European Journal of Pharmaceutics and Biopharmaceutics 191 (2023) 247–258

Contents lists available at ScienceDirect

European Journal of Pharmaceutics and Biopharmaceutics

journal homepage: www.elsevier.com/locate/ejpb

Research paper

Stepping into small shoes: Gaining user perspective on appropriate administration devices for paediatric medication in India

Saba Abidi [a], Sushama Talegaonkar [a,c], Soniya Notani [b], Varsha Pradhan [c], Varsha Pokharkar [c,d], Harvinder Popli [a,c], Jennifer Walsh [b,e], Smita Salunke [b,*]

[a] School of Pharmaceutical Sciences, Delhi Pharmaceutical Sciences and Research University (DPSRU), MB Road, New Delhi 110017, India
[b] European Paediatric Formulation Initiative (EuPFI), University College London School of Pharmacy, 29-39 Brunswick Square, London WC1N 1AX, United Kingdom
[c] Society for Paediatric Medicines and Healthcare Initiative (PMHI), Institute of Chemical Technology, Nathalal Parekh Marg, Matunga East, Mumbai 400019, India
[d] Department of Pharmaceutics, Bharati Vidyapeeth Deemed University Poona College of Pharmacy, Pune, India
[e] Jenny Walsh Consulting Ltd., BioCity Nottingham, Pennyfoot Street, Nottingham NG11GF, United Kingdom

ARTICLE INFO

Keywords:
Administration devices
Dosage form
Paediatrics
Dosing
India
User
Medicines

ABSTRACT

A cross sectional pan-India study about use of administration devices for paediatric oral and inhalation medicines was conducted with a diverse pool of participants of various age groups. Via 634 respondents from more than 15 states in India, this study has identified the administration devices commonly used by parents/caregivers for children 0 to 18 years and by children over 10 years. It has provided insights on device ease of use, challenges faced and recommendations to facilitate the correct use of administration devices for paediatric oral and inhalation medicines. Ethics approval (DPSRU-BREC/2020/A/008)) was obtained from the Biomedical Research Ethics Committee of Delhi Pharmaceutical Sciences and Research University.

The survey was completed by parents only (n = 514) and jointly by both parents and children (n = 120). The mean age of the child was 7.2 ± 4.96 years. 72% of the respondents reported that an oral medicine had been taken recently, 6.3% reported that an inhaled medicine had been taken and the remaining 21.9% reported that both an oral and inhaled medicine had been taken. The use of measuring cup was most prevalent followed by household spoons. The mean of the score for ease of use was found to be highest 4.6 ± 0.50 for oral syringe and lowest (3.8 ± 0.76) for measuring cups. The majority of them found the oral device easy to use. Difficulties were reported mostly for measuring cups and household spoons and were related to a lack of user instructions and measuring difficulties. The respondents who found the device easy to use had mostly received clear instructions from healthcare professionals.

Compared to oral devices, there were very limited responses for inhalation devices (n = 175/634). Nebulisers with facemasks were most frequently used followed by manually actuated Metered dose inhalers with and without spacer. The mean of the ease-of-use score for dry powder inhalers was found to be highest (4.2 ± 0.37) followed by mist inhalers (4.0 ± 0) and manually actuated pressurised metered dose inhalers (4.0 ± 0.71). The nebulisers with facemask were reported to be difficult to use by most of the respondents despite receiving clear instructions from healthcare professionals.

The study findings add evidence to the understudied area of user experiences and perspectives on administration devices for oral and inhalation medicines in India. It highlights a need for initiatives to improve the usability, availability, and affordability of administration devices for children in India. Awareness on the importance of proper use of devices needs to be raised and sustained about the existence of affordable administration devices.

1. Introduction

Administering medications to children can be a challenging task, especially when measuring and delivering the correct dosage. The administration of the required dose of oral liquid medications is crucial to achieving therapeutic goals and ensuring the safe and effective

* Corresponding author.
E-mail address: s.salunke@ucl.ac.uk (S. Salunke).

https://doi.org/10.1016/j.ejpb.2023.09.005
Received 5 June 2023; Received in revised form 4 September 2023; Accepted 6 September 2023
Available online 9 September 2023

delivery of medicines. However, concerns have been raised about the safety and accuracy of administration devices, and their ease of use for both parents and children [1–3]. Ensuring that these devices are easy to use is essential for parents to administer medications correctly and safely, as well as for children to be able to participate in their own treatment, which can help improve treatment outcomes and adherence. Parental dosing errors can arise from a multitude of factors: not understanding that paediatric dosing is based on the child's weight, being rushed or hurried, using the incorrect formulation or concentration, using an inaccurate measuring device such as a household spoon or using a measuring device incorrectly (for example, thinking that the entire medicine dosing cup should be full) [4–6]. In this context, it is important to understand the need for appropriate administration devices, the concerns with their use, and the significance of ease of use for parents and children. Moreover, there are concerns about the variability in practices and preferences regarding the use of different types of administration devices. It is noteworthy that the availability of both medicinal products and administration devices may vary across the globe and from one country to another and this may affect the way in which medicines are administered and overall use of administration devices. Cultural and regional differences can influence the acceptability and usability of different types of devices [7–12]. A lack of understanding of these differences can result in inappropriate or ineffective use of administration devices, which can compromise the safety and efficacy of medication delivery. India has one of the largest populations of children in the world, and the administration of medication to this population is a critical public health issue. Despite the widespread use of administration devices, there is a lack of research on their use and the perspectives and practices of caregivers and children in India. The primary objective of this exploratory study, conducted in collaboration with EuPFI (European Paediatric Formulation Initiative), was to gather information from children and their parents or caregivers in India regarding the use and challenges of different administration devices, and to obtain suggestions for future improvements.

2. Methods

2.1. Study design and setting

This descriptive cross-sectional study was conducted in India from November 2020 to May 2021, using an internet-based survey designed using Qualtrics software (Qualtrics, Provo, UT, USA) [13]. The study was aimed at parents or caregivers of children aged less than 18 years, and children over 10 years old in India. Participation in the survey was voluntary.

2.2. Questionnaire

A validated questionnaire created by the EuPFI and was modified for the Indian context in collaboration with Delhi Pharmaceutical Sciences and Research University (DPSRU) and the Society for Paediatric Medicines and Healthcare Initiative (PMHI) [7]. The survey questionnaire was structured into three parts, with the first part containing questions pertaining to demographic information and was presented to all respondents. The second part was directed at parents/caregivers, while the third part was aimed at children aged between 10 and 18 years. Parents of children aged 0 to 9 years only received the first two parts of the questionnaire. The questions and structure of the second (parent/caregiver) and third (child) parts of the survey were similar. Each part consisted of two sections, one focused on oral devices and the other on inhalational devices. Questions included recent medication usage, type of administration device employed, frequency and duration of medication, ease of device use, and suggestions for administration device manufacturers. In terms of type of questions included, closed (single-response, multi-response, ranking, and Likert-scale questions) and open-text questions (extension, expansion, and general open questions) were included. Open-ended questions were used for the section of the questionnaire pertaining to challenges and suggestions for the usage of the device. To ensure independent answers, the child and parent completed the survey independently. Parents were asked to complete the survey first and then were instructed to handover the survey to their child (aged more than 10 years) on their consent. The child was asked to complete the assent forms before completing the survey.

2.3. Pilot study

A pilot test was conducted with a small sample of parents or carers (n = 60) on an online platform for validity of the questionnaire. The pilot test assessed the respondents' understanding of the questions and accuracy in reporting answers. Participants were also asked to provide feedback on the clarity and applicability of each item and the survey as a whole. Following the pilot test, modifications were made to the questionnaire, including shortening the consent and assent forms for simplicity, the rewriting of questions with simpler wording, the addition or removal of certain responses, and modification of the survey's introduction. The EuPFI questionnaire was pretested by the Young Persons Advisory Groups [8]. The group highlighted the necessity of using simple terms for very young people and improving the readability of the survey.

2.4. Study population and recruitment

The study employed purposive sampling, with participants selected based on the inclusion criteria of parents/caregivers aged above 19 years, with at least one child aged between 0 and 18 years, and who agreed to participate in the study. Children between the ages of 10 and 18 years and their accompanying parent or caregiver were included. Subjects were excluded based on the absence of a parent/caregiver, lack of consent from parents to complete the survey or the inability to comprehend/ complete the survey instrument. A multimodal recruitment strategy was used to maximise reach and potential responses, including distribution of an email invitation through professional and representative organisation mailing lists, newsletters, social and collegial networks, study advertisements on organisation websites, social media, and word of mouth. Consent from each respondent was obtained through electronic agreement with a consent statement before proceeding to the survey.

2.5. Sample size

Assuming a confidence level of 95% and a margin of error of 5%, with a population size of 327 million children in India aged 0–18 years, the recommended sample size for this survey was least 384 parents of children aged 0–18 years in India.

