recorded. Drug administration was timed and recorded for every drug given. No personal data from either nurses or children was collected. Timings were recorded from when the nurse started to prepare the drug until when the child swallowed it. In cases where it was necessary to use a nasogastric (NG) tube, the time was recorded until the nurse could leave the patient.

Data entry and analysis were done using SPSS version 14. The Mann–Whitney test was used for statistical analysis. Ethical approval for the study was obtained from the Derbyshire Research Ethics Committee with site specific approval in Nottingham.

Table 1 Time taken to administer drugs requiring, and not requiring manipulation

	n	Time (min)	
		Median (range)	IQR
No manipulations	179	2 (1–29)	1.5, 2.5
With manipulations	19	4 (3–6.5)	3.0, 4.5

Results

One hundred and ninety eight drug administrations to 100 children were observed over a 6 week period. Of the 198 administrations, 19 (10%) medicines in ten patients required manipulation by nurses before they were in a suitable form for the child to take. Drugs took significantly longer to administer when manipulation was needed, median time 4 minutes, than when manipulation was not required, median time 2 minutes (Mann–Whitney test, $P<0.001$) (Table 1).

The time taken to administer different drug formulations not needing manipulation was also compared, as was the frequency of administration of each formulation. Drugs that were manipulated were excluded from this analysis. The results can be seen in Table 2. The most common form of medicine required was liquid preparations with 129 administrations (72%), compared to 47 (26%) for tablets. Liquids took significantly longer to administer than tablets, median times 2.3 and 1.5 minutes respectively (Mann–Whitney test, P <0.001). Liquid medicines were administered on almost as many occasions to children of six years and over as to children less than six years. Tablets were mainly administered to children of six years and over (Table 2).

Table 2 Time taken to administer different formulations (manipulated drugs excluded)

Formulation	*n* in children 1–5 years old	*n* in children 6–17 years old	Time (min) Median (range)
Tablet	1	46	1.5 (1.0–2.7)
Liquid	68	61	2.3 (1.0–6.5)
Capsule	0	1	1.0
Powder	1	1	16.5 (4.0–29.0)

Table 3 Drugs that underwent manipulations

Manipulation	Drug name and preparation
Crushed, dissolved, whole amount given	Baclofen, dexamethasone, diazepam, fludrocortisone, furosemide, hydrocortisone and topiramate tablets; prednisolone soluble tablets, sodium valproate crushable tablets
Halved and crushed	Captopril and dexamethasone tablets
Halved	Mesalazine sustained release tablets
Crushed, dissolved, portion given	Omeprazole – MUPS tablets
Capsule opened, dissolved, portion given	Secobarbital capsules

Most manipulations were observed on general medical wards with 14 manipulations out of 101 drugs administered (14%) and oncology wards with four out of 26 (15%). This probably reflects the complex nature of the treatments needed, as although 55 drug administrations were observed on surgical wards no manipulations were needed.

The most frequent manipulation observed was for tablets to be crushed, dissolved in water and the whole resulting solution/suspension administered, accounting for 13 of the 19 (68%) manipulations (Figure 1). The time taken to administer medicines and a comparison of the time taken for different manipulations is also shown in Figure 1. The most time consuming manipulation was tablets needing to be crushed, dissolved and a portion of the resulting liquid given. This took a median of 6.5 minutes, 2 minutes longer than any other manipulation. The 13 different drugs requiring manipulation are shown in Table 3.

The age of patients receiving each formulation was analysed excluding all administrations involving manipulations. As expected, the children who received liquids (median age 4.7 years, range 0.1–16 years) were younger than the children who received tablets (median age 14.2 years, range 5.9–17 years). The wide range from 1 month to 16 years for children requiring liquids demonstrates, however, that they are needed across all age ranges.

Table 4 Age of children requiring manipulated and non-manipulated drugs

Manipulation	*n*	Median (range) (years)
No	179	8.2 (0.1–17.0)
Yes	19	12.0 (0.1–14.2)

The age range was similar for children requiring manipulated drugs (1 month to 14 years) and non-manipulated drugs (1 month to 17 years). The need to manipulate medicines spans the whole of childhood. Table 4 shows the ages of children requiring manipulated and non-manipulated drugs. The results show that the median was 8.2 years for non-manipulated and 12 years for manipulated drugs, the opposite to what may have been predicted. This was explained by the fact that there were several older children requiring liquids for administration through a percutaneous endoscopic gastrostomy tube (PEG) which is likely to have affected the age.

In 48 cases, oral medicines needed to be given by NG or PEG tubes. Of these, 11 (23%) required manipulation. Of the 150 drug administrations when no PEG or NG tube was required, only 8 drugs (5%) were manipulated. This suggests that the use of a NG or PEG tube increases the need for drugs to be manipulated due to the lack of availability of suitable liquid medicines for administration by this route.

