TITLE PAGE

A survey of caregivers of Nigerian children less than 6 years of age to determine the experience and perception of acceptability of oral solid dosage forms.

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Keywords: Flexible solid dosage forms, dispersible tablet, acceptability, preference, children

Running title: Experience and perceptions of acceptability of oral dosage forms for young children in Nigeria

Word count: 4308

Abstract

Objectives

The World Health Organization (WHO) recommends flexible solid oral dosage forms such as dispersible tablet as the preferred formulation for (young) children, especially in developing /low- and middle-income countries, LMIC. The aim of this study was to assess experience, perceptions of acceptability, and formulation preferences, among 10 oral dosage forms for young children in a sample of end-users in Nigeria as an exemplar LMIC.

Methods

Using a semi-structured and validated questionnaire, 148 caregivers were surveyed. Acceptability was assessed by level of liking using a 3-point Likert scale and ease of administration. Preference was assessed from participants' dosage form of choice. Oral dosage forms assessed were those mentioned in in the British National Formulary for children, 2013.

Results

The formulation perceived as the most acceptable was the chewable/suckable tablet. However, preference was for liquids. Specifically with the dispersible tablet, whilst 89% (n=111) of caregivers of young children found it easy-to-administer, only 50% of children liked it.

Conclusion

There is a gap between the proposal of dispersible tablet as the preferred dosage form for young children and caregivers' perceptions of acceptability and preference. Educational strategies to increase acceptability of dispersible tablets as the preferred formulation for young children would be required.

Key words: flexible solid oral dosage forms, acceptability, dosage form preference, children

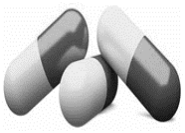
Graphical abstract

Liquid

Chewable tablet

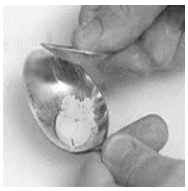
Intact tablet

Dispersible tablet

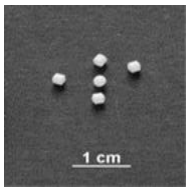


Intact capsule

"Sachet"



Crushed tablet

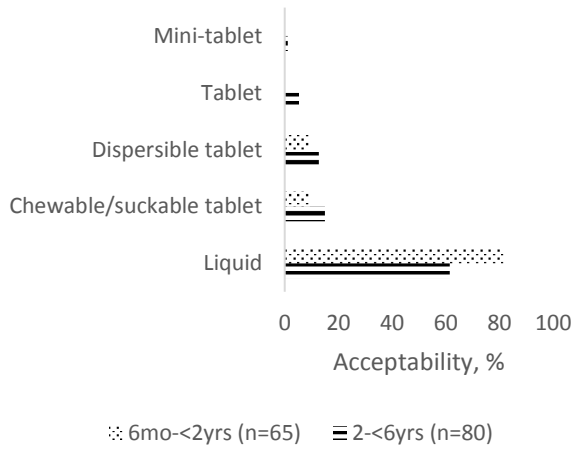


Mini-tablet

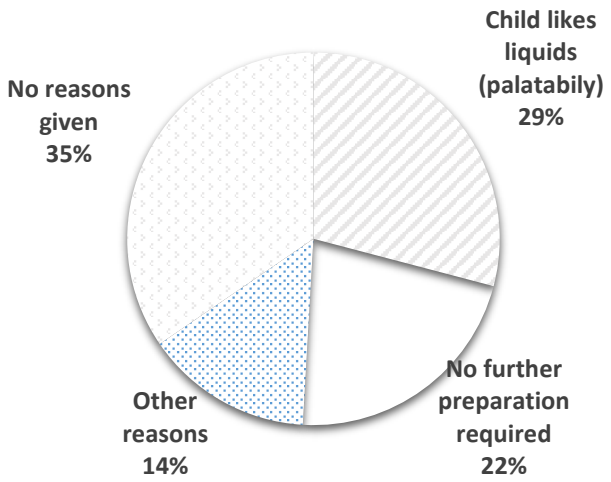
Sprinkle capsule

Orodispersibles

a. Dosage forms surveyed



b. Acceptability of administered oral dosage forms in children under 6 years



c. Reasons given by parents/caregivers for preference for liquid

A survey of caregivers of Nigerian children less than 6 years of age to determine the experience and perception of acceptability of oral solid dosage forms.

Introduction

The oral route remains the most widely preferred route of medicines administration (WHO, 2012; EMA, 2013). For the paediatric population in particular, oral liquid medicines have been traditionally preferred for infants and younger children less than 6 years old due to the limitations in their safe swallowing of conventional tablets or capsules. However the associated shortcomings with oral liquid medicines such as stability problems, difficulties in taste masking, safety of excipients in children, and high storage and transportation costs led to the proposal of flexible solid oral dosage forms (FSODs) by the World Health Organisation (WHO) as the preferred formulations for children (WHO, 2012).

In 2006, the WHO hosted a group of experts in paediatric formulations from the academia, pharmaceutical industry (both innovator and generic), regulators, programme managers and implementers with a view to reaching a consensus on the most suitable formulations for children, with attention to conditions in developing countries. The group recommended FSODs such as dispersible tablets, effervescent tablets, chewable tablets, orodispersible tablets and sprinkle capsules as the most suitable dosage forms, particularly for developing countries (WHO, 2012, WHO, 2014). In September 2010, the United Nations Children's Fund, UNICEF, Supply Division and the WHO further reiterated the preference of solid formulations such as FSODs, with emphasis on the dispersible tablet, that can be administered in more than one form, for example, given whole to older children or

dispersed in water or breast milk for ease of administration to younger children, as the most suitable, or age-appropriate, formulations for children.

Technical, economic and clinical considerations led the WHO proposal. The technical considerations include lower production costs, chemical stability, and potential absence of harmful excipients. Economically, solids, being cheaper to manufacture than liquids, could be more affordable for end-users in developing countries without access to health insurance. Clinically, considering that these dosage forms have a flexible mode of administration, they can be used in different subsets of the paediatric population unable to safely swallow conventional oral solids.