2.6. Ethical considerations

The ethics approval was obtained from the Biomedical Research Ethics Committee of Delhi Pharmaceutical Sciences and Research University (DPSRU-BREC/2020/A/008).

2.7. Data analysis

The survey responses were collected using Qualtrics software and compiled in an Excel sheet for further analysis. The data was analyzed using descriptive statistics, and the mean and standard deviation (SD) were calculated. The means were compared using appropriate parametric and non-parametric tests (Chi-square test, Paired T test) to identify any statistically significant differences. The qualitative data were analysed using thematic analysis. Data were inductively coded and initial themes were generated by identifying broader patterns among the codes and data were collated under headings.

3. Results

A total of 974 people accessed the web link that directed them to the survey and 634 (parents of children aged 0 to 18 years and children over 10 years) completed the survey giving a response rate of 65%.

Participant Characteristics:

The characteristics of the respondents are presented in Table 1. Out of 634 responses, 514 responses were received from parents/caregivers only on behalf of children aged 0 to 18 years and 120 responses were received from parent-child pairs (60 from parents and 60 from children) for children aged between 10 and 18 years. Parents constituted the majority of the respondents (78.4%), 8.2% were guardians and 2.1% were grandparents. The respondents who selected "Others" (6.8%) had a different relationship such as relatives or siblings of the child. The majority of respondents were parents/caregivers of children and children aged 10 to 18 years (33.4%) followed parents/caregivers of children aged 2–5 years (26.8%), 6–9 years (25.5%), 12–23 months (9.4%) and less than 12 months (4.9%). In total, 72% of the respondents reported that an oral medicine had been taken recently, 6.3% reported that an inhaled medicine had been taken and the remaining 21.9% % reported that both an oral and inhaled medicine had been taken. The responses were received from 15 states namely, Delhi, Maharashtra, Madhya Pradesh, Uttar Pradesh, Haryana, Telangana, Karnataka, Kerala, Gujarat, Punjab, Rajasthan, Tamil Nadu, Odisha, Uttarakhand and Goa. The majority of respondents were from Maharashtra (n = 288 [50.2%]), Delhi (n = 161 [28.0%]) and Telangana (n = 26 [4.5%]).

3.1. Oral medicine administration

3.1.1. Type of oral medicine recently used

66% of the respondents reported the use of a liquid dosage form and 34% reported the use of a solid dosage form. The liquid dosage forms included syrups (37.9%), suspensions (19.4%) and drops (8.8%). The solid dosage forms included tablets (31.5%), capsules (1%) and granules (1.5%) (Fig. 1).

Parents/caregivers and children used various dosage forms and no trend was observed with respect to age group and dosage form. Parents/caregivers with children aged greater than 2 years mostly used syrups, suspension or drops, for children aged between 2 and 9 years, syrups were mostly used followed by tablets or suspension and for children over 10 years, tablets were mostly used followed by syrups or suspension (Fig. 2). No statistically significant difference (p = 0.9) was observed between the responses by parent–child pair for the selection of dosage form recently taken. The majority (57.1%) of the respondents reported use of oral dosage forms for short periods of time, such as less than a week or for 1 to 2 weeks. The frequency of taking medicines varied from once a day up to twice a day.

Table 1
Participant Characteristics.

Participant Characteristics	n (%)
Parents of children aged less than 10 years	420 (66.2)
Parent for children aged 10 – 18 years	154 (24.2)
Children responses for aged over 10 years	60 (9.5)
Relationship with the child	
Parents	450 (78.4)
Grandparents	12 (2.1)
Guardian	47 (8.2)
Other	39 (6.8)
No response	26 (4.5)
Age of the child	
Less than 12 months	31 (4.9)
12–23 months	59 (9.3)
2–5 years	169 (26.6)
6–9 years	162 (25.5)
10–18 years	213 (33.7)
Mean ± SD	7.70 ± 6.16
Type of medicine used recently	
Oral	453 (71.5)
Inhaled	40 (6.3)
Both	141 (22.2)

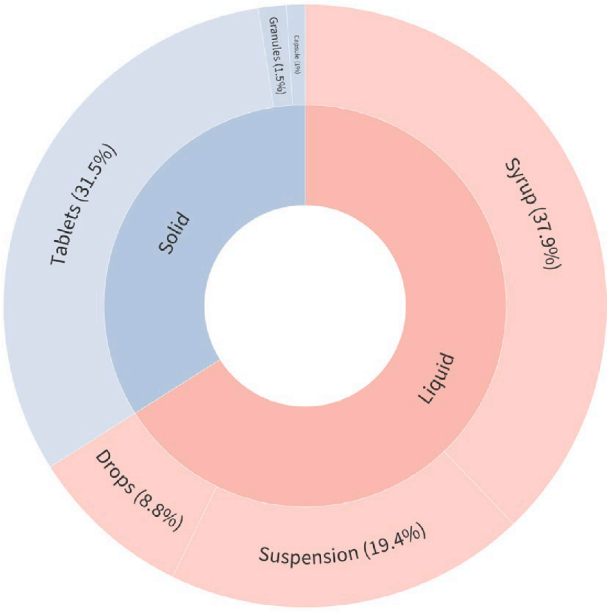

Fig. 1. Type of oral dosage form recently used by the respondents.

3.1.2. Type of device used for oral administration

Out of 593 respondents, 545 (91.9%) reported use of an oral device and 48 (8.1%) did not use any device for the administration of the oral dosage forms. Out of 545 respondents that used devices, a total of 387 (71%) respondents used a device for administration of liquid dosage forms and 158 (29%) used devices for solid dosage forms. 54.9% used measuring cups, 22.4% used household spoons, 13.8% used droppers, 6.4% used measuring spoons and 1.7% used an oral syringe. 0.9% of respondents reported using other types of devices (such as household cup, paladai). No statistically significant difference (P = 2.3) was observed between the responses of parent–child pair for the selection of oral administration device.

Type of oral administration device used according to age is presented in Fig. 3. The parents/caregivers of children aged less than 2 years were reported to be frequently using droppers for administering an oral medicine. Measuring cups were mostly used for children aged 6–9 years followed by 2–5 years and 10–18 years. Household spoons were commonly used for children aged 10–18 years followed by 2–5 years and 6–9 years. Oral syringes were found to be mostly used for children aged less than 5 years. Finally, measuring spoons were mostly used for children aged 2–5 years and 10–18 years followed by 6–9 years.

3.1.3. Ease of use of device

A 5-point Likert scale was used to appraise the ease of use of the oral devices which was coded as "1-very difficult", "2-difficult", "3-Neither easy nor difficult", "4-Easy" and "5-Very Easy". Out of 545, total of 544 parents/caregivers and children responded to the question on ease of use of the device. 55.8% found it easy to use, 20.0% found it very easy to use, 19.4% reported it to be neither easy nor difficult, 0.6% found the device very difficult to use and 4.0% found it difficult to use. The mean and the standard deviation for the ease of use of each device were calculated and evaluated to assess any statistically significant difference between the ease of use of different devices (Fig. 4). The mean (SD) of the ease of use was found to be highest (4.6 ± 0.50) for oral syringe and lowest (3.8 ± 0.76) for measuring cup. The mean of ease-of-use score for household spoon was found to be (4.0 ± 0.84) followed by measuring

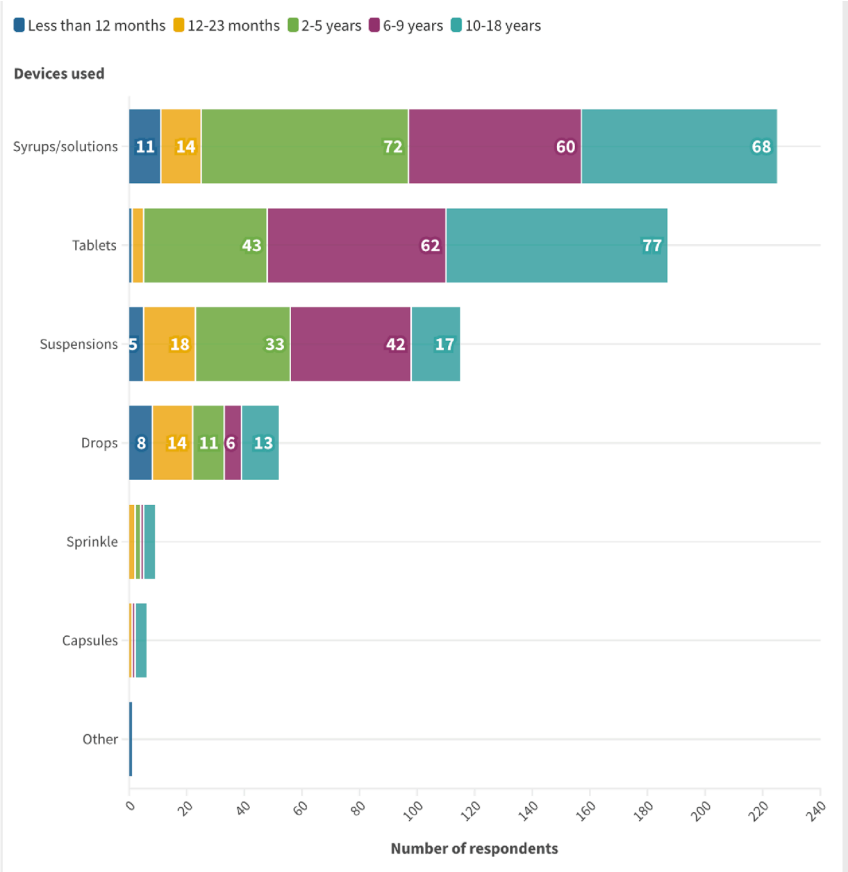

Fig. 2. Type of oral dosage form used according to age groups of the children.

spoons (3.9 ± 0.76) and dropper (3.9 ± 0.67). In addition to these observations, the mean difference in ease of use of oral syringes was found to be statistically significant when compared to measuring spoons (p value = 0.03), measuring cups (p value = 0.005) and droppers (p value = 0.01).

