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REGULAR ARTICLE

In situ coating makes it easier for children to swallow and tolerate tablets and capsules

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ABSTRACT

Aim: Getting children to swallow tablets and capsules is a challenge, and factors that influence their ability to swallow include taste, smell and texture. The aim of this study was to explore how well paediatric patients tolerated and accepted the MedCoat® *in situ* coating for tablets and capsules.

Methods: A nonrandomised intervention study was performed at the Astrid Lindgren Children's Hospital, Karolinska University Hospital, Sweden. We identified 78 paediatric patients, 43 females and 35 males, who had problems swallowing tablets and capsules and evaluated their abilities with questionnaires. The median age of the patients was nine years old, and the range was two to 17 years old.

Results: Swallowing ability and palatability was improved by *in situ* coating. The results showed that 66 of 77 paediatric patients (86%, 95% confidence interval: 76–93%) were able to take the drugs they had been prescribed after *in situ* coating. Swallowing improved in 87% of cases, and palatability improved in 85% of cases.

Conclusion: A study of 77 paediatric patients with a median age of nine years, and a range of two to 17 years, found that 86% were able to take the tablets and capsules they had been prescribed after they were coated with the MedCoat.

INTRODUCTION

Getting paediatric patients to swallow tablets and capsules is a challenge. Factors that influence the child's ability to swallow include taste, smell and texture, their carers' motivation, the clinical status of the patient and whether recent drug treatment involving tablets and capsules has failed.

The olfactory system and taste are well developed even before birth and continue to develop after birth. Many drugs have a bitter taste that is not accepted by most paediatric patients (1–3). In contrast, sweet, salty and sometimes sour tastes are generally more acceptable to children.

Children and older adults have similar issues when it comes to drug acceptability and how well they swallow tablets and capsules. Appropriate formulations are, therefore, crucial in these two age groups, to increase the acceptability of medicines and improve therapeutic outcomes, safety and compliance (4).

New legislation was introduced in the European Union in 2007 due to a lack of paediatric data and as a consequence of widespread off-label use in children (5). One of the aims of the legislation was to require the pharmaceutical industry to develop formulations suitable for children of different ages (5–7).

MedCoat® is an *in situ* coating device designed to facilitate swallowing and hide the unpleasant taste of tablets and capsules. All the ingredients in the coating have been approved as foods and MedCoat contains maltitol syrup, vegetable fat, gelatin, citric acid, sugar, ester, curcumin and flavouring. It was only available in a lemon flavour at the time of the study. A literature search and evaluation performed by Professor Folke Sjöqvist of the Division of Clinical Pharmacology, Karolinska Institutet, found that the ingredients of the MedCoat did not interact with drugs and affect their therapeutic effect (F. Sjöqvist, unpublished data).

A randomised crossover study of 41 healthy adults – 20 males and 21 females – using tablets that were the same

Key notes

- Getting children to swallow tablets and capsules is challenging, and taste, smell and texture have been identified as factors.
- This study of 78 paediatric patients, with a median age of nine years, explored how well they tolerated and accepted the MedCoat® *in situ* coating.
- Swallowing ability (87%) and palatability (85%) were improved by the *in situ* coating, and the majority (86%) could take their medication after it was coated.

size, but had different levels of bitterness, showed that the MedCoat made it easier to swallow the tablets and improved palatability (8). No study has been performed in paediatric patients.

The aim of this study was to evaluate whether the MedCoat *in situ* coating was tolerated and accepted among paediatric patients.

MATERIALS AND METHODS

A nonrandomised intervention study was performed between January 2012 and March 2013 at the paediatric emergency and oncology departments at Astrid Lindgren Children's Hospital, Karolinska University Hospital, Sweden. Paediatric patients and/or their parents were informed and asked whether the children could be included in the study. Only prescribed drug treatment was used during the study. The inclusion criteria were paediatric patients aged from two to 18 years old who had difficulty in swallowing tablets and capsules. The patients who were included were categorised into different age groups: preschool children who were two to six years old, children aged seven to 12 years old and adolescents aged 13 to 18 years old (9). Difficulties were classified as hard or very hard to swallow, discomfort or refusal to swallow the tablet or capsule or when the patients or parents stated that the taste of the tablet or capsule was the reason for the refusal. Children were excluded if they had never swallowed tablets and capsules before, were allergic to any ingredient in the MedCoat or had dysphagia or other diseases due to underlying pathology.