However, a formulation with poor acceptability may have an impact on patient safety, therapeutic outcomes, compliance, prescribing practice and ultimately commercial viability (Ivanoska et al., 2014; Kozarewicz, 2014). It is important to understand the formulation acceptability and preferences of parents/caregivers and children for oral solid dosage forms. Unlike adults, where oral solid dosage forms such as tablets or capsules will generally be acceptable to the majority of patients, potential paediatric patients from neonates to adolescents have differing needs. The qualitative features of formulations, such as form and taste, can affect acceptance and the likelihood of effective administration to paediatric patients. Moreover, certain practical considerations such as awareness of these age-appropriate dosage forms, and ease of administration, can profoundly impact the usability and acceptability of these formulations in resource-limited settings; and yet related knowledge is very limited (Orubu 2016).

While efforts are being made internationally to increase access to age-appropriate medicines for children, FSODs have become increasingly available for children with diseases

like malaria and HIV, but the barriers to implementation of FSODs in low resource settings are still not well understood. The acceptability and preference for dosage forms may vary widely between different cultural settings, socioeconomic contexts and literacy levels. For example, a national survey of medicines administration practices and preferences in Tanzania in 2013 demonstrated that forms such as dispersible tablets and granules in sachets were unfamiliar. Parents/caregivers and healthcare workers were accustomed to crushing portions of adult pills and mixing with water to attain a liquid solution (Adams et al., 2013). Similarly, other studies have demonstrated commercial unavailability, or lack of awareness of an age-appropriate medicine, forcing end-users to use medicines in ways that can affect acceptability and efficacy (Best et al., 2011, Thee et al., 2014). For instance, parents/caregivers may wish to administer dispersible tablets by means other than intended, that is, as a normal tablet without any prior dispersion. At the same time, children may not directly swallow any given tablet, but decide to keep the tablet in their mouth for a period of time thereby using it as an orodispersible tablet.

Specifically with the dispersible tablet, apart from experiential knowledge of the dosage form, there are many other obstacles such as unavailability of safe drinking water to disperse tablets, poor palatability, and cost, that impact the acceptability and effective administration of dispersible tablets to sick children in resource-limited settings (UNICEF, 2008; WHO, 2015a). Access to quality (improved) water sources is generally low in developing countries (UNICEF, 2008; WHO, 2015a). Where there is poor access to clean water, liquids may be regarded as the dosage form of choice for young children, despite the disadvantages mentioned earlier. Poor knowledge of the correct means and method of administering the dispersible tablet, appropriate dispensing device, volume of water, rinsing

out the dosing device after use also can have an effect on acceptability. In 2012, poor understanding of the dispersible tablet was identified as a barrier to their proper use (UN Commission on life-saving commodities for women and children, 2012).

In addition to the capacity to use the formulation as authorised, preference can be determined by other factors such as an "overall appeal" (related to medicine presentation, or packaging), medicine belief systems, and cost (Ward and Kynvin, 2015, WHO, 2015b). While appeal and belief systems are largely subjective, cost is not. In developing countries, cost can be a major, though not much studied, driver of both acceptability and preference. If offered a choice of several products of the same medicine, a patient or caregiver who pays for their medicine out-of-pocket is likely to find the lowest-cost product most acceptable and preferred (Ward and Kynvin, 2015). Literacy levels, access to quality water, and the ability to pay for medicines show a rural-urban divide and can influence acceptability and preference for medicines. Given the critical role these aforementioned factors play in the acceptability and preference for medicines, it is important that the acceptability of FSODs is assessed among end-users living in both urban and rural areas in a developing country. In this study, Nigeria was conveniently selected as an exemplar developing country.

Materials and methods

Study design

The study was designed as a cross-sectional descriptive survey of parents and caregivers of children less than 6 years old for their experience with and perception on acceptability and preference among several oral dosage forms for children.

Study instrument and validation

The study instrument was a semi-structured questionnaire divided into three parts comprising 13 items (Table 1). Part I collated participants' demographic information. Part II assessed experience with 10 types of paediatric oral dosage forms identified from the British National Formulary for children (BNFc), 2014, of which five (dispersible tablets, oro-dispersible tablets, chewable tablets, sprinkle capsules, and multi-particulates in sachets) can be regarded as FSODs (Table 1). Part II required participants to indicate which of the 10 formulations had been administered in the past three to six months, the acceptability of each, and a preferred dosage form for children in each of two age sub-groups as described in section 2.4.1. Acceptability was assessed as described in section 2.5. Pictures of the dosage forms were included in this part to facilitate comprehension. Part III was specific for the dispersible tablet and elicited participants' knowledge of the name of the dispersible tablet prescribed, acceptability, ease of preparation, preference, and water source for administering medicines. In parts II and III, participants were allowed to make free-text comments.

Questionnaire validation was carried out by vetting and pre-testing. Vetting was performed by experienced healthcare professionals – a consultant paediatrician, hospital and academic pharmacists – to test appropriateness of the questions. The vetted questionnaire was pre-tested on 22 participants for validation: a minimum of 80 % of participants reporting the questionnaires as easy to fill was taken to mean good comprehension. Data from this stage provided information for modification of the study instrument.

Study settings

Study settings were chosen based on convenience to include urban and rural locations in two, out of 37 federating units, in Nigeria (Table 2). The urban setting selected was a tertiary-level health facility in metropolitan Lagos, Lagos State The peri-urban location with a mix of urban and rural areas was chosen as Bayelsa State; facilities surveyed included secondary and tertiary hospitals, schools, community pharmacies and places of worship. With more than 85% of its population living in the urban metropolitan Lagos, Lagos State can be described as urban; while Bayelsa State with a mix of rural and urban locations can be described as peri-urban (Lagos State Government, 2011; Iaquinta and Drescher, 2000).

Participants

Inclusion criteria

Criteria for inclusion were parents/caregivers of children aged 6 months – < 6 years with an acute condition (malaria) or a chronic condition (HIV/AIDS) prescribed, respectively, branded dispersible artemether/lumefantrine and generic dispersible lamivudine/nevirapine/zidovudine and/or co-trimoxazole. Children who had not been weaned were excluded from the study. Children were stratified into two age-groups: 6 months - < 2 years (infants and toddlers), and 2 - < 6 years (pre-school children) according to the EMA classification (EMA, 2006).