3.1.4. Instructions on use of oral device

The participants were asked if and who had given them the instructions on the proper usage of the device and 544 responded to this question. As presented in Fig. 5, more than half of the respondents (73.7%) reported that they had received instructions on device use, whilst 24.3% respondents reported that they had not received instructions on how to use the device. Amongst the respondents who received instructions, 40.4% received them from their doctor, 20.7% from the patient information leaflet, 14.7% from a pharmacist, 5.5% from a nurse and 5.5% from parents. No statistically significant difference was observed between the responses of parents and children about receiving of the device instructions (p = 0.8).

3.1.5. Clarity of the instructions

Parents/caregivers and children were asked to rate the clarity of the instructions received on a scale of 1–5 where 1 was "very clear" and 5 was "Not clear". A total of 377 parents and children responded on the clarity of the instructions received (Fig. 5). 58.9% respondents reported that the instructions were clear and 17.5% reported the instructions to be very clear. Only 1.9% of the parents responded that the instructions were not clear and 4.5% selected neither clear nor not clear. No statistically significant difference (p = 0.62) was observed between parents and children about the clarity of the instructions.

3.2. Challenges in and suggested improvements for the usability of oral devices

Content analysis of the open-ended questions regarding challenges associated with device use or suggestions for improvement showed consistent underlying three key themes with both parents and children. Challenges associated with the device design were the most common theme followed by user instructions and accessibility. These challenges were prioritized on basis of the frequency of a problem reported by the respondents as presented in Fig. 6. The unique challenges reported for each device is summarised in Table 2.

3.3. Device design

Practical medication problems related to device design included: difficulty in measuring the medicine due to the poor visibility of the graduation on a dosing device (e.g., measuring cup), liquid spillage while pouring the liquid from bottle onto the spoon or while administering the medicine to children with measuring cup or spoon, difficulty with cleaning the device (eg. measuring cup) as the medicine usually adhered to the inside of the cup, difficulty with holding the device (eg. measuring spoon with small handles, measuring cup with no grip) and quality of the plastic or material of construction of the device. One parent reported limited usefulness of droppers because the total liquid capacity of the dropper did not match the prescribed dose and it was difficult to measure viscous liquids with droppers.

3.3.1 User instructions

Respondents expressed concerns regarding a lack of appropriate user instructions since most medicines appeared to be supplied without leaflet and so user instructions were not available. Respondents

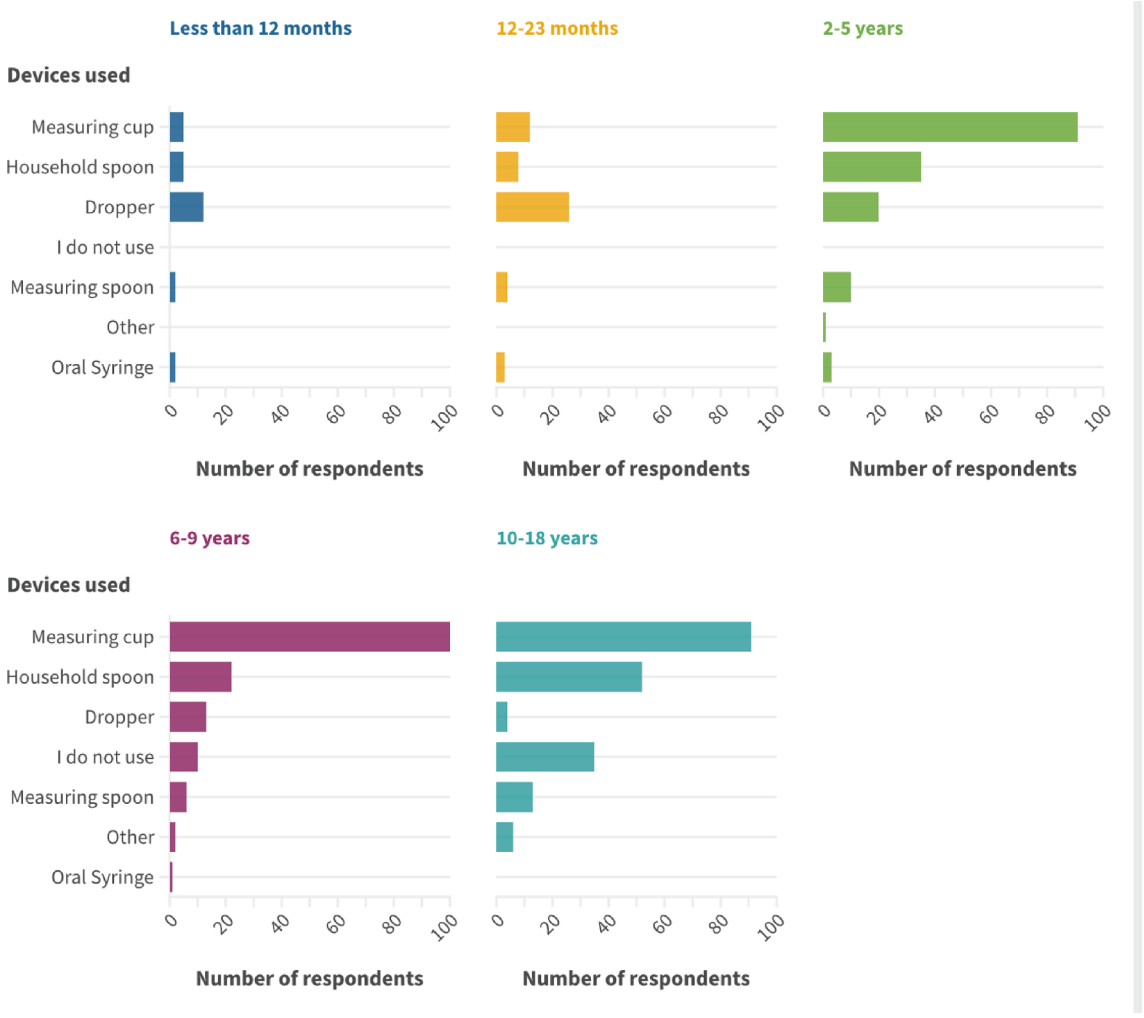

Fig. 3. Type of oral device used according to age groups of the children.

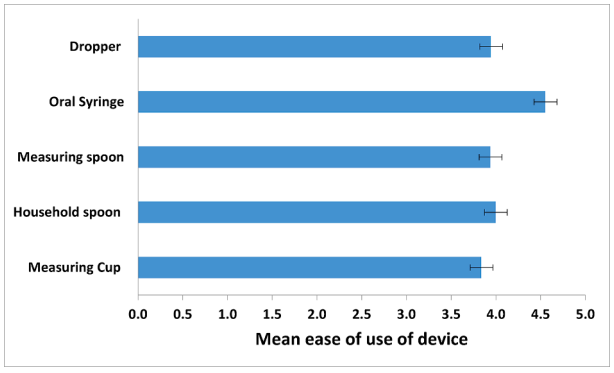

Fig. 4. The mean of the ease of use of each oral device.

recommended that companies create user instructions that are clear, informative, and easy-to-use. Cleaning and maintenance instructions should be provided, especially how to clean and maintain the dosing device, including any recommended cleaning solutions or procedures. The other recommendations include,

- providing clear, step-by-step instructions on how to use the dosing device, including any measurements or markings on the device;
- using visual aids such as diagrams or pictures to help illustrate the instructions and
- provide important safety information, such as how to store the dosing device safely out of reach of children and what to do if the device is damaged or broken;
- provide clear instructions on how to measure the correct dosage of medication using the dosing device.