The MedCoat *in situ* coating enables the patient or parents to apply a thin flavoured coating to tablets and capsules before oral administration. The coating makes the tablet or capsule more slippery and easier to swallow. A pharmacist instructed participants on how to use the MedCoat and answered any questions or concerns. The patients or parents were then asked to fill in the first questionnaire about how the child experienced taking medicine without the MedCoat. The duration of the patients' drug treatment determined the number of questionnaires that needed to be filled in. If patients received all or part of their drug treatment at home, questionnaires were given to the patients or parents to be filled in at home and they were then returned to the research team.

Patients or parents evaluated the tolerance of the MedCoat (the facilitation of drug treatment, swallowing ability and drug palatability) either using a simplified form of the Faces Pain Scale–Revised (FPS-R), a variety of facial expressions, or using a numeric score presented in scale form (10).

All the patients' personal information was coded and entered into a database, and no individuals could be directly identified. The study was approved by the local ethical committee (Dnr: 2011/505-31/2).

Statistical analysis

The statistical analysis was carried out using Kruskal–Wallis, with the Dunn's post hoc test performed for multiple comparisons of independent groups of samples. The Friedman nonparametric ANOVA test and the Dunn's post hoc test were performed for multiple comparisons of dependent groups of samples. The 95% confidence intervals for proportions were calculated (11). Classified data from two independent populations were compared by Fisher's exact test. All statistical tests were two-sided, and the minimum level of statistical significance was $p < 0.05$.

RESULTS

We asked 79 paediatric patients who had difficulty in swallowing tablets and capsules to participate in the study, and these comprised 61 from the paediatric emergency department and 18 from the oncology department, Table 1. There was only one refusal, and 78 children were included in the study. The median age was nine years old, and the range was two to 17 years old. Some of the patients or parents did not answer all the questions, Figure 1. There were 17 different oral formulations used in the study, mainly antibiotics and pain relief tablets and capsules, with sizes ranging from 3.6 mm to 18 mm, Figure 2. The reasons given for having difficulty in swallowing the tablets and capsules included their unpleasant taste and size, Table 1.

Before *in situ* coating, 53 patients took complete tablets, 18 patients took tablets that had been split into smaller sizes, and seven patients did not answer the question.

Many children included in our study were able to swallow tablets and capsules larger than those proposed by the European Medicines Agency, Figure 2.

All paediatric patients included in the study had initially reported a problem with their oral drug treatment, but 66 of the 77 paediatric patients (86%; 95% CI: 76–93%) who commented on the MedCoat reported they were able to

Table 1 Demographic data and reasons for swallowing problems in paediatric patients

Parameters	N	Preschool children 2–6 years	Children >6–12 years	Adolescents > 12–18 years
Patients	78	27	26	25
Male/female	35/43	18/9	10/16	7/18
Problem swallowing tablet/capsules	76	27	24	25
Problem due to big tablet	42	12	16	14
Problem due to rough tablet	35	10	14	11
Problem due to bad taste	56	22	17	17
Problem due to after taste	45	17	11	17
Problem due to less salvia	2	0	1	1
General refusal to swallow	48	21	15	12

Median age: 9 years (range: 2–17 years).

