Science Article

A DESCRIPTIVE SURVEY OF THE PACKAGING CHARACTERISTICS OF ORAL LIQUID PAEDIATRIC MEDICATION AVAILABLE IN RETAIL MEDICINE OUTLETS IN KADUNA, NIGERIA

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ABSTRACT

Background: Accurate & well-presented information on product packaging, and proper selection of medication measuring devices by manufacturers are all important in ensuring safe and rational use of medications. The aim of this study was to describe the general characteristics and presentation of information on the packaging of oral liquid paediatric medications, available in retail medicine outlets located in Kaduna state.

Methods: A cross-sectional survey was carried out between June and September 2018, in sixty pharmacies and patent medicine shops selected through multistage sampling. All medications that were marketed for use in children, encountered during the survey were included in the study. Data was collected on the formulation type, country of manufacture, type of measuring device included and presence of expiry dates & National Agency for Food and Drug Administration and Control (NAFDAC) registration. Information was also collected on the wording and presentation of instructions on drug packaging. Data collected was then coded and entered into a Microsoft Excel 2013 sheet for analysis, and descriptive statistics used to report the data collected.

Results: Two hundred drugs were encountered-81 suspensions and 119 solutions. Most of the suspensions were anti-infectives, while majority of solutions were cold and cough medication and multivitamins. Majority of the drugs had NAFDAC registration numbers (94%) and expiry dates (99%), although up to 24% did not have leaflets. Over half (59%) of the drugs were manufactured in Nigeria. Eighty-two percent of the drugs contained a medication-measuring device-the most common of which was a measuring cup. Dosing instructions allowing teaspoons/tablespoons to be used to measure out doses were frequently encountered (45%). Only five (26.3%) out of 19 paracetamol-containing drugs them had instructions that they not be used concurrently with other paracetamol-containing products. While seventy-one (87.6%) of the suspensions had instructions to shake before use, the instruction was the same size and colour as surrounding text in majority of cases.

Conclusion: While some of the observed characteristics were adequate, quite a few potentially problematic ones were identified. There is a need for NAFDAC to develop more comprehensive guidelines on drug packaging within the country.

Keywords: Measuring device, Nigeria, Oral Liquids, Packaging, Paediatric,

Introduction

Paediatric medications include a wide range of medicines usually formulated and marketed for disease prevention or treatment in children. Use of these medicines allow for safe and accurate dose administration, reduce the risk of medication errors and improve therapeutic outcomes in children[1]. They are predominantly oral liquids to help ease swallowing difficulties, improve drug palatability and ensure dosing accuracy[1-2]. Paediatric liquid oral medications can be broadly classified into two groups: non-solutions e.g. emulsions & suspensions and solutions such as drops, syrups, elixirs etc. These formulations have distinct advantages and disadvantages, even though solutions are preferred over suspensions because they allow for more accurate dosing[3].

Medication labeling refers to the label on the drug container and all printed materials on/in the package that accompany a medicinal product[4]. Medication labels usually provide important information including: indications, usage directions and information about adverse effects- in addition to other relevant details. Proper drug labeling is important because it can help ensure rational drug use, especially in instances when medicines are dispensed to patients by healthcare professionals without the provision of relevant information on how to use them safely and effectively[5]. Many drug regulatory bodies e.g. The Nigerian National Agency for Food and Drug Administration and Control (NAFDAC) [6], The American Food and Drug Administration (FDA) [7], and the Canadian Government[8] all provide guidelines for the proper labelling of most types and/classes of medication.

Medication measuring devices (MMDs) on the other hand, include a wide range of tools used to dispense liquid oral medication such as measuring cups, dosing spoons, syringes and droppers. These tools help to simplify medication administration- especially to children, and facilitate accurate dosing[9]. Several drug regulatory agencies[6-8] also require that oral liquid medication be packaged with a suitable measuring device.

Medication errors are quite common in children, and can cause significant morbidity and mortality[10]. Sub-optimal drug labelling and packaging has been identified as a causative factor for medication errors[11-12]. This is because good drug packaging and label design can improve the legibility of dosing instructions and other relevant information, and increase the chances that the product will be safely used by the end user. In addition, paediatric administration errors - a type of medication error caused by administering either too much or too little of a drug- have also been reported in the literature. These can be caused by the use of common household spoons to administer medicines or wrong measurement techniques when using some medication measuring devices[9,13].

A few studies have reported problems with the medication measuring devices and information on drug packaging provided by paediatric medication manufacturers[14-15]. In Nigeria, an earlier study by Ogaji and colleagues[16] described the availability of information leaflets and medication measuring devices in oral paediatric medicines available in Jos. However, their study only assessed the presence of these items, and did not provide any further information on their specific characteristics.