Sample size

Sample size was 50 participants per age-group in each study location for a total of 100 per location, or 200 for the study. As this was an exploratory study, this sample size was considered sufficient (Hertzog, 2008, van-Riets et al., 2010). In order to overcome

recruitment pitfalls, an extra 30-50% was added and 130 – 150 participants were targeted per location.

Socioeconomic classification

Participants were grouped into an upper and a lower socioeconomic class using a combination of highest educational attainment and occupation of the breadwinner (the parent or caregiver who primarily provided for the family) (Kehinde et al., 2013). Participants whose breadwinner had at least a secondary school education and who were working as artisans – hairdressers, fashion designers, etc., or were junior school teachers were classified as upper class. Those with at most a primary school education working as small-scale traders, labourers or messengers were classified as lower class (Oyedeji, 1985, Aronu and Ojinnaka, 2009, Fetuga et al., 2010, Frank-Briggs and Alikor, 2011).

Criteria for assessing acceptability and preference

Acceptability was assessed using a 3-point Likert scale of "disliked", "neither disliked nor liked", or "liked" to indicate level of liking and ease of administration of dosage form rated as either "easy" or "difficult" as modified from Bayer, *et al*., (1988). While palatability was not directly assessed, the Likert scale was thought a good proxy for assessing the taste of the medicine administered in the study period, and hence of the child's willingness to take the medicine. During questionnaire administration, the researchers were careful to express this in a way that conveyed that palatability/taste was implied. The rationale for inclusion of ease of administration was the fact that it is listed as an important consideration in the development of paediatric medicines, and as a measure of the ability of the end-user to use the medicine as intended (WHO, 2012). Dosage forms that were liked by ≥80% of children and rated as "easy to administer" by ≥80% of parents/caregivers were considered

acceptable. Where the dosage form was either liked by ≥80% of children or rated as "easy to administer" by ≥80% of parents/caregivers, the dosage form was considered maybe acceptable (acceptable for the parent/caregiver, but not for the child).

Preference was evaluated from the parent/caregivers' dosage form of choice in the urban setting. For the peri-urban setting, participants were asked to rank the top four most preferred dosage forms identified from the urban setting.

Ethics

Ethical approvals were obtained before study commenced. Ethical approval was received from the Health Research and Ethics Committee of Lagos University Teaching Hospital (ADM/DSCT/HREC/1589); and from the Head of Clinical Services at Federal Medical Centre, Bayelsa State via an internal memo dated April 8, 2014. Verbal informed consent was obtained from participants before questionnaire administration. The purpose of the study and what was required of participants were explained in local languages (*Yoruba*, *Ibo*, or *Ijaw*, as the case was) or Pidgin English before consent was obtained. Participants in the urban area who agreed to partake were rewarded with a pack of noodles.

Questionnaire administration

The questionnaires were mostly administered by trained researchers (pharmacy students, intern or qualified pharmacists). A few, less than 5%, were self-administered by the parents/caregivers.

Data analysis

Data was anonymised. The results from part II of the questionnaire that considered all oral dosage forms for perceptions on acceptability and preference were aggregated for the

urban and peri-urban settings and described as percentages. Dosage forms for which there were less than 10 respondents were treated as not common and, thus, were not included in the analysis. Results from part III for the dispersible tablet were analysed for differences between study arms (acute vs chronic condition) and settings using the Chi square test. A two-tailed p value < 0.05 was considered statistically significant. The results for preference for the dispersible tablet was descriptive and expressed as percentages.

Results

Questionnaire validation was conducted from September 24 – October 20, 2013. All respondents (100%, n=22) reported the questionnaires as easy-to-fill. However, from the answers recorded it was observed that there were some problems with understanding of some of the questions. These questions which included whether the age and gender in part I of the questionnaire referred to the child or the parent/caregiver, and issues with easy or difficult to administer and preferred dosage form were modified. The modifications allowed for parents/caregivers to provide both ages and genders of the child and the parent/caregiver. In addition, parents/caregivers were made to give reasons for difficulty in administration of the dosage form; and the wording of the question for dosage form of choice clarified such that participants chose only one preferred dosage form.

Questionnaire administration was performed for the urban setting in October 2013, and in the peri-urban setting in July, 2014. In the urban setting, it was observed that participants had no experiential knowledge of oro-dispersible tablets, so the chewable and oro-dispersible tablets were combined into a single “chewable/suckable” dosage form, or

tablets used in the mouth, category in the questionnaire used for the study in the peri-urban setting. This left nine oral dosage forms to be assessed. Similarly, with no mini-tablet (2-4 mm in diameter) tablet available at the time of the study, folic acid tablets (a widely-known medicine among mothers as it is given out during pregnancy) which is actually a medium-sized tablet (≈ 8 mm in diameter) was used as the "closest" example. A second modification to the questionnaire used in the peri-urban setting allowed participants to rank the four most preferred dosage forms as identified from the survey in the urban area.

Demographics

The study included 148 children aged 6mo – 6 years and their parents/caregivers in two different settings (Table 3). In the urban setting, participants' socioeconomic class varied with the disease condition, being of the upper socioeconomic class for the acute condition and of the lower socioeconomic class for the chronic condition. In the peri-urban setting, participants were mostly of the upper-socioeconomic class. The median age of parents/caregivers was 32 years (range 21 – 63 years). Almost all were mothers of the child.

Experience, perceived acceptability, and preference for oral dosage forms

Participants had experience with all nine dosage forms, though a wider variety of dosage forms had been administered to children aged 2-<6 years (Figure 1).

Acceptable dosage forms were the suckable/chewable tablets and liquids, depending on age-group. For both age-groups, the suckable/chewable tablet was liked by >80% of children to whom it had been administered (Figure 1) and also found easy to administer by >90% of parents/caregivers (Figure 2). On the other hand, liquids were less liked by children (70 % of children <2 years, and 65% of children 2-<6 years were reported to have liked the liquids

administered in the past), while 91% of parents/ caregivers of children aged 2-<6 years old found it easy to administer (compared to 76% for children aged 6mo-<2 years).