3.4. *Inhalation devices*

A total of 175 (out of 634) responses from parents/caregivers and children were received for inhalation devices. Out of 175 responses, 12 responses were received from parent-child pairs, whereas 151 responses were received from parents only.

3.5. *Type of inhalation devices used*

A nebulizer with facemask was found to be the most commonly used administration device for respiratory medicines (54.6%), followed by manually actuated pressurized metered-dose inhalers (17.8%). 9.8% respondents reported that breath-actuated inhalers were used and 9.2% reported the use of dry powder inhalers. Mist inhalers and spacers were used by 3.7% and 4.3% respectively. 4.9% selected pressurised metered dose inhalers. In addition to this, 3.1% reported to be using a combination of different devices. No statistically significant difference ($p = 0.9$) was observed between the selection of the inhalation device by parents/caregivers and children.

As presented in Fig. 7, the use of nebulizer with facemask was

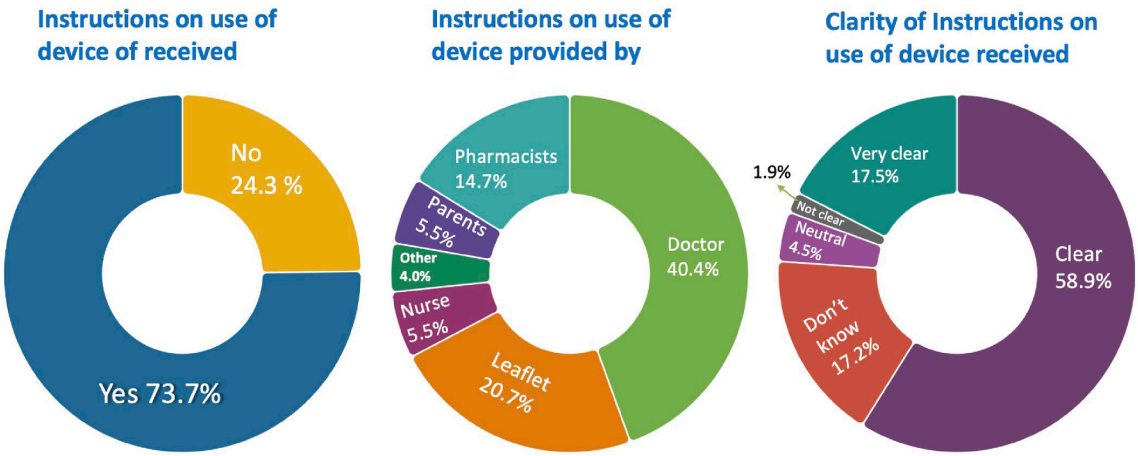

Fig. 5. Responses (%) on instructions received and clarity of instructions for oral devices.

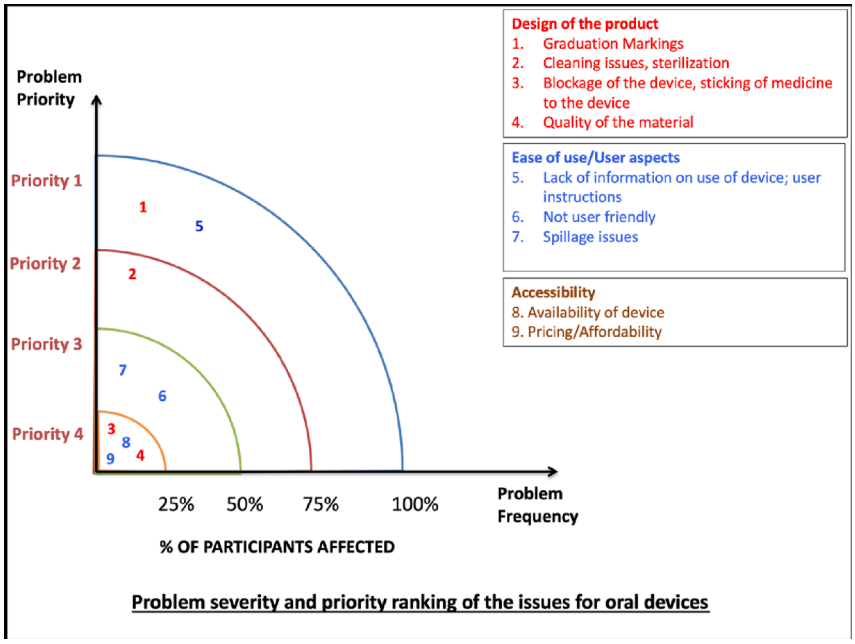

Fig. 6. Problem severity and priority ranking of the issues for oral devices.

observed to be highest in the 2–5 years age group, followed by 6–9 years. Pressurised metered dose inhalers were found to be commonly used by children aged 6–9 years. Dry Powder Inhalers were also found to be commonly used in 6–9-year-olds, whereas mist inhalers were frequently used in 10–18 years age group. Spacers were reported to be mostly used by children of 6–9 years.

The inhalation devices were found to be mostly used for one week or less (41.7%) followed by 1–2 weeks (25.2%), as reported by parents/caregivers and children. The frequency of the device used was majorly twice a day followed by once a day.

3.6. Ease of use

Respondents rated the ease of device use on a Likert scale from 1 (very difficult) to 5 (very easy). A total of 173 participants responded to this question. The responses were mixed; however, most (42.8%) of the respondents found it easy to use. The mean of the ease of use of dry powder inhalers, pressurised metered dose inhalers and mist inhalers was observed to be same (4.0 ± 0.00). The use of nebuliser and facemask was reported to be less easy than others with a mean value of 3.2 ± 0.92. The mean of breath actuated metered dose inhalers was found to be 3.9 ± 0.92 and that of spacers was observed as 3.7 ± 0.45. (Fig. 8) A statistically significant difference in mean ease of use was observed between nebuliser and manually actuated pressurised metered-dose inhalers ($p = 0.00$) and nebuliser and dry powder inhalers ($p = 0.00$).

Instructions received for the usage of the device.

172/175 responded to the questions on device instructions, 7.6% of the respondents did not receive any instructions, whilst 79.7% respondents reported being instructed on the use of the device and 12.8% of the respondents selected 'don't know". When further asked about the source of instructions, 58.1% received them from a doctor, 22.1% selected nurses and 13.2% of respondents were instructed by a pharmacist, 3.7% received them from a patient information leaflet and 2.9% received them from parents. (Fig. 9) No statistically significant difference was observed between the responses by parents and children ($p = 0.4$).

Clarity of the instructions.

A total of 118 responses were obtained for the question on clarity of the instructions, out of which, the majority of the respondents (65.3%) reported that the instructions were clear and 25.4% reported the

Table 2
Device-specific challenges reported by parents and children.

Administration Device	Challenges reported by parents and children
Dropper	Make metered dosing easier for droppers; provide visual illustration; Marking are not clear; Dropper with colored marking will be good; need clear instructions on how to use; need information on type of material used for droppers, need graduation scale on dropper as well; need ml and drops instructions; medicine sticks to dropper tip; Viscous solutions adhere to the walls of the dropper so a residual volume remains in the dropper unable to be expelled; droppers were difficult for measuring viscous liquids; modification needed to avoid leaks during administration with droppers; difficulty in cleaning the device;. design of dropper should be more attractive; inbuilt dropper fixed with bottle could be of more benefit to deliver one time accurate dose;
Household spoon	Correct dose measurement is not possible using household spoon; The size of household spoons may vary so dose measurement is not done properly; spoon is easy to use but the size of spoons should be same because the chances of dose variability is more with them; household spoons are not graduated; dose accuracy is the main problem with household spoons.
Measuring cup	user friendly and fit of purpose, however, should have clear markings and clear instructions e.g. pictures. Also, the material should be environment friendly; measuring cups for oral administration cause loss as it sticks to cup and difficulty to child below 8 years age; need handle or proper grip as it is difficult to hold the device and administer medicine. add more readings to the cup to make it more accurate say intervals 0.5 mL;
Oral syringe	not available in India, purchased from abroad; make it attractive so children are not scared of syringe; the writing should be more permanent. It fades away after few washes, make reusable syringe with easy cleaning / sterilization protocol;
Measuring spoon	It can be a non-spill system and also attract a kid to hold on and have medication by himself or herself because most kids after 7 years do not allow elders to administer medicine to them; there are more chances of drug spillage because of the design of spoon; need clear instructions on measurement and use of device; need environmental friendly material and avoid plastic.

instructions to be very clear. However, 3.4% respondents said that they did not know about the clarity of the instructions. Only 1.7% reported the instructions to be not clear (Fig. 9). Most of the children responded that the instructions were clear. However, 4.2% parents responded they were neither clear nor not clear. A statistically significant difference was observed in the responses to the question related to the clarity of the instructions between parents/caregivers and children ($p = 0.02$).