Therefore, the aim of this study was to describe the general characteristics (E.g. type of formulation, country of manufacture, presence of NAFDAC registration number and type of medication measuring device present etc.), and the wording and/ presentation of information on the packaging of oral liquid paediatric medications available in retail medicine outlets located in Kaduna state.

Methods

Study Site

The study was carried out in Kaduna state, the fourth largest state - by land mass- in Nigeria. The state has 23 local government areas and a population of over six million inhabitants according to 2006 official census figures[17]. The state comprises of three major urban areas: Kaduna metropolis, Kafanchan and Zaria[18]. Over 95% of all the registered pharmacies in the state are located within two of these areas-Kaduna metropolis and Zaria[19], hence this study was carried out in those areas.

Study Design

A cross-sectional survey was carried out on selected pharmacies and patent medicine shops from June to

September 2018. Multi-stage sampling was used to select pharmacies and patent medicine stores to be visited. Given the large size of Kaduna metropolis, it was divided into two major areas - Kaduna north and Kaduna south. These two areas plus Zaria town were then subdivided into ten major suburbs each, making a total of 30 suburbs. Registered pharmacy premises in the state[19], were then classified based on their locations into one of these 30 suburbs. One pharmacy premise was then randomly sampled from each group, making a total of thirty pharmacies. There is currently no similar list of registered patent medicine shops in the state, so convenience sampling was used to select thirty patent medicine shops from these thirty suburbs.

All selected pharmacies and patent medicine shops were eligible to participate if they were willing to allow the researchers access to their shops, if not, they were excluded and another pharmacy/patent shop randomly selected.

Data Collection Instrument

A form was designed to collect data. Information was collected on: type of liquid dosage form; generic name(s) and strength of drug; country of manufacture; presence of medication leaflet; presence and type of medication measuring device (MMD) etc. Data were also collected on the wording and presentation of information on the drug packaging. These included whether the indication for use of the medicine was written on the pack; presence of NAFDAC registration number and expiry dates, in addition to other relevant information.

Data Collection

Shop owners or other personnel working in the visited premises were initially approached and informed about the objectives of the study. Afterwards, their permission was sought to collect data from their shops. If they agreed, the researcher identified paediatric medications and proceeded to fill the data collection form. Pictures of all the medication packs encountered were also taken- using a mobile phone camera, and a phone scanning application used to scan images of the medication leaflets included in the packs.

Data were collected from any medication that was marketed for use in children. This was defined as medication containing dosage information - either on the pack or leaflet - showing that it could be used in children aged 6 years or younger. In addition, information was only collected once for each medication, irrespective of how many times it was encountered.

Data Analysis

Data was coded and entered into a Microsoft Excel 2013 sheet for analysis. Descriptive statistics (frequencies and percentages) were then used to report the data collected.

To decide whether a drug is an over the counter medicine or a prescription only medicine, Essential Medicine Index[20] 2016/2017 edition was used.

Ethical Considerations

Ethical approval was obtained from the Human Research Ethics Committee of Ahmadu Bello University (Approval number: ABUCUHSR/2018/UG/003). No information that could be used to identify the visited premises was collected, and the study did not involve any patient contact.

Results

General Drug Characteristics

Of the 200 oral liquid paediatric medications encountered, 119 (59.5%) were solutions while 81 (40.5%) were suspensions. Several types of formulations were grouped together under the solutions category, and these included syrups, drops, elixirs, emulsions and mixtures. Majority of the suspensions were anti-infective agents - either antibiotics or antimalarials - while the solutions were mostly cold and cough medication or multivitamin preparations (Figure 1).