The least acceptable dosage form in terms of level of liking was the “mini-tablet” (actually a medium-sized tablet in this setting) in children <2 years and the sachet in children aged 2-<6 years, while in terms of ease of administration, it was the crushed tablet in both age-groups.

The preferred dosage form was liquid (Figure 3).

Dispersible tablet: knowledge, perspectives on acceptability and preference

Participants in the urban setting demonstrated good knowledge of the names of the dispersible tablets they had administered to their children, although in some cases they had to be prompted to recall the names. This was not the case with the peri-urban area.

The dispersible table was found to be maybe acceptable in the sample studied (n=111). While almost all parents/caregivers in both settings found it easy to prepare (Figure 4), only about 50% of the children were reported to have liked the dispersible tablet that was administered in the past (Figure 5).

When participants in the urban setting were asked if they would prefer all medicines for their children to be made as dispersible tablets, majority, 65% (47/72), said “no”. The results were the same in the peri-urban setting where liquids were ranked as the dosage form of first choice for both age-groups (Figure 3). The major reasons given by parents/caregivers for the preference for liquids over dispersible tablets were: “these are sweet; or child likes liquids”, and “no further preparation required” (Figure 6).

Discussion

Acceptability of oral dosage forms

Of all nine oral dosage forms assessed, the chewable/suckable tablet was perceived as the most acceptable in both age-groups. The chewable/suckable tablet was better liked than liquid which is traditionally considered the de-facto dosage form for children in these age-groups. As deduced from the free-text comments, the main reason liquid was not liked by all had to do with taste: parents/caregivers said children only liked a liquid if it tasted sweet; none mentioned bulkiness of the container for liquids, or storage conditions as reasons why liquids were not liked, though these were not provided as options. On the other hand, the chewable tablet formulation(s) that the caregivers would have administered to their children – and which was used as an example during questionnaire administration – was chewable vitamin C tablets which do not contain a necessarily unpleasant-tasting API (vitamin C has an acidic taste), and is often sweetened and flavoured. This was also the case with the example of the "orodispersible" tablet used, Strepsils® lozenges, which again is sweetened and flavoured. These two medicines are available as over-the-counter (OTC) products and so may not necessarily be considered as medicines in these settings. Thus, these results as to liking for the chewable/suckable tablet have some degree of bias. How much of the perceived acceptability depended on taste, and how much depended on the view as "not medicines" is not known. However, these results show that the taste of the medicine was an important determinant of acceptability, as was expected.

Somewhat surprisingly, in children less than 2 years old, the chewable/suckable tablet was reported as having been administered and as acceptable (well liked). However, there is the concern that as teething is only complete by the age of 2 years; there might be possible

safety issues with swallowing these dosage forms that are meant to be chewed in this age group. No parent/caregiver mentioned issues with this though. The literature on the safety of chewable tablets in young children is scant, and there is so far only one review establishing the safety of chewable tablets in children above the age of 2 years (Michele et al., 2002). The same concern applies for the lozenge used as an example of the oro-dispersible tablet in this study.

In terms of ease of administration, the chewable/suckable tablet was the dosage form found easiest to administer; with liquids found easy to administer by >80% caregivers only to children 2-<6 years old. On the other hand, the crushed tablet was considered the most difficult to administer, most probably because of the aversive taste of tablets not meant to be administered in this manner. The crushing of tablets is a common manipulation used to facilitate the oral administration of medicines in young children. In this study, the medium used for dispersing the crushed tablet for administration to the child was not investigated but was most likely water. In this, the results differ from that reported for the administration of anti-tuberculosis (anti-TB) drugs to children in South Africa where most caregivers, 88% (n=83), who crushed tablets and administered with beverages or food reported the crushed tablets as easy to administer (Bélard et al., 2015). However, there are issues with crushed tablets dispersed in beverages, food, or water. For example, reduced bioavailability had been reported for crushed lopinavir/ritonavir tablets (Best et al., 2011), and is suggested for crushed ofloxacin and levofloxacin tablets (Thee et al., 2014). It is important, therefore, that the effects of mixing paediatric medicines with food/drinks as occurs in practice is studied. Another issue with the use of crushed tablets dispersed in food

might arise if all the food is not given leading to loss of dose, and potentially reduced efficacy.

Oral dosage form preferences

Parents/caregivers preferred liquid over other oral dosage forms for children less than 6 years old. These results for preference are similar with that reported for Tanzania where there was clear preference for liquids in children less than 2 years (76%, 147/185), while caregivers were divided between liquids (48%, 93/185) and crushed tablets/sprinkled capsules (30%, 59/185) for 2-6 year olds (Adams et al., 2013). The results are, however, different from that reported for Kenya, where preference was for the dispersible tablet formulation of artemether-lumefantrine tablet as opposed to the liquid formulation for the same age group (Ogutu, et al., 2014).

Factors identified from this study as influencing acceptability and preference for oral dosage forms were mainly taste and the age of the child or familiarity with the dosage form. Most parents/caregivers in their free-text comments reported taste as the main factor influencing whether the child readily takes a medicine or not. Taste or palatability is a known determinant of acceptability and adherence with prescribed medicines in young children as well as of preference (Marriot, 2013; Bryson, 2014). With preference, the age of the child as a factor in the dosage form of choice may derive from traditionally-held views and might be related to prescribing habits of physicians who may routinely prescribe liquids for young children. As the results show, it was indeed the most commonly administered oral formulation in the sample surveyed.

Dispersible tablets: acceptability, preference, and barriers

While not as well-liked as the chewable/suckable tablets or liquid, the dispersible tablet was perceived as easy to prepare or use in both the urban and peri-urban study locations. With an average 89% of participants (99/111) reporting the dispersible tablets as easy to prepare, these results are in close agreement with that reported for other developing countries of Kenya and Bangladesh. In Kenya, 98% (122/126) of caregivers of children less than 5 years old with malaria reported dispersible artemether-lumefantrine tablets as either "acceptable" (15%), "simple" (68%), or "very simple" (14%) on a 5-point scale accessing difficulty or ease of use, while only 2% found it "difficult" and none found the product "very difficult" to use (Ogutu, et al., 2014). The study in Bangladesh reported that most caregivers (98%, n=303) followed the correct procedure to dissolve dispersible zinc tablets (Nasrin et al., 2005). Together, these results indicate that the dosage form is easy to prepare.