Challenges in and suggested improvements for the usability of inhalation devices.

The responses to the question regarding ways in which the inhalation device could be improved were as per the oral devices, predominantly around device design and user instructions for nebulizer and facemask.

Device design: Parents suggestions on improvement of device design of nebulizers included modification of the size of the facemask to make it comfortable for children of different age groups, portable so that it is easy to carry, reduction in the noise/sound produced by the nebulizers as it is frightening for children which makes which makes it challenging for parents to use the device effectively. Additionally, identifying ways to reduce the treatment time was noted. Finally, respondents suggested considering a reduction in cost.

User Instructions: The proposition to improve user instructions for nebulizers included the use of clear and simple language and including visual aids such as diagrams or videos to demonstrate how to use a nebulizer effectively. In addition, the provision of hands-on training to ensure that parents and caregivers understand how to use a nebulizer properly was suggested. Other suggestions included to provide instructions in multiple languages to ensure that parents and caregivers who speak different languages are able to use nebulizers effectively and provide follow-up support through phone calls or visits to healthcare professionals, to ensure that nebulizers are used correctly over time or assess the need for further training. The respondents expressed concerns on a lack of detailed of instructions provided on cleaning and maintaining the nebulisers. For pressurised metered dose inhalers, the coordinated effort between the child's inhalation and the activation of the device was reported to be challenging, especially for young children. Parents/caregivers reported difficulties in determining if the child is receiving the full dose of medication or if the device is being used correctly.

4. Discussion

A cross sectional pan-India study about use of administration devices for paediatric oral and inhalation medicines was conducted with a diverse pool of participants of various age groups. Via 634 respondents from more than 15 states in India, this study has identified the administration devices commonly used by parents/caregivers for children 0 to

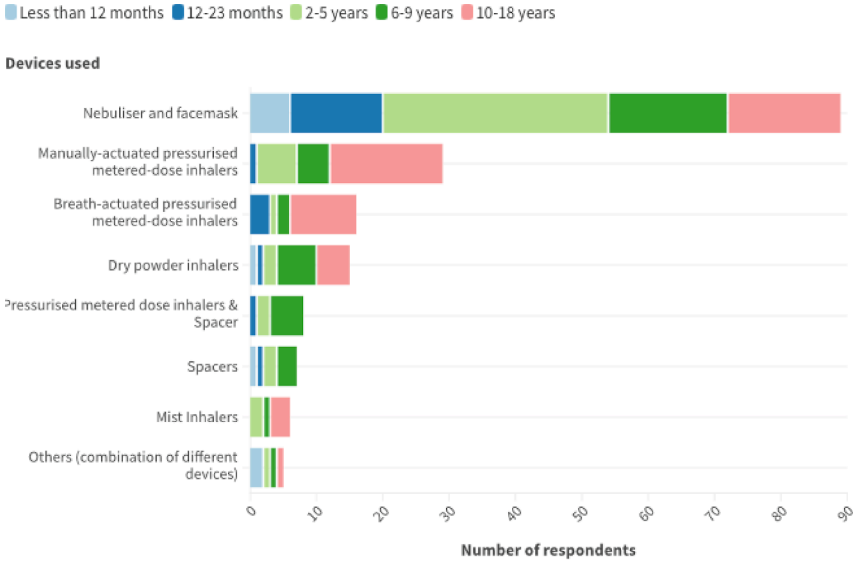

Fig. 7. Type of inhalation device used according to age group.

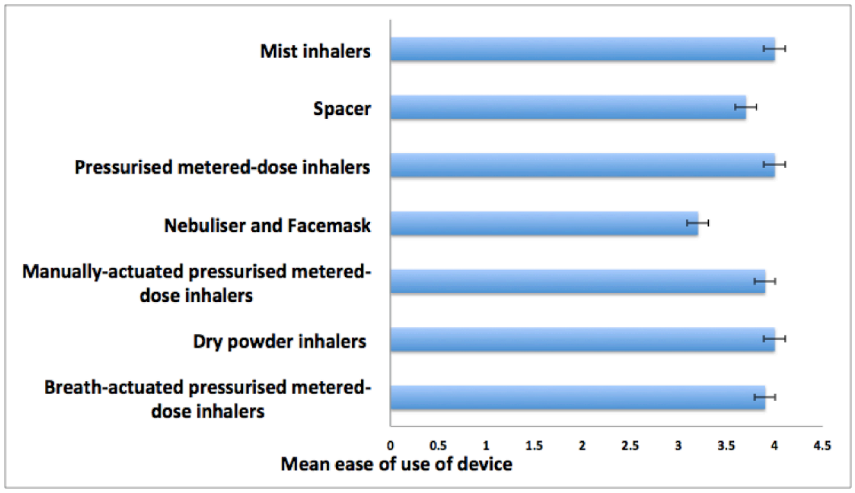

Fig. 8. Mean values of the ease of use of the inhalational devices.

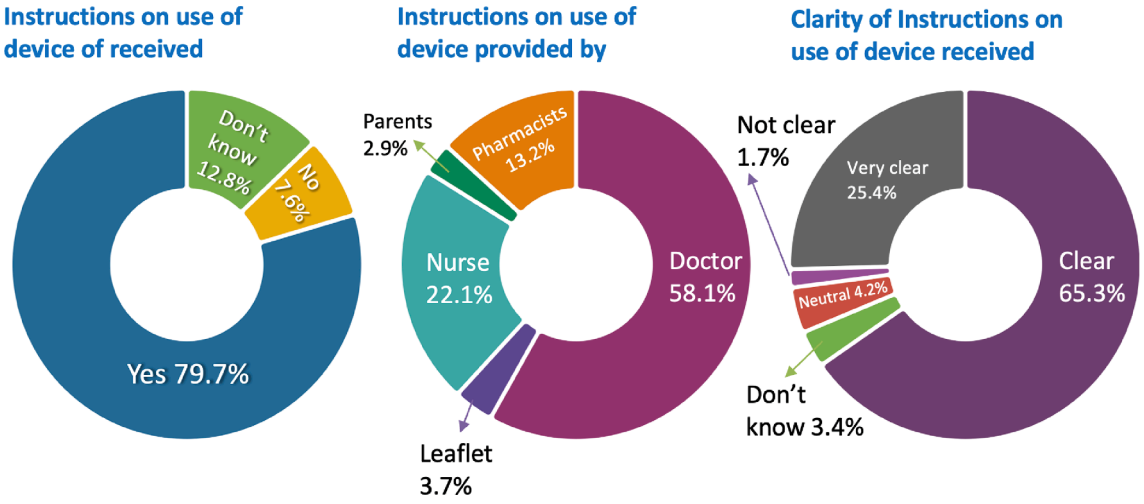

Fig. 9. Responses (%) on instructions received and clarity of instructions for inhalation devices.

18 years and by children over 10 years. It has provided insights on device ease of use, challenges faced and recommendations to facilitate the correct use of administration devices for paediatric oral and inhalation medicines.

4.1. Oral medicine administration

As reported in other studies [14,15], the findings of this survey found that oral liquids were predominantly used by the youngest children (60.3 % age groups 0 to 8 years). Conversely, tablets and capsules were commonly used for the 12 to 18 years age group. The variations in use of different dosage form could be related to age of the child, market availability, prescriptions, and acceptability by children [13].

The findings on the use of oral devices are supported to some extent by previous studies in India and other Low Middle-Income Countries (LMICs) that evaluated the most-preferred drug administration device [12,16–20]. Medicine cups were the most frequently reported measuring device used by participants in these studies [18,21], which is consistent with our findings, especially for 2- to 5-year-olds. In Europe, oral syringes are the most commonly supplied administration device by healthcare professionals to paediatric patients and caregivers for the administration of oral liquids, and the predominant use of oral syringes in the UK and Europe has been previously reported by children and their caregivers [2,7]. In Japan, powders are frequently prescribed to children less than 10 years old and are commonly administered using a dropper in patients less than 12 months old and using a household spoon in those aged 12 months to less than 6 years [10]. Thus, the prevalent use of measuring cups in our study could be influenced by dosage form and the availability of device with the medicine.

The second most often used device to administer liquid medications in this study was a household spoon, probably as it is the most accessible device at home. This indicates a trend toward low awareness of the potential for error when using a household spoon or unfamiliarity with other available devices [20]. Indeed, household spoons have been shown to be inaccurate, and their use as a medicine administration/measuring device has been referred to as obsolete and should no longer be recommended [22]. Unlike other countries, for example the USA, where warnings about the use of household spoons for liquid medicines have been documented [23], no such efforts have been made in India or other LMICs to raise the awareness on the importance of appropriate use of proper administration devices.