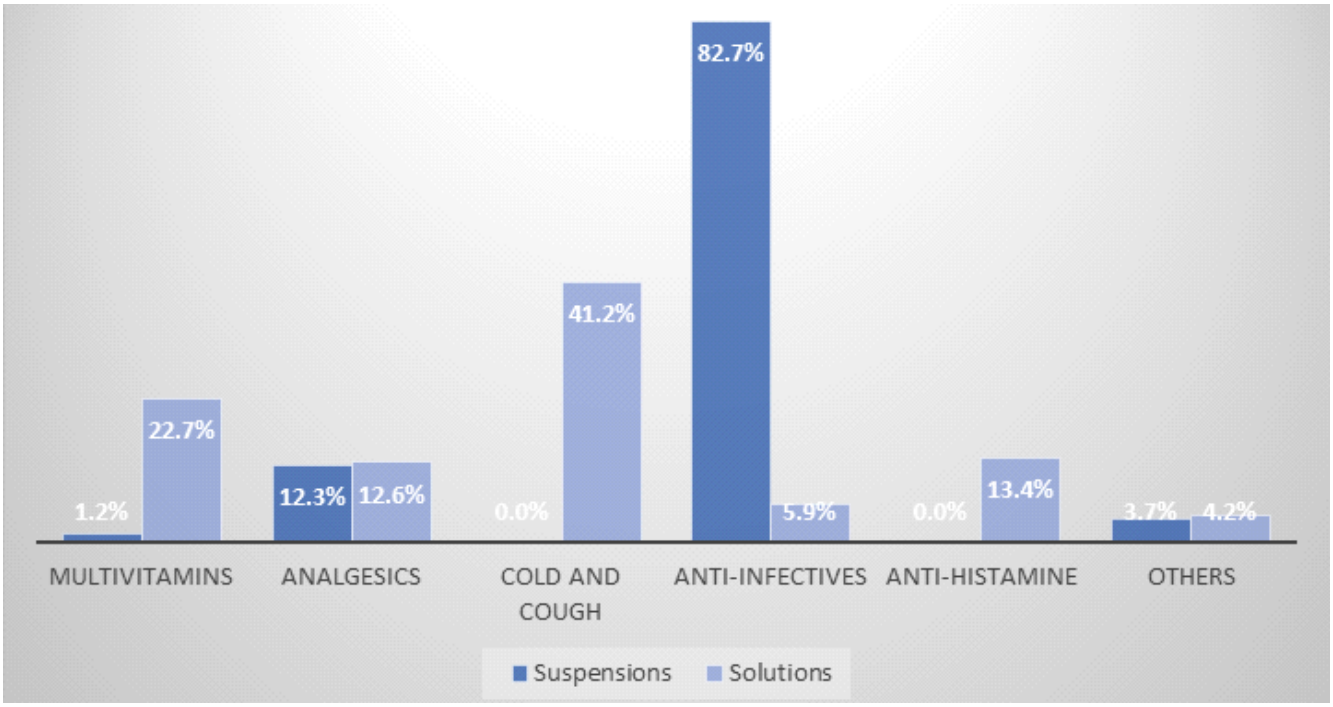


Figure 1: Pharmacological Classification of the Liquid Paediatric Medications Encountered

Generally, most of the drugs had expiry dates and National Agency for Food and Drug Administration and Control (NAFDAC) registration numbers written on their packs (Table 1). Majority of the drugs encountered were manufactured in Nigeria (59%) and India (21%). While the rest were manufactured in various countries including the United Kingdom, China, Egypt, Pakistan and so on.

Characteristic	Present n (%)	Absent n (%)
Leaflet*	152 (78.8)	41 (21.2)
Expiry Date	198 (99)	2 (1)
NAFDAC Registration Number	188 (94)	12 (6)

Table 1: General Characteristics of the Liquid Paediatric Medications Encountered

* Values in this row do not sum up to the total because seven drugs were sealed and could not be opened

Information Contained on the Packaging of Encountered Medication

Majority of the medication packs encountered had storage instructions on them. Conversely, less than 10% of packs in either category had either written information or a sign indicating whether the drug was an over-the-counter (OTC) drug or a prescription-only-medicine (POM). In addition, almost half of the OTC medications had dosing instructions allowing teaspoons/tablespoons/dessertspoons to be used to measure out doses (Table 2). Nineteen (19) of the medication encountered were paracetamol-containing drugs. Only five (26.3%) of them had instructions on their packs that they not be used alongside other paracetamol-containing products.

Discussion

This study described the general packaging characteristics of oral liquid paediatric medications available in retail medicine outlets in Kaduna state. Study findings revealed that most of the drugs encountered were registered by NAFDAC and had storage directions and expiry dates. Almost half of the OTC medication had dosing instructions allowing the use of teaspoons/tablespoons to be used to measure out doses. In addition, while many suspensions had instructions for shaking before use, the instruction was not properly worded and could not be easily seen. Furthermore, the most common type of measuring device included in the medication were measuring cups.

Majority of the medications encountered during this study were registered by NAFDAC and had storage instructions and expiry dates on their packs. Leaflets were slightly less common, with just under 80% of packs in this study containing them. This is similar to earlier results reported by Ogaji and colleagues[16], even though their study reported a lower percentage (69.3%) of medications containing leaflets. It should however be noted that current NAFDAC labelling guidelines[6] only require POMs to have leaflets, and most of the drugs that did not have leaflets in our study were OTC medicines. In the same vein, estimates of medication measuring device inclusion in packs for both studies were also very close.