Despite this, participants included in this study showed some reluctance to reconstitute the dispersible tablet. This reluctance, and palatability (as noted in section 3.3 and 4.2) constituted barriers to acceptability and preference for the dispersible tablet in these settings.

Participants showed willingness to invest in a source of quality water for administering medicines (data not included), as had been reported for another developing country with access to water concerns (Adams et al., 2013).

Limitations

There were some limitations with this study. Firstly, several of the dosage forms were not known to the participants. These were: oro-dispersible tablets, mini-tablets, and sprinkle capsules. Thus the researchers had to improvise and used examples that were technically

not the dosage forms mentioned for these three. This would have introduced some bias for the results for these dosage forms, as had been mentioned. In addition, the dispersible tablets administered by parents/caregivers might have differed in their formulation and taste-making properties and this would have influenced acceptability by the child. No effort was made to match formulation with acceptability (level of liking).

Secondly, as the study relied on experience, and not on actual dosage form administration, the results reflect attitudes which might be different from what the parents/caregivers might do in actual practice.

Thirdly, this study did not assess cost. Participants on ARVs/Co-trimoxazole received their medicines for free, and artemether/lumefantrine was subsidised, as such the cost of medicines as a factor in acceptability or preference could not be evaluated.

Conclusion

There is a gap between the WHO proposal of the dispersible tablet as the preferred formulation for young children and end-users' oral formulation preferences in these settings at the time of study. While the dispersible tablet was found easy to administer, parents/caregivers preferred liquid formulations for children aged 6mo-<6 years. The major reasons for preference for liquids over the dispersible tablet was that the children preferred liquids (as these were sweet), and reluctance to prepare the dispersion of tablet for administration. These reasons constituted barriers in this setting.

To overcome these barriers, dispersible tablet formulations should be made to demonstrate that the products are suitably taste-masked. To change perceptions and facilitate

usage/uptake, educational strategies for parents/caregivers emphasising the benefits of the dispersible tablets would be needed.

Though not studied, it would also be necessary to provide guidance as to the reconstitution of dispersible tablets in milk or fluids other than water, as bioavailability could be altered.

Acknowledgments

Dr Dan Orumwense of the Federal Medical Centre, Yenagoa, Bayelsa State, and Edith Kpokiri of the UCL School of Pharmacy are acknowledged for facilitating the conduct of the survey in Bayelsa State. Prof Edna Iroha of the Paediatrics Department, Lagos University Teaching Hospital and Dr Ehijie Enato of the University of Benin, Nigeria are acknowledged for useful insight in the preparation of the questionnaires.

Funding

This work was supported as part of a PhD by the Niger Delta Development Commission, Nigeria and the Niger Delta University, Bayelsa State, Nigeria.

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Table 1 Summary of questionnaire

Part	Questions	Specific items	Response Type/ Options
Part 1	Socio-demographic information	Age, gender; highest education level and occupation of caregiver (or breadwinner[1]) and relationship of caregiver to child.	Self -completion
Part 2 (2a)	Experience with oral dosage forms Level of liking Ease of administration	Oral dosage forms[2]: i. liquids ii. intact tablets, iii. chewable tablets*, iv. orodispersible tablets*, v. dispersible tablets*, vi. minitablets, vii. crushed tablets viii. intact capsules, ix. sprinkle capsules*, x. "sachets"*[3].	Not administered. Administered, and: • Liked • Neither liked nor disliked • Disliked Easy to administer. Difficult to administer, because: • Bad (unpleasant) taste • Needed an administration device • Long dispersion times

	Preference		Closed question, with options for comments
Part 3 (2b)	Use of the dispersible tablet	Name of dispersible tablet prescribed; Difficulties during preparation, if any; Level of liking for the dispersible tablet; Preference for dispersible tablets.	Closed and open-ended
	Water source	Tap, bottled, sachet, stream, well	Closed question

Notes:

1. Where the caregiver is not the person who provides for the family.
2. As identified from the British National Formulary for children, 2014.
3. Multi-particulates or powders packed in sachets.

* FSODs

Table 2 Study locations in Nigeria

Study stage	State in Nigeria	Institution(s)	Study sites within each state or institution

			Acute arm	Chronic arm
Stage I (Pre-test)	Lagos State	Lagos University Teaching Hospital (LUTH)	(In this stage, patients as well as health-care practitioners were consulted. The questionnaires were filled in by a convenience sample of patients).	
Stage II (Urban)	Lagos State	Lagos University Teaching Hospital (LUTH)	Paediatric Out-patient (POP) Clinic; Children's Emergency (Olukoye Ransom Kuti Children's Emergency, ORKCE); Ward; Children Medical Ward (D3)	AIDS Preventive Initiative in Nigeria (APIN) Clinic

Stage III (Peri-urban)	Bayelsa State	Various	General Hospital, and homes in Amassoma in Southern Ijaw Local Government Council; community pharmacies, homes, schools, and a church premise in Edepie, Amarata, Onopa, and Kpansia – suburbs of Yenagoa Local Government Council.	HIV/AIDS pharmacy of the Federal Medical Centre (FMC)

Table 3 Demographic characteristics of participants in stages II and III of the study

	Urban		Peri-Urban+		
	Acute	Chronic	Acute	Chronic	N
6 mo. - < 2 years					
Number of participants (n)	13	30	12	10	65
Socioeconomic class, upper (%)	62	33	63	70	
2 - < 6 years					
Number of participants (n)	27	21	16	19	83
Socioeconomic class, upper (%)	48	43	62	83	
					148

+ An on-going industrial action in the hospitals and the threat of Ebola at the time the study was conducted limited participants numbers.