Although oral syringes are recommended when oral liquid dosage forms are prescribed, this is not regularly practised in India as seen from this study, compelling parents to use measuring cups or spoons. Previous studies have demonstrated the superior accuracy of syringes compared to cups, and spoons. Hence it can be difficult to measure and dose small volumes correctly with these devices [9,20]. The use of oral syringes may be critical for medications with narrow therapeutic index where

small inaccuracy in doses could lead to toxicity or therapeutic failure of for example antibacterial agents which should be in a consistent steady state concentration at the site of infection [16,24–26]. The US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have provided guidance regarding the supply and appropriateness of measuring devices for oral liquids [27,28]. However, no national guidelines exist on dosing devices in India. Regulatory authorities in India should demand that an appropriate administration device is provided with liquid dosage forms of medicines, according to required dose volumes. Manufacturers should ensure that dosing devices that accompany oral liquid medicines have all the relevant volume markings that correspond to indicated doses on their products, and pharmacies should stock appropriate liquid medication measuring devices to facilitate optimal dosing [29,30]. It is recognised that dosing accuracy is also dependent upon handling and usage of the measuring instrument and not just device type and design. Hence, the provision of appropriate instructions and training on use of devices is equally as important as the availability of appropriate devices with medicines.

The respondents' opinions on ease of use of the devices were broadly similar. The majority of them found the oral device easy to use. Difficulties were reported mostly for measuring cups and household spoons and were related to a lack of user instructions and measuring difficulties; 18 out of 27 respondents that reported difficulty in using the device had not received instructions on using the device. The respondents who found the device easy to use had mostly received clear instructions from healthcare professionals. This further affirms that providing instructions on use of administration devices is essential to ensure appropriate use and mitigate any potential health risks of under or overdosing in children, as shown in previous studies [31,32]. Peacock et al. found that pharmacist's advice about the use of dosing instrument decrease the incidences of dosing error [31]. In addition, it is important that parents understand and use instructions provided with the medication. Specific to paediatric liquid medications, strategies such as using pictogram-based instructions [33–37] and color-coded instructions [38], have been shown to decrease the likelihood of caregiver dosing errors. Studies have shown that the correct use of dosing devices was not linked to age, or ethnicity [32]. Awareness and training sessions are suggested to be essential factors in developing skills required for proper dosing and use of administration devices for children.

4.2. Use of inhalation devices

Compared to oral devices, there were very limited responses for inhalation devices (n = 175/634). Nebulisers with facemasks were most frequently used followed by manually actuated Metered dose inhalers with and without spacer. Studies of prescription patterns in Europe have found large differences among countries in choice of inhalation device. For example, a study published in 2011 concluded that approximately 90% of inhaled corticosteroid devices used in Sweden were Dry powder inhalers, whereas in the UK and Italy, approximately 80% were Metered dose inhalers and liquids for nebulisation, respectively [39]. A European study on the usability of inhaler devices found that manually actuated Metered dose inhalers with and without spacer were the most used, followed by the breath-actuated Metered dose inhalers [7]. The predominant use of Nebulisers with facemask in India may be because inhalers are not commonly prescribed in LMICs due to the absence of medication availability [11]. However, recommending the use of a nebulizer is a difficult proposition for a developing country like India because of economic constraints. Nebulizers are cumbersome, expensive and require a power supply. In a developing country like India, uninterrupted power supply and cost concerns, both reparative and maintenance related, preclude the widespread use of nebulizers. Interestingly, studies in other countries have shown a significant reduction in hospital costs following the substitution of metered dose inhalers with spacer for nebulizer. While inhalers are generally more affordable than nebulisers, the cost of the medicine used in inhalers can be expensive. On the other hand, nebulisers may have a higher upfront cost, but they can use cheaper generic medicines. Additionally, nebulisers can deliver higher doses of medication than inhalers, making them more effective for children with severe respiratory problems. Mist inhalers were least commonly used by the respondents in this study.

The use of different types of inhalation devices according to the different age groups of children was broadly similar with other studies conducted in different part of the world [3,7]. The use of Nebulizer with facemask was observed to be highest in the age group of 2–5 years, followed by 12–23 months. Dry powder inhalers were used in 6–8 year-olds and Metered dose inhalers were often used by older children aged 12–18 years. Age is an important patient factor for selection of inhalation device by doctors, as children aged less than 3 years are generally unable to adopt the required inhalation techniques and are therefore treated with either nebulizers with a facemask or pressured metered dose inhalers with a spacer and a facemask. For children aged 3–6 years, pressurised metered dose inhalers with a spacer and a facemask is the most appropriate device for use. After that age (greater than6 years), children are gradually more capable of effectively using Dry powder inhalers and breath-actuated pressurised metered dose inhalers. All the metered dose inhaler systems require coordination of activation and inhalation and may be difficult to use, particularly for younger children, resulting in incorrect device use. For this reason, it is recommended a pressurised metered dose inhalers should be combined with a spacer device in young children [40,41]. However, our study showed that only one fifth of respondents used spacer with Metered dose inhalers. This could be due to additional cost associated with commercial spacers, which are categorised as add-on devices, extension devices, or holding chambers. Studies estimate that more than half of children who use Metered dose inhalers without devices, such as spacers and valved holding chambers (VHCs) with mouthpieces or masks, gain little to no clinical benefit from their medication because of incorrect inhaler technique [42]. Hence, the long-term cost–benefit of using a metered dose inhaler and spacer should be explained to parents in India. Use of improvised spacer devices (such as toilet paper roll, paper towel roll, rolled paper, plastic bottle spacer, bottle-holding chamber) can alleviate the cost of a spacer device without loss of efficacy of inhaled medicines in children. However, they are only recommended in case of an emergency or the absolute non-availability of a spacer as it has been shown that such improvised devices may affect the therapeutic benefits of the pressurised metered dose inhalers selected. At present there is insufficient evidence regarding the most clinically and cost-effective spacer (e.g., small or large volume), which is reflected in the current lack of standardisation and variations in the usage of these devices.

The mean of the ease-of-use score for dry powder inhalers was found to be highest (4.2 ± 0.37) followed by mist inhalers (4.0 ± 0) and manually actuated pressurised metered dose inhalers (4.0 ± 0.71). The nebulisers with facemask were reported to be difficult to use by most of the respondents despite receiving clear instructions from healthcare professionals. User suggestions for nebulisers and facemask included improving the ease of cleaning and assembly/disassembly, device size, shape and weight, ease of operation and overall desirability. Apart from the user instructions from the manufacturers, it was suggested that educational leaflets and/or a short audio-visual aid, e.g., video, demonstrating the appropriate and effective use of nebulizers, including the setting up and operating, cleaning, and disinfecting, and maintenance would greatly help caregivers. Manually actuated pressurised metered dose inhalers users frequently reported difficulties with coordination of inhaler actuation and inspiration whereas the breath-actuated pressurised metered dose inhalers users found them easy to use and free from coordination problems. Our study is not the first study to highlight the challenges faced by inhalation device users. Ravikiran et al. demonstrated the significance of patient education and face-to-face training in decreasing the percentage of errors on using an inhalation device [17]. Kelling and colleagues reported that physicians were generally unable to use Metered dose inhalers properly despite their

frequent prescription of such devices to patients [43]. A systemic review by Lavorini et al. showed that up to 25% of patients never receive verbal instructions on how to use their devices [39]. Our study confirms and extends these findings, showing that priority must be given to developing easy to use inhalers with structured and detailed inhaler technique training. The appropriate selection and use of the inhaler device appears as important as the choice of treatment.

4.3. Challenges and recommendations on improvement of devices

The common challenges and recommendations reported for all the devices were grouped into three categories (1) device design (2) user aspects (3) accessibility.

Device design: Many of the challenges/recommendations reported for device design were consistent with findings from previous studies including for example, improvements in the markings on the oral device, particularly making them clearer, and adding graduations to be able to measure medicines in 0.5 mL. In addition, respondents reported difficulty in measuring and administering viscous liquids with droppers due to blockage of the tip or leaking, and difficulties in measuring and administering exact doses when using cups due to the medicine sticking to the measuring cup walls. These issues were consistent with those reported by Monk etal in 1997 [44]. In 2023, these issues remain the same for users in India. For inhaler devices, as previously reported by others, problems were noted with assembling nebuliser equipment, duration of nebulisation, noise, weight, and non-portability of equipment. Suggestions for improving the design of oral devices included adding handles to cups for easier administration, longer handles for spoons, and beaks on spoons or cups to avoid spillage. For inhaler devices, respondents suggested modification of the size of the facemask to fit different paediatric age groups. In addition, it was suggested that the design of devices should enable easy cleaning and a dose detector or auto stopper should be added to medicine bottles.