The current version of the NAFDAC guidelines[6] require that all OTC products have information about the indication(s) of the drug, and a statement to the effect that a physician be consulted if symptoms persists. Also required for paracetamol containing preparations, is the warning that they not be used concurrently with other paracetamol-containing products. While most of the OTC medicines in this study had indications written on their packs, almost half of these indications contained at least one medical term, with plenty of them containing several such terms. Health literacy- the degree to which individuals have the capacity to process, and understand basic health information - has been reported to be low worldwide, even in developed countries[21]. Using medical terminology, has been identified as one of the reasons why health related information is so difficult for patients/consumers to understand[22]. Also, while several of the OTC medications had some instructions on seeking further medical care, inconsistencies were observed in how these statements were worded. In some cases, the instruction was to seek further care if symptoms persisted, without specifying a time period. In other cases where a specific duration was indicated, the number of the days to wait before seeking further care- even for the same drug although manufactured by different companies - varied widely. While some medicines specified two days, others specified three days and so on. This is a potential problem that can cause parents to delay seeking proper medical attention for their sick children. It was also observed that only about a quarter of paracetamol containing products had instructions that they should not be used alongside other paracetamol containing products. This was a low rate of compliance to the NAFDAC regulations, and also potentially very dangerous given the risk of hepatotoxicity associated with paracetamol overdosing[6].

Dosing of medications is a very common source of medication errors in children. NAFDAC labelling guidelines[6] require that an appropriate measuring device be included in the packaging of paediatric medication, and a good number of medication seen during the course of this study complied with that directive. However, majority of the included devices were measuring cups. This is worrisome because several studies have shown that dosing mistakes are made more frequently when parents use dosing cups to measure medication, than when other measuring devices are used[23-24]. In one of these studies, less than 20% of parents were able to correctly measure the required volume using a measuring cup[23]. Also observed was the fact that almost half of the medications seen during this study had dosing instructions that allowed teaspoons/tablespoons be used to measure doses. The use of household utensils like spoons to measure doses is very common[25], and has since been identified as a leading cause of liquid medication dosing errors in children[26]. Interestingly, findings from several studies[27-28] suggest that indicating dosing directions only in milliliters (mLs), can discourage the use of household spoons to measure doses and eliminate the confusion faced by some parents in distinguishing between teaspoons and tablespoons.

Bottles containing oral suspensions

Table 2: General Information Contained on all of the Medication Packs Encountered

Item	Drug Status	Solutions n (%)	Suspensions n (%)
Indication(s) for use written on pack	POM	7/18 (38.9)	22/75 (29.3)
	OTC	76/101 (75.2)	6/6 (100)
Indication(s) contained at least one medical term		39/83 (47 .0)	22/28 (78.6)
Presence of dosing instructions on pack	POM	5/18 (33.3)	21/75 (28 .0)
	OTC	71/101 (80.2)	5/6 (83.3)
Presence of tablespoonful/teaspoonful in dosing instructions on pack		40/76 (52.5)	5/26 (19.2)
Storage instructions on pack		111/119 (93.3)	77/81 (95 .0)
"*Instruction to see physician if symptoms do not improve (OTC's only) on pack"		34/47 (72.3)	3/6 (50 .0)
Drug status on pack		7/119 (5.9)	6/81 (7.4)

POM- Prescription only medicine, OTC- Over the counter, * This analysis was only carried out for medication requiring this type of information specifically cough and cold preparations and analgesics

Seventy one (87.6%), of the 81 suspensions encountered had instructions to shake the bottle before use. However in most cases, the instruction was written in the same font size and colour as surrounding text. In addition the instructions did not always specify what should be shaken and how often. Almost 80% of the dry powders for suspension had reconstitution instructions on their packaging, however pictograms showing how to reconstitute these powders were not common (Table 3). On the 42 packs that had reconstitution instructions, only 13.2% of packs had directions that were numbered or written using bullet points to make them easily readable. In addition, out of the eight suspensions that had instructions specifying that a defined amount of water be added to reconstitute them, only two provided devices that could easily measure the specified amount of liquid to be added.