Figures

Captions

Figure 1 Experience, and level of liking for oral dosage forms as reported by a sample of caregivers of children aged: (a) 6 mo-<2 year-olds, (b) 2-< 6 year-olds. Though all 9 had been administered, intact and sprinkle capsules were not common dosage forms, as were tablets in children <2 years. The acceptable dosage form in both age-groups was the suckable/chewable tablet which was the only dosage liked by >80% of children to whom it had been administered.

Figure 2. Ease of administration of oral dosage forms as reported by a sample of caregivers of children in the age-groups: (a) 6 mo-<2 years, (b) 2-< 6 years. The dosage forms perceived as easy to administer by ≥80% of caregivers were: (i) the chewable/suckable tablet in both age-groups, and (ii) liquid in the 2-< 6 years age-group.

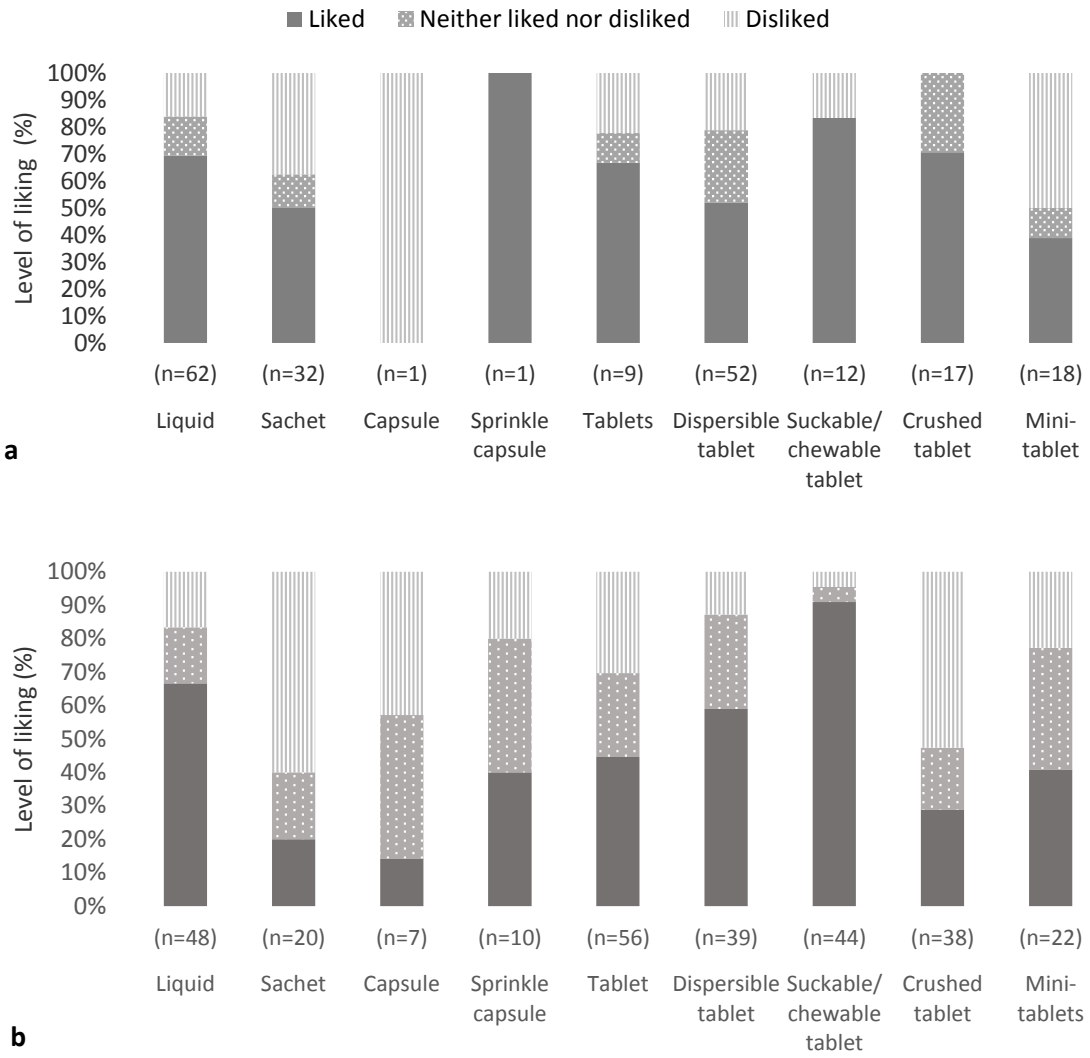
Figure 3. Oral dosage form preferences for: (a) 6 mo - < 2 year-olds, (b) 2-< 6 year-olds. For both age-groups, caregivers chose liquid as the preferred dosage form over the chewable/suckable and the dispersible tablets.

Figure 4. Ease of preparation of the dispersible tablet in a sample of caregivers of children < 6 years old with an acute (malaria) or chronic (HIV/AIDS) condition in an urban (Lagos State) and peri-urban (Bayelsa State) setting in Nigeria. n is the number of participants who have administered/used the dosage form. There was no difference in the ease of preparation of the dispersible tablet among study participants, p=0.95.

Figure 5. Level of liking for the dispersible tablet as reported by caregivers of children < 6 years old with an acute (malaria) or chronic (HIV/AIDS) condition in an urban (Lagos State)