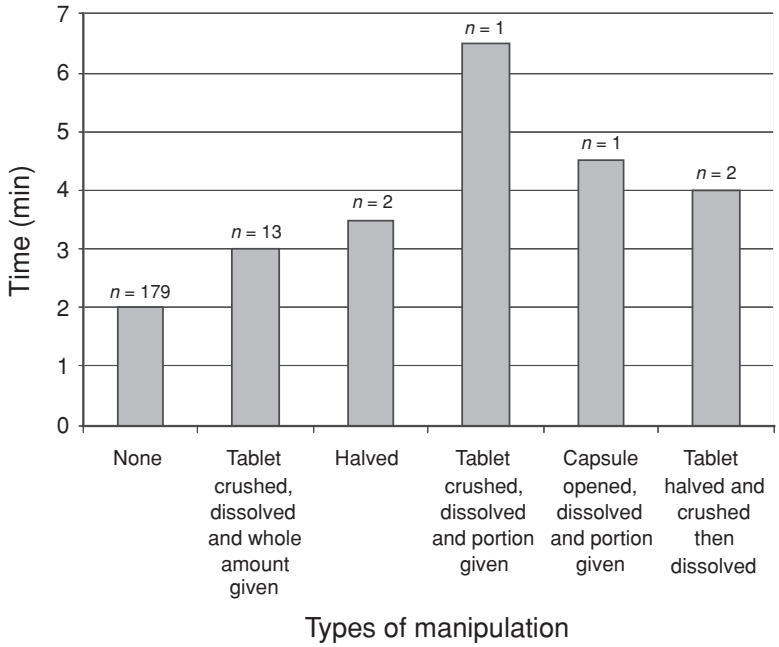

Figure 1 Median time taken to administer medicines: comparison of different manipulations

Discussion

This study found that one in 10 drug administrations require the manipulation of the medicine before administration to children in hospital, and one in ten children receive manipulated drugs whilst in hospital. Although a small study, it is the first time that this important consequence of the lack of availability of suitable formulations for children has been examined. Drugs requiring manipulation took twice as long to administer as those not requiring manipulation. Most hospitals require two trained paediatric nurses to check all children's medicines. Therefore this must represent a major impact on nursing staff resources.

The main manipulation required was the manipulation of tablets, including combinations of cutting, crushing and dissolving the resulting powder. For six of the drugs involved (captopril, fludrocortisone, hydrocortisone, omeprazole, prednisolone and topiramate) the main reason was because they are not available in a licensed liquid formulation. Other studies have shown the lack of availability of appropriate formulations for children[7]. Liquid preparations of such drugs may be prepared or obtained as unlicensed products by the pharmacy. Alternatively the tablets are left to be manipulated by nurses on the wards.

When manipulations are necessary, there are potential problems of inaccuracy of the dose the child receives. One example observed was an omeprazole tablet being crushed in a syringe, shaken with 10 ml of water until it seemed to have dissolved and 1 ml given to the patient. The tablet was very difficult to dissolve and the actual dose the child received is unlikely to have been accurate. This method of administration is unreliable as many tablets disperse rather than dissolve, increasing the inaccuracy of the dose[6]. More research is needed in this area but early studies suggest that there may be an increase in adverse drug reactions when off label or unlicensed medication is prescribed[8, 9].

Another drug seen to cause problems was secobarbital which is only licensed in a capsule form. Administration involved opening the capsule, dissolving the contents, and giving the child a portion of the liquid solution produced. This is very time consuming, holds potential for error and the resulting solution is unpleasant to take, therefore patient refusal and subsequent failure of sedation for scans is common.

Prednisolone is available as a soluble tablet which would be anticipated to be a useful formulation for children without the need for manipulations. However, our observations showed that this preparation was crushed by nurses before attempting to dissolve as the tablets took so long to dissolve when whole.

The other drugs which were manipulated are all available in a licensed liquid form. It was therefore surprising that these were given as manipulated tablets. Reasons include cost – the liquid formulation of dexamethasone is very expensive compared to the tablets[10]; availability on the ward and the volume of the liquid to provide the required dose of sodium valproate for one patient was 25 ml. Despite liquid preparations being available they are not always of a useful strength, particularly for older children and those needing administration through a PEG. A study in the Netherlands found that even in 12–16 year olds 50% of unlicensed drugs were liquid preparations. This was thought to be because the available licensed oral solutions are not concentrated enough so the pharmacy had to prepare them[7]. Other reasons for using solid rather than liquid formulations are short shelf lives of some liquids and difficulties in carrying and storing large volumes of liquid. A three months supply of one medicine equates to a small box of capsules or 18 containers of liquid[11].

Nurses need to spend significantly more time administering liquids rather than tablets even when manipulations are not required. This is because liquid preparations involve calculating the volume needed to provide the required dose and drawing up the dose accurately in a syringe. Tablets are generally simply taken straight out of a bottle or packet and administered. More than two thirds of our patients required liquid formulations with significant time implications for paediatric nursing staff. Another factor affecting the time taken to administer drugs was the child's cooperation. On many occasions they did not want to take the drug and had to be persuaded to take it very slowly in small amounts or using a dummy to encourage a very young child to swallow.