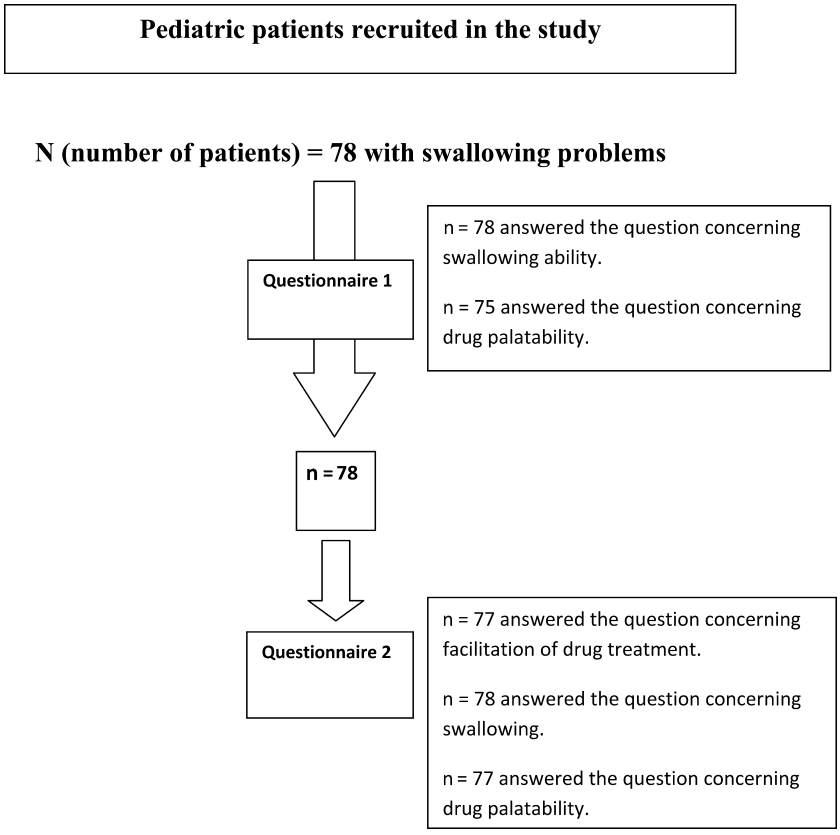

Figure 1 Consort flow diagram. The total number of patients who answered the questions concerning drug treatment, swallowing ability and palatability in the two questionnaires.

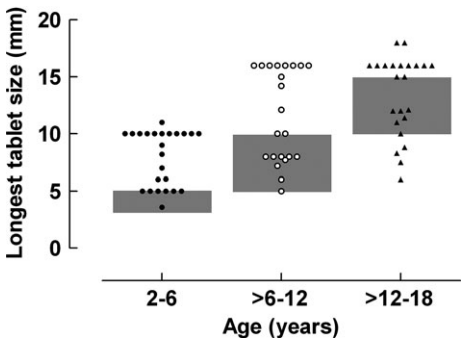

Figure 2 Tablets and capsules sizes swallowed by different age groups. The longest tablets and capsules sizes that were swallowed by the three study groups before they used the *in situ* coating. The shaded part of each study groups refers to the size interval proposed by the European Medicines Agency.

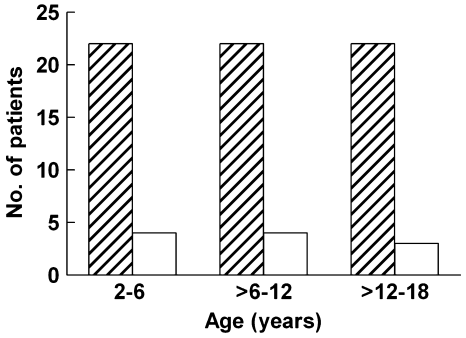

Figure 3 Facilitation of *in situ* coating by the different age groups. All paediatric patients reported difficulty in swallowing tablets and capsules before the use of the *in situ* coating. The striped columns show the number of patients who reported that drug treatment improved, and the open columns show not improved drug treatment after the first *in situ* coating.

take the drug treatment after *in situ* coating, Figure 3. Similar levels were reported by all three age groups.

Many paediatric patients had difficulties in swallowing tablets and capsules without the *in situ* coating, and this was more pronounced in children aged two to six years compared to children aged seven to 12 years ($p = 0.02$), Figure 4.

The ability to swallow improved in 68 of 78 patients (87%, 95% CI: 78–94%) after *in situ* coating, but 14 still had difficulties in swallowing the tablets and capsules, reporting a score of three or four. The improvement did not differ between the age groups ($p = 0.78$), Figure 4.