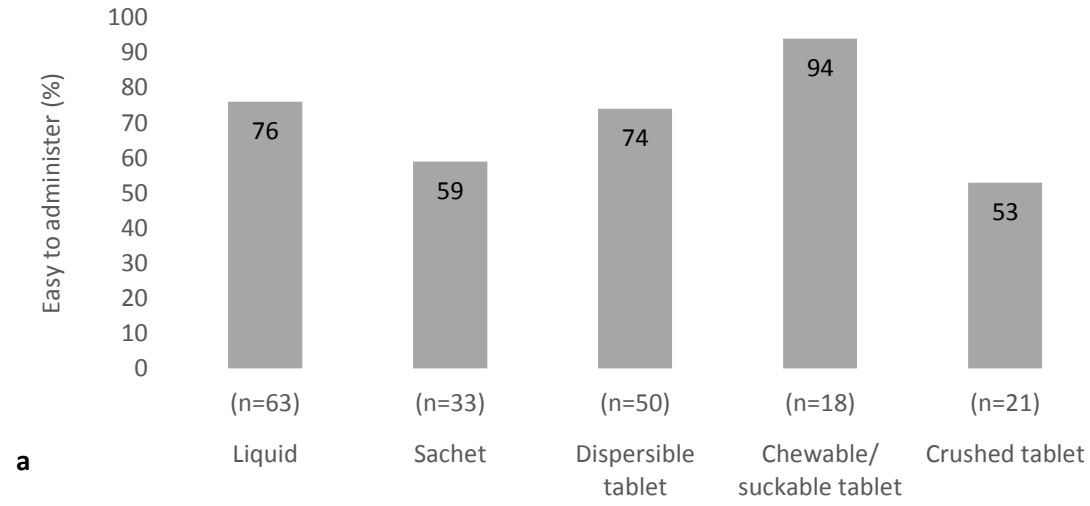
and peri-urban (Bayelsa State) setting in Nigeria. n is the number of participants who have administered/used the dosage form. The level of liking for the dispersible tablet was independent of disease condition and study setting, p=0.86.

Figure 6. Reasons given for the choice of liquids as the preferred dosage form for children less than 6 years old.

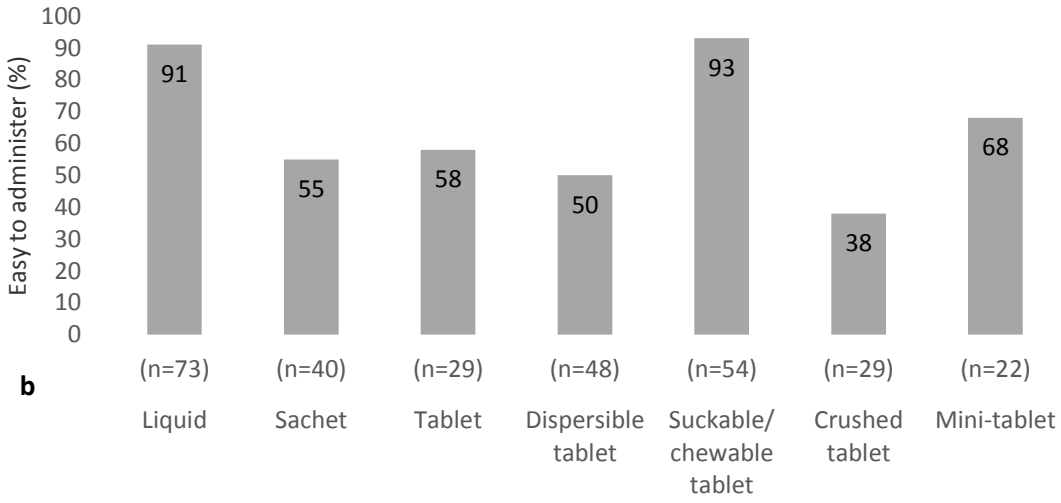


Note: n is the number of participants that had administered the dosage form

Figure 1



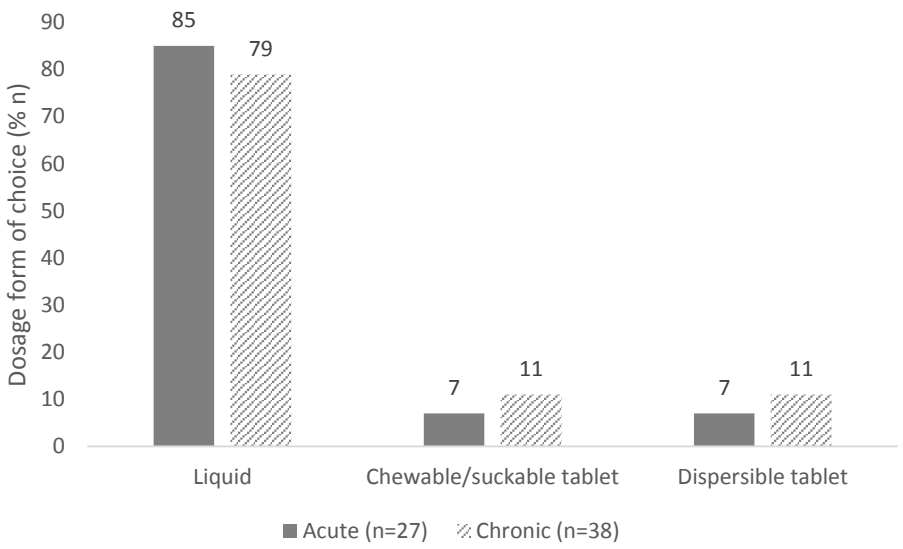
a



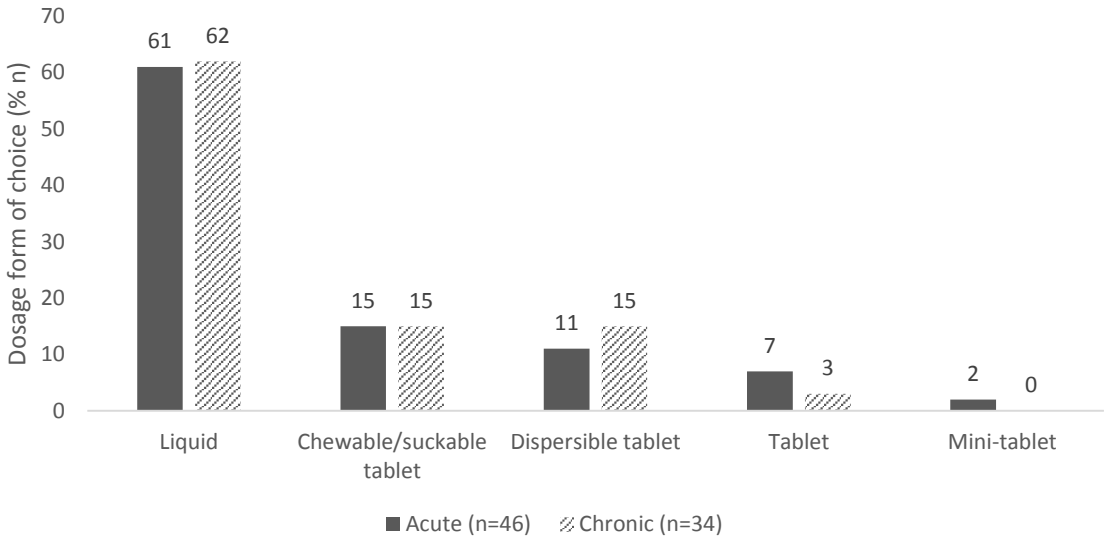
b

Note: n is the number of participants that had administered the dosage form. Easy to administer is the proportion of participants, %, who found the dosage form easy to administer.