Table 3: Information Contained on the Paediatric Suspension Packs Encountered

Item	Yes n (%)	No n (%)
Instructions to "shake before use"	71 (87.6)	10 (12.4)
Font size of text for instruction to "shake" was bigger when compared to surrounding text	21 (29.6)	50 (70.4)
Font colour of text for instruction to "shake" was different when compared to surrounding text	10 (14.1)	61 (85.9)
Instruction specified to 'shake the bottle'	17 (23.9)	54 (76.1)
Instruction specified to 'shake before each use'	15 (21.1)	56 (78.9)
*Reconstitution instructions were written on pack	42 (79.2)	11 (20.8)
*Pictograms on pack showing how to reconstitute suspension were present	2 (3.7)	51 (96.3)
Reconstitution instructions specified to initially shake the bottle to loosen powder	22 (52.4)	20 (47.6)
Reconstitution instructions specified to initially add water to the halfway mark	14 (33.3)	28 (66.6)

*Only 53 of the suspensions were powders for reconstitution

Problems observed with some of the medication encountered

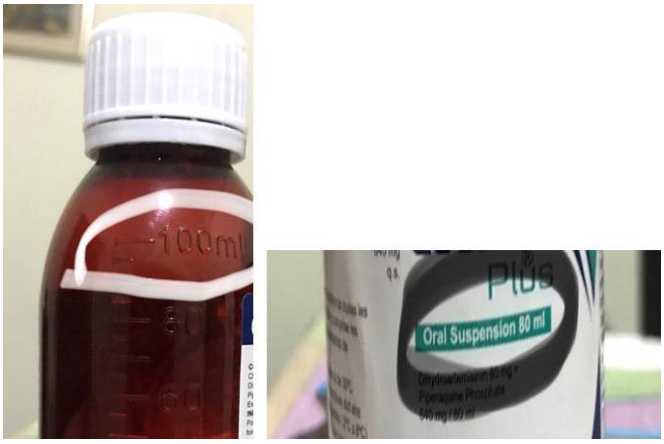


Figure 2: The bottle for this medication was calibrated up to the 100ml mark, but the dry powder for suspension was only supposed to be reconstituted to 80mls. In addition, it contained no reconstitution instructions on its pack or leaflet.

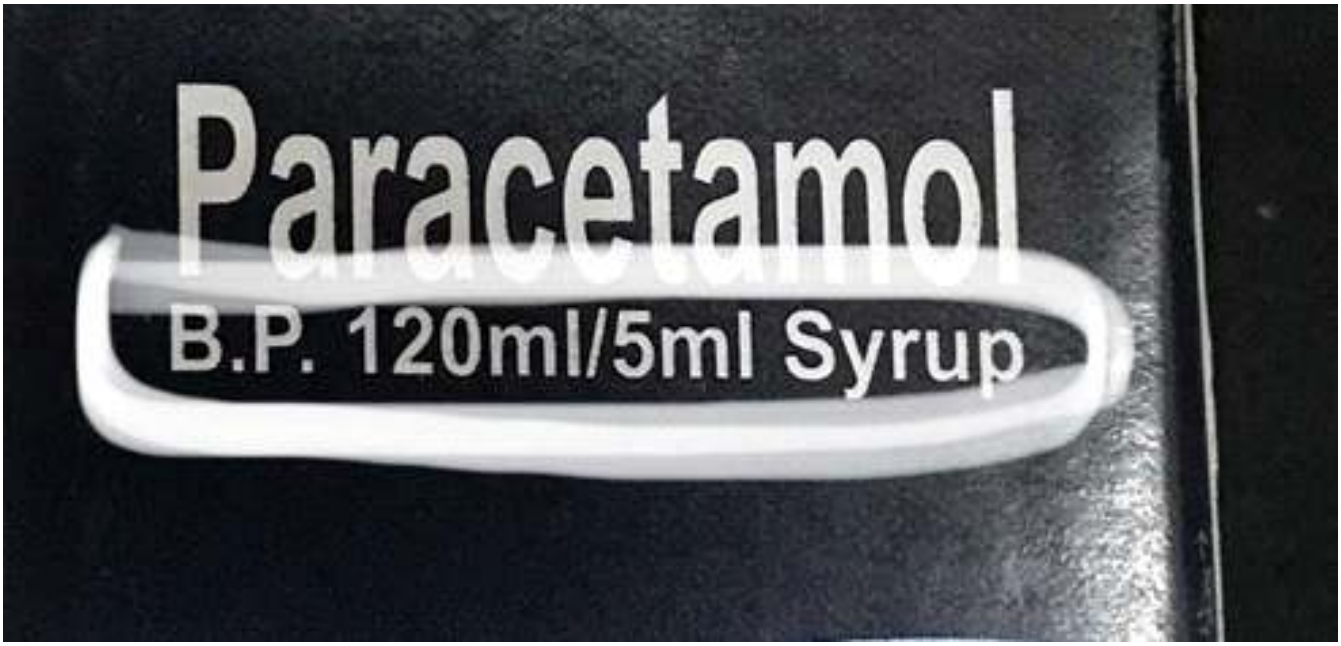
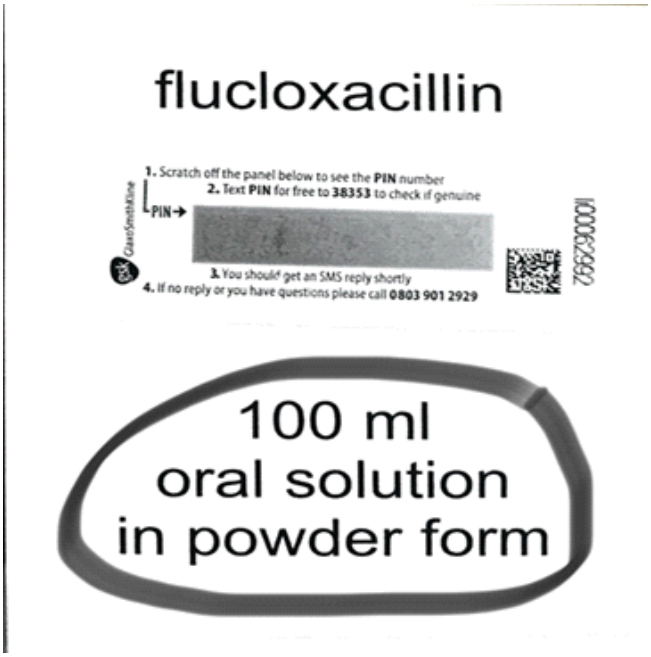