User aspects: The lack of appropriate user instructions and training/education for users were the most commonly reported user related issues with administration devices. Providing instructions in different formats such as pictures, you tube video with QR codes, and clear leaflets were common suggestions for improvement of user instructions. Specific to paediatric liquid medications, strategies such as using pictogram-based instructions [37,38,39,40,41] and color-coded instructions [42] have been shown to decrease the likelihood of caregiver dosing errors [32,44]. However, the level of health literacy among caregivers is a significant factor that impacts the comprehension of medications' instructions [37,45,46]. Pictograms are used to enhance understanding of written instructions [45]. However, scientific evidence remains limited with a lack of research investigating parental comprehension of patient information leaflets and the impact of using pictorial aids at the national and regional levels in India.

Accessibility: The Indian healthcare system continues to be impacted by aspects of availability, affordability, and quality of health services and this was seen for the administration devices as well. The challenges reported by the respondents indicate that the lack of access to administration devices is due to a number of factors including high costs, limited availability, and lack of governance, as well as a widespread lack of awareness. Despite acknowledgement of the importance of administration devices that are affordable and accessible, within the existing literature there appears to be little focus on the ways to improve the accessibility of appropriate administration devices in India. New and innovative administration devices may reach western and high-income countries populations in a matter of months or years; they rarely reach LMICs at the same pace and quality. Most of the respondents suggested providing the devices with the product. Currently most of the products in India come with measuring cups. The market potential is huge for developing and producing the right administration devices at an affordable cost. There are some efforts by the Indian pharmaceutical industry in developing innovative devices that can be provided with the medicine. Abbott's Innovation and Development Center in Mumbai has pioneered LiDoCon, (Liquid Dosing Concept), a first of its kind device for liquid medicines that provides accurate, hygienic, and convenient dosing. LiDoCon was born of a practical need felt by a parent so that monitoring of dosage and hygiene could be made easy [47]. This novel technology is currently being used for a cough syrup and will be extended to different types of liquid formulations in the near future. In the meantime, parallel efforts are needed to include oral dosing syringes with products. All major multinational administration devices manufacturers are based in developed countries, although much of their manufacturing is done in the developing world, in countries such as China and India. They are primarily focused on devices that can be marketed in high-income countries at a premium price. Lack of governance including legislation, policies and national programmes is a key barrier to the availability of administration devices. Many Indian states have not put in place the relevant legislation or policies relating to the provision of administration devices. This creates a bottleneck in the availability of devices. In addition, there is a lack of adequate regulation on proper dosing and use of appropriate devices, as well as a need for India to adopt regulatory mechanisms to ensure that administration devices on the market meet the relevant standards and are safe, effective, and appropriate. Poor quality devices can lead to secondary health complications and abandonment of the device. For instance, the parents reported that the droppers either did not function properly or leaked badly and could not be used, indicating the need to ensure appropriate quality. The respondents expressed a concern with plastic used for spoons and suggested using environment friendly material for devices. The cost of the administration devices was another challenge reported by parents. Cost analysis is an important factor when it comes to choosing between inhalers and nebulisers for children in India. The cost can be prohibitive in low-income contexts and lack of economic means could be identified as a primary barrier to access devices. Most of the respondents were not aware of the range of available administration devices and their benefits. Limited awareness or purchasing capacity leads to a limited demand, which results in few incentives to engage in production. Hence, awareness needs to be raised and sustained about the existence of affordable administration devices. Public health policy makers should implement educational programs from district to national level in India for health professionals and patients.

4.4. Limitations and future areas of research

A small number of children and parents participated in the study as compared to the population of India, due to the high attrition rate from eligible participants. This high attrition rate may have been due to the requirement for parents to handover the survey to children for completion once they had completed the survey, and children preferring to complete the survey in their own time. Therefore, the results of the present study are not representative of the general population, and these demographic trends may have affected our data. Although the majority of children and parents may share similar opinions on use of administration devices, a moderate proportion viewed ease of use differently. This finding confirms that it may be beneficial to obtain both parent and child perspectives on use of administration devices. The open comments on some occasions were difficult to interpret and had limitations. The study highlighted the need of further research on a larger scale with more diverse participants from different LMICs with different socioeconomic status to examine the perceptions of children and their parents of usability of administration devices. Hence, a pan India study was conducted through workshops to engage a broader cross-section of society and assess the need for innovative administration devices for liquid orals in India and understand factors (e.g., socioeconomic, environmental, design, and technical) [12]. Additionally future studies are needed to identify user instructions strategies (e.g., pictograms, videos, training) and to test these strategies in real-world settings. The PMHI (non-profit orginisation) in Mumbai, India has now adopted this as an

area of work they will take forward. They are developing a roadmap to help raise awareness of the issues among healthcare professionals and parents, and they are developing a series of leaflets and activities to support this.

5. Conclusion

The study findings add evidence to the understudied area of user experiences and perspectives on administration devices for oral and inhalation medicines in India. Key considerations for device selection and use include healthcare professional knowledge of all the devices; patient's knowledge and ability to use their device correctly (factors such as age, availability, affordability, awareness or training play an important role) and their personal preferences. There is clearly a need for initiatives to improve the usability, availability, and affordability of administration devices for children in India. Local pharmaceutical companies in developing countries should be encouraged to develop administration devices. Public health policy makers should implement educational programs for health professionals and patients for raising awareness and training sessions for improving skills required for proper dosing and use of administration devices for children in India.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The data that has been used is confidential.

References

[1] J. Walsh, D. Bickmann, J. Breitkreutz, M. Chariot-Goulet, Delivery devices for the administration of paediatric formulations: overview of current practice, challenges and recent developments, Int. J. Pharm. 415 (1–2) (2011) 221–231.

[2] J. Walsh, M.-C. Math, J. Breitkreutz, T. Zerback, H. Wachtel, Devices for oral and respiratory paediatric medicines: What do healthcare professionals think? Int. J. Pharm. 492 (1) (2015) 304–315.

[3] H.S. Yin, B.P. Dreyer, H.A. Moreira, L. van Schaick, L. Rodriguez, S. Boettger, A. L. Mendelsohn, Liquid medication dosing errors in children: role of provider counseling strategies, Acad. Pediatr. 14 (3) (2014) 262–270.

[4] T. Litovitz, Implication of dispensing cups in dosing errors and pediatric poisonings: A report from the American Association of Poison Control Centers, Ann. Pharmacother. 26 (7–8) (1992) 917–918.

[5] A. Lopez-Pineda, J. Gonzalez de Dios, M. Guilabert Mora, G. Mira-Perceval Juan, J. J. Mira Solves, A systematic review on pediatric medication errors by parents or caregivers at home, Expert Opin. Drug Saf. 21 (1) (2022) 95–105.

[6] H.S. Yin, A.L. Mendelsohn, M.S. Wolf, R.M. Parker, A. Fierman, L. van Schaick, I. S. Bazan, M.D. Kline, B.P. Dreyer, Parents' medication administration errors: Role of dosing instruments and health literacy, Arch. Pediatr. Adolesc. Med. 164 (2) (2010).

[7] Alessandrini E, Walsh J, Herman E, Salunke S. Usability of administration devices for oral and respiratory paediatric medicines: opinions of caregivers and children. . European Paediatric Formulation Conference 2021 proceedings Available at: http://wwweupfiorg/past-conferences/13th-eupfi-conference-virtual-2/. 2021.

[8] E. Alessandrini, J. Walsh, S. Salunke, Usability of administration devices for oral and respiratory medicines: Views from a UK primary school, Eur. J. Pharm. Biopharm. 178 (2022) 150–158.

[9] P. Joshi, S.B. Bavdekar, Liquid Drug Dosage Measurement Errors with Different Dosing Devices, Indian J. Pediatr. 86 (4) (2019) 382–385.

[10] J. Saito, H. Nakamura, J. Walsh, A. Yamatani, S. Salunke, A Survey to Understand Parent/Caregiver and Children's Views on Devices Used for the Administration of Oral Pediatric Medicines in Japan, Children (Basel) 9 (2) (2022) 196.

[11] M. Stolbrink, H. Thomson, R.M. Hadfield, O.B. Ozoh, R. Nantanda, S. Jayasooriya, B. Allwood, D.M.G. Halpin, S. Salvi, M.M. de Oca, K. Mortimer, S. Rylance, The availability, cost, and affordability of essential medicines for asthma and COPD in low-income and middle-income countries: a systematic review, Lancet Glob. Health 10 (10) (2022) e1423–e1442.

[12] S. Talegaonkar, A. Chitlangia, V. Pradhan, S. More, S. Salunke, Uncovering Caregiver Concerns: 5 key issues that still remain unresolved in administration of oral medicines for children in India, Eur. J. Pharm. Biopharm. 187 (2023) 166–174.

[13] Qualtrics software, Version XM of Qualtrics. Copyright © 2023.

[14] E. Alessandrini, F. Brako, M. Scarpa, M. Lupo, D. Bonifazi, V. Pignataro, M. Cavallo, O. Cullufe, C. Enache, B. Nafria, J. Claverol, L. De Taeye, E. Vermeulen, J. Preston, C. Tuleu, Children's Preferences for Oral Dosage Forms and Their Involvement in Formulation Research via EPTRI (European Paediatric Translational Research Infrastructure), Pharmaceutics. 13 (5) (2021) 730.