Without the *in situ* coating, difficulties in swallowing due to drug palatability were most pronounced in the two- to

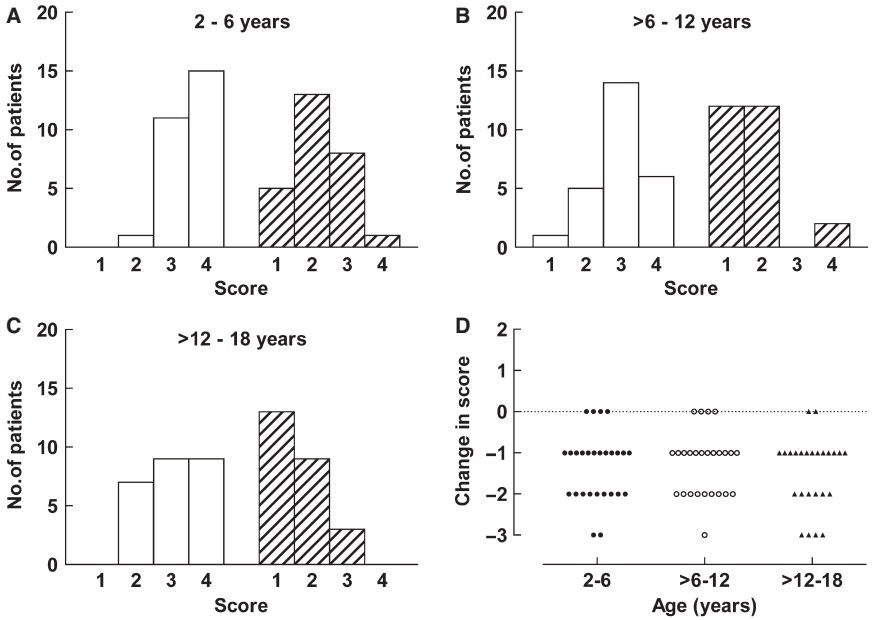

Figure 4 Swallowing ability. (A–C) show swallowing ability before the first *in situ* coated dose. The open columns show the concerns that patients and parents reported about swallowing ability before the use of the *in situ* coating. Striped columns show the results after the first *in situ* coating. Scores for swallowing tablets or capsules range from one to four and refer to: very easy, easy, hard and very hard, respectively. D shows the change in swallowing ability after the first *in situ* coated dose. A score of zero refers to no change in score, a negative change in the score refers to improvements, and a positive change in the score refers to worsening in swallowing ability.

six-year-old age group ($p = 0.0009$), Figure 5. Drug palatability was improved in 63 of 74 paediatric patients with the coating (85%, 95% CI: 75–92%), and the improvement was most pronounced in children over six years old ($p = 0.0031$), Figure 5. However, 10 patients still had palatability problems after *in situ* coating, reporting a score of three or four, and one patient felt the *in situ* coating made palatability worse.

Before the use of the *in situ* coating, 52 of 78 patients (63%, 95% CI: 55–77%), $p > 0.99$, had exactly the same scores for swallowing and palatability, compared with 49 of 74 patients (66%, 95% CI: 54–77%), $p = 0.57$, after the *in situ* coating.

None of the patients found the coating technique very hard to carry out (score of four), 21 patients found it hard (score of three), 36 found it easy (score of two), and 21 found it very easy (score of one).

Seventy patients of 78 repeated the use of *in situ* coating. Repeated use gave further improvements in the ability to swallow and in drug palatability, most pronounced in children over 6 years of age. Four patients of 70 reported that the drug coating reduced their ability to swallow, and nine of 67 patients reported that the drug palatability was worse with the coating.

DISCUSSION

The main finding of this study was that coating of tablets and capsules was well tolerated among children and improved overall drug administration. It has been established that children use a similar swallowing method to adults from the age of five, and it has also been suggested that children under six years old find it harder to swallow tablets and capsules (12,13). Despite this, it has been shown that preschool children can swallow tablets at the age of three, with training (14), and our study also found that preschool children could often swallow tablets and capsules before the use of the *in situ* coating. We included patients from the age of two that managed to swallow whole tablets and capsules following *in situ* coating. Initially, all paediatric patients had difficulty in swallowing tablets and capsules, but it was most pronounced in the two- to six-year-old age group, compared to those aged seven to 12 years ($p = 0.02$).