Figure 3: This drug had a volume by volume measurement (ml/ml) instead of weight by volume (mg/ml)



Figures 4 & 5: Medication packs with contradictory information about their formulation type

Figure 6: Dosing instructions for this drug are in dessertspoonful only

Medication Measuring Devices

A total of 164 medications had measuring devices provided in their packs. The most common type of measuring device was the measuring cup (Figure 7). In about a quarter of cases (25.6%), the included device could not measure all of the doses recommended by the manufacturer. The maximum volume (in milliliters) measurable by most devices was 10mls (63.2%).

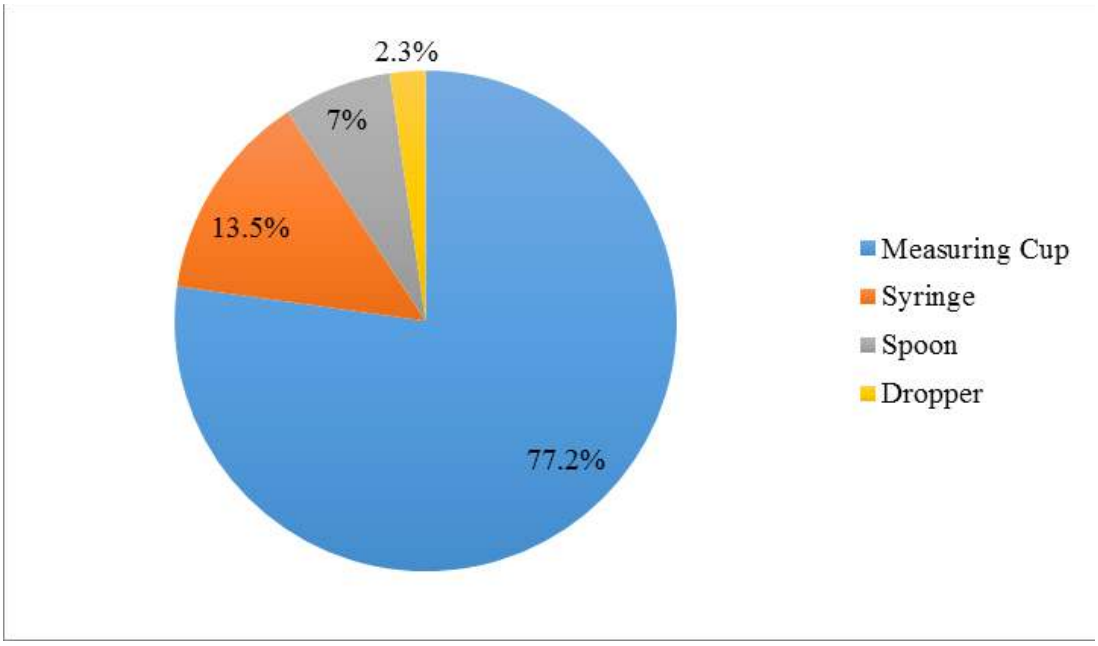


Figure 7: Types of Medication measuring devices available in paediatric liquid dosage forms