Figure 2


Dosage form of choice (% n)
90
80
70
60
50
40
30
20
10
0
85
79
7
11
7
11
Liquid
Chewable/suckable tablet
Dispersible tablet
Acute (n=27)
Chronic (n=38)

a.


Dosage form of choice (% n)
70
60
50
40
30
20
10
0
61
62
15
15
11
15
7
3
2
0
Liquid
Chewable/suckable tablet
Dispersible tablet
Tablet
Mini-tablet
Acute (n=46)
Chronic (n=34)

b.

Figure 3

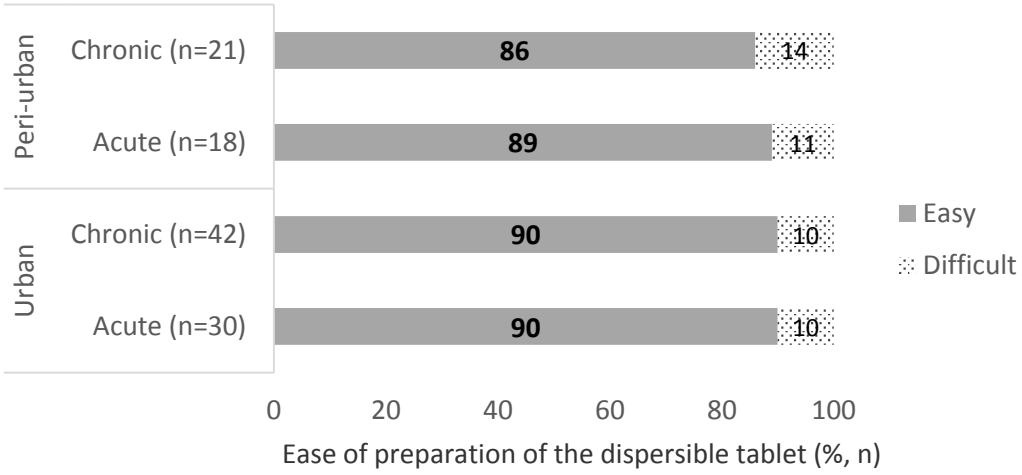

Peri-urban
Chronic (n=21)
Acute (n=18)
Urban
Chronic (n=42)
Acute (n=30)
86
14
89
11
90
10
90
10
Easy
Difficult
0
20
40
60
80
100
Ease of preparation of the dispersible tablet (%, n)

Figure 4

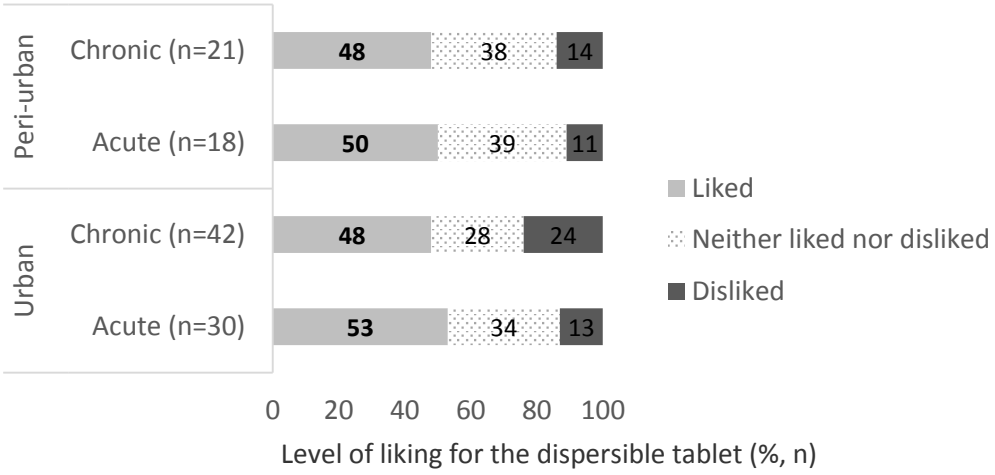
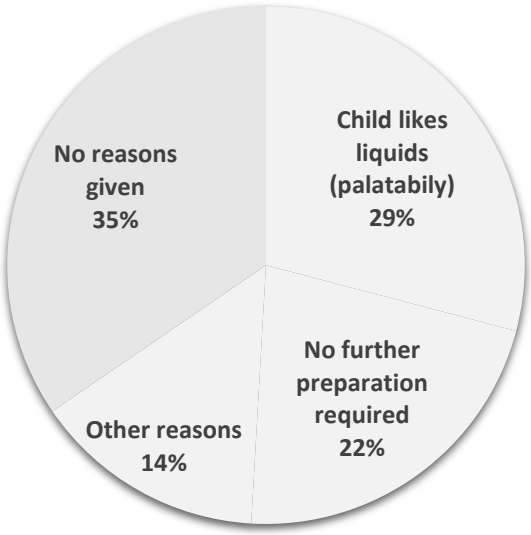

Peri-urban
Chronic (n=21)
48
38
14
Acute (n=18)
50
39
11
Urban
Chronic (n=42)
48
28
24
Acute (n=30)
53
34
13
Liked
Neither liked nor disliked
Disliked
0
20
40
60
80
100
Level of liking for the dispersible tablet (%, n)

Figure 5



Notes:

1. n = 72.
2. Other reasons included a combination of child's liking for liquids and no further preparations required before administration of liquids

Figure 6