Children have a well-developed sensory system before birth. Within hours of birth, infants prefer sweet and savoury tastes and reject bitter tastes, a reflection of their basic biology. Some data suggest that exposure to bitter tastes develops postnatally and that children are more sensitive to bitter tastes than adults (1).

The difference in how children experience perception compared to adults remains unknown. Our study found that drug palatability was initially more pronounced in the two- to six-year-old age group compared to all age groups ($p = 0.0009$), Figure 5 and Table 1.

Drug size was reported to be a common reason for swallowing problems in patients of seven years of age or more, Table 1. It has been proposed that acceptable tablet sizes are correlated to age. Preschool children aged two to five years old can swallow small tablets (3–5 mm), children aged six to 11 years old can swallow medium tablets (5–10 mm) and adolescents aged 12–18 years old can swallow large tablets (10–15 mm). No information about capsules has been published (9). Most of the

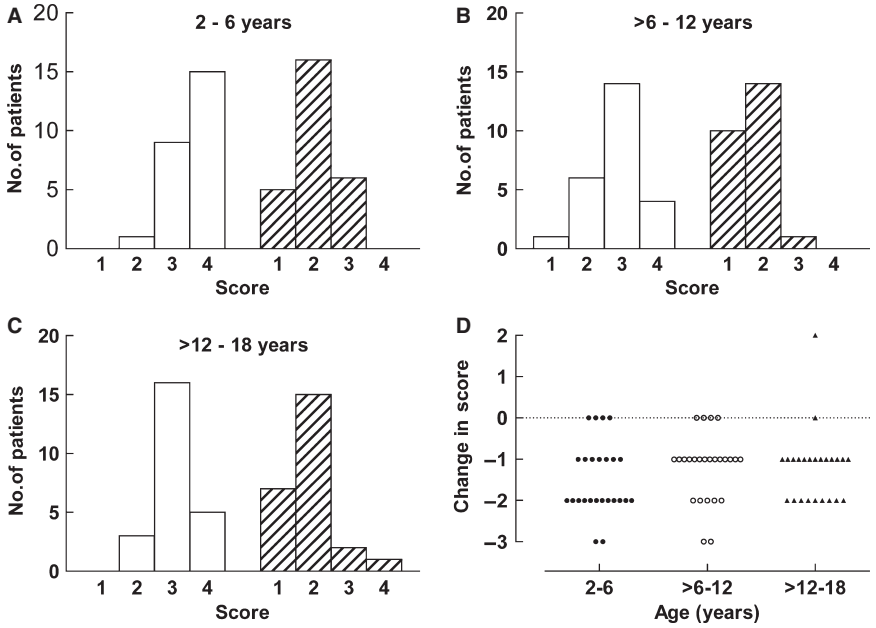

Figure 5 Drug palatability. (A–C) show drug palatability before the first *in situ* coated dose. The empty columns show what patients/parents reported concerning drug palatability before the use of the *in situ* coating. Striped columns show the results after the first *in situ* coating. A score of 1 refers to very good palatability, 2 to good palatability, 3 to bad palatability and 4 to very bad palatability. (D) shows drug palatability after the first *in situ* coated dose. A score of zero refers to no change in score, a negative change in the score refers to improvements, and a positive change in the score refers to worsening drug palatability.

children in our study, who ranged from two to 17–years of age, managed to swallow tablets and capsules. Many children could swallow significantly larger tablets than the size recommended by the European Medicines Agency, Figure 2 (9). In a clinical situation, tablets and capsules should even be considered as suitable for children who are younger than six years of age. Using an *in situ* coating improved swallowing and drug palatability in most patients. We did not see any difference in the ability to swallow between the age groups. Drug palatability differed between the groups and was most pronounced in two- to six-year-old patients ($p = 0.0009$). Repeated use of the *in situ* coating improved the ability to swallow, but it became worse in a few patients. The ability to swallow is an interplay between physiological and psychological factors, and training is not the only solution for improving the swallowing ability. Therefore, we believe that *in situ* coating could prove a useful tool for initiating drug treatment in children of all ages. However, we did note that one patient with braces had difficulty in swallowing *in situ* coated tablets because the coating stuck to their braces.