need to be shaken to re-disperse drug particles, because of the non-homogenous nature of this type of pharmaceutical formulation. While most of the suspensions seen had some form of instruction to shake before use, in most cases the instruction was not easily identifiable as it was written with font that was the same size or colour as surrounding information. To avoid this, several product labelling guides[7-8] for other countries recommend the judicious use of colour and different font sizes on product packaging to highlight important information. Furthermore, the actual wording of this instruction on many packs was rather vague - either they did not specify that it was the suspension bottle that should be shaken, and/ they did not specify that the bottle needed to be shaken before every use. An example of this can be seen in the instruction "shake before use" provided on many of the packs seen during the study.

Reconstitution of dry powders for suspension can be complicated for untrained individuals[29], yet it is an important step in ensuring that the final product contains the correct dose for the patient. While the packs for most of the dry powders for reconstitution seen during this study had some sort of instructions on how to reconstitute them, wide variations in the content of these instructions were also seen. In many cases, the instructions on the packs were written as sentences in paragraph form. Current best practice is to break complex information into understandable chunks, either by using numbers or bullet points[22]. Similarly, pictograms showing how to reconstitute these powders were very rare. Pictograms are important because pictures closely linked to written text can enhance patient understanding and improve adherence to instructions[30]. With respect to the actual content of the instructions, only about half suggested that the bottle be shaken before water was added, and that water was initially added halfway or less. These are important steps because they ensure that the powder is not caked, and improve the chances of producing a uniformly dispersed suspension.

The major limitation of this study was the sampling method used. Although medicine shops were randomly sampled, there may be factors that were not accounted for that would limit the generalizability of our results to other places.

Conclusion

Findings from this study showed that most of the drugs encountered were registered by NAFDAC and had storage directions and expiry dates. Many of them also had medication measuring devices included in their packs, and the most common type of measuring device seen were measuring cups. Almost half of the OTC medications had dosing instructions allowing teaspoons/tablespoons to be used to measure out doses. In addition, while many suspensions had instructions for shaking before use, the instruction was incorrectly worded and could not be easily identified. The Nigerian drug regulatory body needs to develop detailed, more comprehensive and standardized regulations for paediatric drug packaging, and ensure proper compliance with these guidelines.

References

1. Ivanovska V, Rademaker CM, van Dijk L and Mantel-Teeuwisse AK (2014). Pediatric Drug Formulations: A Review of Challenges and Progress. Pediatrics 134(2); 361-372. doi: 10.1542/peds.2013-3225
2. Van Riet-Nales DA, Schobben AF, Vromans H, Egberts TC and Rademaker CM (2016). Safe and effective pharmacotherapy in infants and preschool children: importance of formulation aspects. Archives of Disease in Childhood 101(7); 662-669. doi: 10.1136/archdischild-2015-308227
3. Maldonado S and Schaufelberger D 2011: Pediatric Formulations (American Pharmaceutical Review) https://www.americanpharmaceuticalreview.com/Featured-Articles/37186-Pediatric-Formulations/ Accessed January 1, 2019
4. Christensen ML, Helms RA and Chesney RW (1999). Is Pediatric Labeling Really Necessary? Pediatrics 104(Suppl 3); 593-597.
5. Wells L and Metherell M (2017). Consumer medicine information. Australian Prescriber 40(2); 44-45. doi: 10.18773/austprescr.2017.015
6. NAFDAC (2018). Drug and Drug Product Labelling Regulations 2018 (pp. 1-16). National Agency for