[15] L.V. Adams, S.R. Craig, E.J. Mmbaga, H. Naburi, T. Lahey, C.T. Nutt, R. Kisenge, G. J. Noel, S.P. Spielberg, I. Choonara, Children's medicines in Tanzania: a national survey of administration practices and preferences, PLoS One1 8 (3) (2013) e58303.

[16] A. Nadeshkumar, G. Sathiadas, S. Sri Ranganathan, V. Suppiah, Administration of oral dosage forms of medicines to children in a resource limited setting, PLoS One1 17 (12) (2022) e0276379.

[17] S.R.S.Y. Ravikiran, Dosing ability of Indian parents for liquid medication, Indian Pediatr. 48 (2) (2011) 153–154.

[18] Y. Saaka, D.M. Nyamadi, H. Amekyeh, A. Mensah, R. Melchio, Assessment of the Availability and Accuracy of Dosing Devices Packaged with Oral Liquid Medications in the Ho Municipality of Ghana, Scientifica. 2022 (2022) 1–8.

[19] Smit Patel SK, Hemal Magdalia, Sandipkumar Bhatt*, Rohit Patel. Liquid Medication Dosing Error amongst Parents/ Caregivers at Outpatient Clinic. Indian Journal of Pharmacy Practice. 2022;15(3):235-43.

[20] P. Sobhani, J. Christopherson, P.J. Ambrose, R.L. Corelli, Accuracy of oral liquid measuring devices: comparison of dosing cup and oral dosing syringe, Ann. Pharmacother. 42 (1) (2008) 46–52.

[21] A. Sil, C. Sengupta, A.K. Das, P.D. Sil, S. Datta, A. Hazra, A study of knowledge, attitude and practice regarding administration of pediatric dosage forms and allied health literacy of caregivers for children, J Family Med Prim Care. 6 (3) (2017) 636–642.

[22] E. Younas, M. Fatima, A. Alvina, H.A. Nawaz, S.M. Anjum, M. Usman, M. Pervaiz, A. Shabbir, H. Rasheed, Correct administration aid for oral liquid medicines: Is a household spoon the right choice? Frontiers, Public Health 11 (2023).

[23] NCPDP recommendations for standardizing dosing in metric units (mL) on prescription container labels of oral liquid medications, version 2.0. Am J Health Syst Pharm. 2021;78(7):578-605.

[24] S. Arenas-López, K. Gurung, S.M. Tibby, M. Calleja Hernández, C. Tuleu, Accuracy of enteral syringes with commonly prescribed paediatric liquid medicines, Arch. Dis. Child. 102 (7) (2017) 655–659.

[25] H.S. Blix, K.K. Viktil, T.A. Moger, A. Reikvam, Drugs with narrow therapeutic index as indicators in the risk management of hospitalised patients, Pharm Pract (Granada). 8 (1) (2010) 50–55.

[26] J.E. Juárez-Hernández, B.C. Carleton, Paediatric oral formulations: Why don't our kids have the medicines they need? Br. J. Clin. Pharmacol. 88 (10) (2022) 4337–4348.

[27] EMA. European Medicines Agency Committee for Medicinal Products for Human Use. Guideline on pharmaceutical development of medicines for paediatric use. . Availablle at: https://wwwemaeuropaeu/en/documents/scientific-guideline/guideline-pharmaceutical- development-medicines-paediatric-use_enpdf. 2013.

[28] FDA. Guidance document - Dosage Delivery Devices for Orally Ingested OTC Liquid Drug Products. Available at : https://wwwfdagov/regulatory-information/search-fda-guidance-documents/dosage-delivery-devices-orally-ingested-otc-liquid-drug-products. 2011.

[29] Gildon BL, Condren M, Phillips C, Votruba A, Swar S. Appropriateness of oral medication delivery devices available in community pharmacies. Journal of the American Pharmacists Association. 2016;56(2):137-40.e1.

[30] S. Mohanasundaram, P. Rutter, A. Fox, K. Wood, M. Roldo, Reduction of oral liquid controlled drugs discrepancy in day-to-day practice, Int. J. Pharm. Pract. 29 (4) (2021) 356–361.

[31] G. Peacock, S. Parnapy, S. Raynor, S. Wetmore, Accuracy and precision of manufacturer-supplied liquid medication administration devices before and after patient education, J. Am. Pharm. Assoc. 50 (1) (2010) 84–86.

[32] G.S. Ryu, Y.J. Lee, Analysis of liquid medication dose errors made by patients and caregivers using alternative measuring devices, J. Manag. Care Pharm. 18 (6) (2012) 439–445.

[33] A.M. Algabbani, K.A. Alzahrani, S.K. Sayed, M. Alrasheed, D. Sorani, O. A. Almohammed, A.S. Alqahtani, The impact of using pictorial aids in caregivers' understanding of patient information leaflets of pediatric pain medications: A quasi-experimental study, Saudi Pharmaceutical Journal. 30 (5) (2022) 544.

[34] H.K. Chan, M.A. Hassali, C.J. Lim, F. Saleem, W.L. Tan, Using pictograms to assist caregivers in liquid medication administration: a systematic review, J. Clin. Pharm. Ther. 40 (3) (2015) 266–272.

[35] P. Patidar, A. Mathur, A. Pathak, Can use of pictograms reduce liquid medication administration errors by mothers? An interventional study, BMC Psychology. 9 (1) (2021) 99.

[36] H.S. Yin, B.P. Dreyer, L. van Schaick, G.L. Foltin, C. Dinglas, A.L. Mendelsohn, Randomized controlled trial of a pictogram-based intervention to reduce liquid medication dosing errors and improve adherence among caregivers of young children, Arch. Pediatr. Adolesc. Med. 162 (9) (2008) 814–822.

[37] H.S. Yin, A.L. Mendelsohn, A. Fierman, L. van Schaick, I.S. Bazan, B.P. Dreyer, Use of a pictographic diagram to decrease parent dosing errors with infant acetaminophen: a health literacy perspective, Acad. Pediatr. 11 (1) (2011) 50–57.

[38] K.S. Frush, X. Luo, P. Hutchinson, J.N. Higgins, Evaluation of a method to reduce over-the-counter medication dosing error, Arch. Pediatr. Adolesc. Med. 158 (7) (2004) 620–624.

[39] F. Lavorini, C.J. Corrigan, P.J. Barnes, P.R.N. Dekhuijzen, M.L. Levy, S. Pedersen, N. Roche, W. Vincken, G.K. Crompton, Retail sales of inhalation devices in European countries: so much for a global policy, Respir. Med. 105 (7) (2011) 1099–1103.

[40] NICE. National Insititute for Health and Care Excellence, Guidance on the use of inhaler systems (devices) in children under the age of 5 years with chronic asthma. Available at https://www.nice.org.uk/guidance/ta10/resources/guidance-on-the-use-of-inhaler-systems-devices-in-children-under-the-age-of-5-years-with-chronic-asthma-pdf-2294389002949 2000.
[41] Wanda Hagmolen of ten Have, N.J. van de Berg, P.J.E. Bindels, W.M.C. van Aalderen, J. van der Palen, Assessment of inhalation technique in children in general practice: increased risk of incorrect performance with new device, J. Asthma 45 (1) (2008) 67–71.
[42] A. Volerman, U. Balachandran, M. Siros, M. Akel, V.G. Press, Mask Use with Spacers/Valved Holding Chambers and Metered Dose Inhalers among Children with Asthma, Ann. Am. Thorac. Soc. 18 (1) (2021) 17–22.
[43] J.S. Kelling, K.P. Strohl, R.L. Smith, M.D. Altose, Physician knowledge in the use of canister nebulizers, Chest 83 (4) (1983) 612–614.
[44] P.M. Monk, P.A. Ball, The Accuracy of a Paediatric Dosing Device, The Australian Journal of Hospital Pharmacy. 27 (4) (1997) 323–324.
[45] M.G. Katz, S. Kripalani, B.D. Weiss, Use of pictorial aids in medication instructions: A review of the literature, Am. J. Health Syst. Pharm. 63 (23) (2006) 2391–2397.
[46] D. Schubbe, P. Scalia, R.W. Yen, C.H. Saunders, S. Cohen, G. Elwyn, M. van den Muijsenbergh, M.-A. Durand, Using pictures to convey health information: A systematic review and meta-analysis of the effects on patient and consumer health behaviors and outcomes, Patient Educ. Couns. 103 (10) (2020) 1935–1960.
[47] Available at https://www.abbott.in/media-center/press-releases/abbott-pioneers-new-liquid-dosing-device-lidocon-in-india.html. 2023.