In situ coating of tablets and capsules is easy to carry out, and the patients and parents using the coating found that their technique improved after training and repeated use. Children accepted the lemon taste of the coating, but suggested that a raspberry flavour should also be offered.

The only drawback of this study was that the duration of the treatment after repeated use of the *in situ* coating was not documented, and this could be a crucial factor in the outcome.

The main strength of this study was that the cohort covered a range of ages in two different clinical settings. The majority were recruited in the emergency department before they saw a doctor, and the remainder were already receiving oncology treatment.

CONCLUSION

Our study of 77 paediatric patients with a median age of nine years found that 86% were able to take the tablets and capsules they had been prescribed after they were coated with the MedCoat. Swallowing improved in 87% of cases and palatability improved in 85%.

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CONFLICT OF INTERESTS

MedCoat AB supported the study by providing samples and placebo tablets and instructions for training purposes. No funding was received from the company.

References

1. Mennella JA, Beauchamp GK. Optimizing oral medications for children. *Clin Ther* 2008; 30: 2120–32.
2. Mennella JA, Pepino MY, Beauchamp GK. Modification of bitter taste in children. *Dev Psychobiol* 2003; 43: 120–7.
3. Maldonado S, Schaufelberger D. Pediatric formulations. *Am Pharm Rev* 2001; 1–6, Available from http://www.americanpharmaceuticalreview.com/Featured-Articles/37186-Pediatric-Formulations (accessed February 24, 2015).
4. Liu F, Ranmal S, Batchelor HK, Orlu-Gul M, Ernest TB, Thomas IW, et al. Patient-centred pharmaceutical design to improve acceptability of medicines: similarities and differences in paediatric and geriatric populations. *Drugs* 2014; 74: 1871–89.
5. Kimland E, Nydert P, Odlind V, Bottiger Y, Lindemalm S. Paediatric drug use with focus on off-label prescriptions at Swedish hospitals - a nationwide study. *Acta Paediatr* 2012; 101: 772–8.
6. Kolch M, Schnoor K, Fegert JM. The EU-regulation on medicinal products for paediatric use: impacts on child and adolescent psychiatry and clinical research with minors. *Eur Child Adolesc Psychiatry* 2007; 16: 229–35.
7. Kimland E, Bergman U, Lindemalm S, Bottiger Y. Drug related problems and off-label drug treatment in children as seen at a drug information centre. *Eur J Pediatr* 2007; 166: 527–32.
8. Uloza V, Uloziene I, Gradauskiene E. A randomized cross-over study to evaluate the swallow-enhancing and taste-masking properties of a novel coating for oral tablets. *Pharm World Sci* 2010; 32: 420–3.
9. EMA. Clinical Investigation of Medicinal Products in the Paediatric Population; 2001. Available from http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500002926.pdf (accessed February 24, 2015).
10. Hicks CL, von Baeyer CL, Spafford PA, van Korlaar I, Goodenough B. The Faces Pain Scale-Revised: toward a common metric in pediatric pain measurement. *Pain* 2001; 93: 173–83.
11. Ott L, Mendenhall W. *Understanding statistics*, 4th ed. Boston, MA: Doxbury Press, 1985.
12. Ruark JL, McCullough GH, Peters RL, Moore CA. Bolus consistency and swallowing in children and adults. *Dysphagia* 2002; 17: 24–33.
13. Ranmal S, Tuleu C. Demonstrating evidence of acceptability: the "catch-22" of pediatric formulation development. *Clin Pharmacol Ther* 2013; 94: 582–4.
14. Yeung VW, Wong IC. When do children convert from liquid antiretroviral to solid formulations? *Pharm World Sci* 2005; 27: 399–402.