Food and Drug Administration and Control.
7. FDA 2018: Labeling (U.S. Food and Drug Administration) https://www.fda.gov/drugs/guidancecompliancereguratoryinformation/guidances/ucm065010.htm Accessed January 1, 2019
8. Health Canada 2016: Good Label and Package Practices Guide for Prescription Drugs (Health-Canada) https://www.canada.ca/en/health-canada/services/drugs-health-products/reports-publications/medeffect-canada/good-label-package-practices-guide-prescription-drugs.html#a1.1_Accessed January 1, 2019
9. Johnson A and Meyers R (2016). Evaluation of Measuring Devices Packaged With Prescription Oral Liquid Medications. Journal of Pediatric Pharmacology and Therapeutics 21(1); 75-80. doi: 10.5863/1551-6776-21.1.75
10. Rinke ML, Bundy DG, Velasquez CA, Rao S, Zerhouni Y, Lobner, K. et al. (2014). Interventions to Reduce Pediatric Medication Errors: A Systematic Review. Pediatrics 134(2); 338-360. doi: 10.1542/peds.2013-3531
11. Jeetu G and Girish T (2010). Prescription Drug Labeling Medication Errors: A Big Deal for Pharmacists. Journal of Young Pharmacists 2(1); 107-111. doi: 10.4103/0975-1483.62218
12. TGA (2013). Labelling and packaging practices: A summary of some of the evidence, Version 1.0. Therapeutic Goods Administration, Australia.
13. Wojewoda E and Chou KJ (2017). Factors Associated With Dispensing Dosage Delivery Devices. Journal of Pediatric Pharmacology and Therapeutics 22(4); 251-255. doi: 10.5863/1551-6776-22.4.251
14. Yin HS, Wolf MS, Dreyer BP, Sanders LM and Parker RM (2010). Evaluation of Consistency in Dosing Directions and Measuring Devices for Pediatric Nonprescription Liquid Medications. JAMA 304(23); 2595-2602. doi: 10.1001/jama.2010.1797
15. Abdulrazaq N, Anwer Ali A, Mowloud M, Hamada D and Quraishi U (2014). Evaluation of clarity and consistency in dosing directions and measuring devices for pediatric over the counter liquid medications used in United Arab Emirates. African Journal of Pharmacy and Pharmacology 8(5); 168-174. doi: 10.5897/ajpp2013.3907
16. Ogaji JI, Otutu KO and Iranloye TA (2013). A survey on the provision of package inserts in pediatric oral formulations by pharmaceutical manufacturers in Nigeria. Journal of Basic and Clinical Pharmacy 4(1); 10-13. doi:10.4103/0976-0105.109400
17. NPC (2010). Population Distribution by Sex, State, LGA & Senatorial District (p. 10). Abuja: Nigerian Population Commission
18. KDSG 2018: Demographics (Kaduna State Government). https://kdsg.gov.ng/demographics/ Accessed January 1, 2019
19. PCN (2016). List of Licensed Pharmacists and Licensed Pharmaceutical Premises (pp. 667-670). Abuja: Pharmacists Council of Nigeria.
20. Emdex (2016). Drug Information. Volumes 1&2. Lagos: Emdex limited
21. Kickbusch I, Pelikan JM, Apfel F and Tsouros AD (2013). Health literacy-The Solid Facts (pp. 1-11). Copenhagen, Denmark: World Health Organization;
22. ODPHP (2005). Plain Language: A Promising Strategy for Clearly Communicating Health Information and Improving Health Literacy (pp. 1-11). Rockville, MD: Office of Disease Prevention and Health Promotion, U.S. Department of Health and Human Services.
23. Sobhani P, Christopherson J, Ambrose PJ and Corelli RL (2008). Accuracy of Oral Liquid Measuring Devices: Comparison of Dosing Cup and Oral Dosing Syringe. Annals of Pharmacotherapy 42(1); 46-52. doi:

10.1345/aph.1k420
24. Yin HS, Parker RM, Sanders LM, Dreyer BP, Mendelsohn AL, Bailey S et al. (2016). Liquid Medication Errors and Dosing Tools: A Randomized Controlled Experiment. Pediatrics, 138(4); e20160357. doi: 10.1542/peds.2016-0357
25. Madlon-Kay DJ and Mosch FS (2000). Liquid medication dosing errors. Journal of Family Practice 49(8); 741-744.
26. Yin HS, Dreyer BP, Ugboaja DC, Sanchez DC, Paul IM, Moreira HA et al. (2014). Unit of Measurement Used and Parent Medication Dosing Errors. Pediatrics 134(2); e354-e361. doi: 10.1542/peds.2014-0395
27. Yin HS, Parker RM, Sanders LM, Dreyer BP, Mendelsohn AL, Bailey S. et al. (2016). Effect of Medication Label Units of Measure on Parent Choice of Dosing Tool: A Randomized Experiment. Academic Pediatrics 16(8); 734-741. doi: 10.1016/j.acap.2016.04.012
28. van Ittersum K and Wansink B (2016). Stop spoon dosing: milliliter instructions reduce inclination to spoon dosing. BMC Research Notes 9(1), 33. doi: 10.1186/s13104-015-1809-1
29. Batchelor HK and Marriott JF (2015). Formulations for children: problems and solutions. British Journal of Clinical Pharmacology 79(3); 405-418. doi: 10.1111/bcp.12268
30. Houts PJ, Doak CC, Doak LG and Loscalzo MJ (2006). The role of pictures in improving health communication: A review of research on attention, comprehension, recall, and adherence. Patient Education and Counseling 61(2); 173-190. doi: 10.1016/j.pec.2005.05.004