"Children may refuse anything that, to them does not smell or taste good, therefore palatability is one of the most important factors in determining compliance in young children"[12].

On these occasions the time taken to administer the medicine could be twice as long as usual. The need for drug formulations acceptable to children can be seen to be very important. In a study regarding compliance of oral antibiotic therapy it found that the type of antibiotic had a highly significant association with compliance[13]. A suggested reason for this was the palatability of different antibiotics[13].

The median age of children taking medicines in tablet form was 14 years and for liquids almost

5 years. This would be expected as most younger children struggle to take medicines in solid form. Research with antiretroviral medicines in chronic patients showed that 7 years was the age when most children transferred to solid formulations[11]. Our own study showed that although liquids are needed across all age ranges, conversely, tablets were taken by a child of under 6 years. Assumptions, therefore, should not be made of the age when children should take solid dose forms and who should have liquids. Ideally, children should be given a choice.

Manipulation of medicines was needed in all age groups but the median age for children needing manipulated drugs was higher than those that did not. This is unexpected but can be explained as there were many older children using a PEG tube which increased the overall median age.

The main limitation to the study was the time available. Therefore, numbers are relatively small and not all administrations in the study period could be observed. The researcher, therefore, had to target wards which had the highest numbers of patients with prescribed drugs. This may have affected the types of drugs being administered. Despite this, a range of ward types including surgical, medical, oncology and neurology wards and an ambulatory day case unit were studied giving a wide range of patients. The total number of drugs administered in these areas over the study period is not known.

Conclusion

The manipulation of drugs by nursing staff to produce a suitable formulation for children was needed in 10% of drug administrations and for 10% of children receiving drugs in hospital. These manipulations may result in an inaccurate dose being given to the child with the danger of toxic or sub-therapeutic doses. Drugs requiring manipulation took significantly longer to prepare and administer, on average twice as long. This has implications for nursing staff resources as two trained paediatric nurses are needed to administer each medicine to children. More than two thirds of drug administrations involved liquids, which take significantly longer than solid formulations to administer. The main reasons for drugs needing to be manipulated were because they were unavailable in a licensed liquid form; liquid forms being too low strength and the unavailability of the liquid product when needed on the wards. Patients using a NG tube or PEG were four times more likely to require a manipulated drug.

Further research is required to look at this issue in higher patient numbers and in different areas. The aim would be to provide information to the pharmaceutical industry for drugs to target for the development of suitable licensed preparations for children.

Acknowledgements

Thank you to all nurses, children and families who allowed us to observe them during this study.

Disclosures

There are no conflicts of interest for either author and there was no financial support for this project.

References

1. Cuzzolin L, Zaccara A, Vashlow F. Unlicensed and off label use of drugs in paediatrics: a review of the literature. Fund Clin Pharmacol 2003;17:125-130.
2. Turner S, Longworth A, Nunn AJ et al. Unlicensed and off label use of drugs in paediatric wards: A prospective study. BMJ 1998;316:343-345.
3. Conroy S, McIntyre J, Choonara I. Unlicensed and off label drug use in neonates. Arch Dis Child Fetal Neonatal Ed 1999;80:F142-F145.
4. Conroy S, Choonara I, Impicciatore P et al. Survey of unlicensed and off label drug use in paediatric wards in European countries. BMJ 2000;320:79-82.
5. Turner S, Nunn AJ, Choonara I. Unlicensed drug use in children in the UK. Paed Perinat Drug Ther 1997;1:52-55.
6. Nunn AJ. Medicines that children can take. Arch Dis Child 2003;88:369-371.
7. Schirm E, Tobi H, De Vries TW et al. Lack of appropriate formulations of medicines for children in the community. Acta Paediatr 2003;92:1488-1489.
8. Neubert A, Dormann H, Weiss J et al. Unlicensed and off label drug use in paediatrics. Drug Safety 2004;27:13.
9. Turner S, Nunn AJ, Fielding K et al. Adverse drug reactions to unlicensed and off-label drugs on paediatric wards: a prospective study. Acta Paediatr 1999;88:956-958.
10. British National Formulary Publications. BNF for children 2007. Royal Pharmaceutical Society of Great Britain, London 2007.
11. Yeung VW, Wong ICK. When do children convert from liquid antiretroviral to solid formulations? Pharm World Sci 2005;27:399-402.
12. Hoover RN, Strasser PH. Artificial sweeteners and human bladder cancer: preliminary results. Lancet 1980;1:837-840.
13. Hoppe JE, Blumenstock G, Grotz W et al. Compliance of German paediatric patients with oral antibiotic therapy: results of a nationwide survey. Pediatr Infect Dis J 1999;18:1085-1091.

CrossRefs are available in the online published version of this paper:
http://www.librapharm.com
Paper PPDT-0205_3, *Accepted for publication:* 9 January 2008
Published Online: 13 February 2008
doi:10.1185/146300908X254206