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Research Article

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Excessive Dilution of Oral Antibiotic Suspensions and Oversized Bottles: An Exploratory Survey Based on Pediatrician's Experiences in Kabul

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Abstract

Medication errors in the reconstitution of oral suspensions, which include excessive dilution, may affect the treatment outcome despite the correct diagnosis and selection of appropriate treatment.

Objective: *To document the practice of parents/caregivers adding more than double the recommended volume of water to oversized bottles of oral Azithromycin or Cefixime suspensions.*

Method: *An exploratory survey was conducted using self-administered anonymous questionnaires. It involved the participation of 32 pediatricians from different pediatrics departments at Maiwand Teaching Hospital, an inner-city hospital in Kabul. The survey aimed to gather pediatricians' experiences with parents/caregivers adding excessive water to Azithromycin or Cefixime oral suspensions to approximately twice the recommended concentration*

Results: *Twenty-five participating pediatricians (78.1%) reported encountering at least one instance where more than double the recommended amount of water was added to Azithromycin or Cefixime suspensions. The majority of these cases (84%) were observed in the outpatient department. Eighteen participants (72%) thought the issue was rare or infrequent, while seven (28%) thought it was frequent.*

Conclusion: *Bottles of oversized oral antibiotic suspensions had been filled up with water to nearly their full volumes, which reduced the concentration of active substances to half or less, and may threaten the treatment outcome. This problem is not confined to any particular country but can arise in any situation where non-healthcare professionals reconstitute pediatric oral suspensions using oversized bottles. Improved reconstitution education, separate diluent bottles for oral suspension, and the establishment of standards and ceilings relative to total dose volume for oral suspension bottles are recommended.*

Keywords: Reconstitution, Oral Suspensions, Pediatrics, Antibiotic Resistance, Medication Error.

1. Introduction

Medication errors by patients may affect the treatment outcome even if a correct diagnosis was made and an appropriate treatment was selected. Drug use in pediatrics needs particular attention, not only from prescribers and dispensers but also from the pharmaceutical industries and parents/caregivers. Children are considerably more vulnerable to medication errors [1]. Many studies about medication errors/irrational drug use have been published, some of them about inappropriate reconstitution of oral suspensions [2-7]. Pediatric dosage forms are characteristically complex due to various factors, including the diverse patient population, challenges with patient compliance, and safety concerns specific to children [8]. These dosage forms must adhere to specific criteria to meet the requirements of both patients and caregivers. It is frequently observed that "appropriate dosage forms of medication are often not available for use in newborns, infants, and young children [9]." Oral suspensions are considered more suitable dosage forms for children. Numerous pediatric medications are available in powder form, which is reconstituted with a specific amount of liquid. Appropriate use of suspensions

involves correct reconstitution, appropriate concentration, accurate dose administration, adherence to the recommended duration of treatment, and proper storage conditions [6]. A study conducted in France revealed a high incidence of errors in reconstituting liquid oral preparations, with approximately half of the caregivers incorrectly reconstituting the medication [7]. Given that the reconstitution of oral suspensions is typically performed by parents or caregivers in Afghanistan, as in many other countries, there is a higher likelihood of inappropriate reconstitution of suspensions occurring [7,10]. The issue becomes particularly concerning when it comes to antibiotics, which are commonly available as powders for reconstitution for oral suspensions [9]. Antibiotics are among the most commonly used drugs in pediatrics [11]. underdosing antibiotics can have severe health implications, not only for the patient but also in terms of promoting antibiotic resistance [12,13]. While the majority of oral antibiotics for pediatric outpatients are in powder form for oral suspensions, there are limited reports about their appropriate use [10]. Several factors, including the volume of the reconstituted liquid, have been identified as potential contributors to reconstitution problems [10]. A prospective observational study reported a caregiver error prevalence of 46% in the reconstitution of amoxicillin suspension [7].

As previously reported, the practice of adding excessive water to oral suspensions results in a reduction in the concentration of active ingredients to some degree. The problem becomes more severe when the concentration is reduced to half or less during reconstitution. This occurs when bottles with empty spaces exceeding the total dose volume are filled with water up to nearly their full volume. Currently, standards or maximum volume for empty space in oral suspension bottles to facilitate shaking could not be identified. Some suspensions have packaging sizes that are disproportionately large, with bottle volumes exceeding twice the total dose volume.

In recent years, concerns have emerged regarding the excessive dilution of some oral antibiotic suspensions due to the oversized bottles. Oversized bottles may contribute to overdilution that can lead to suboptimal dosing, while, potentially compromising patient safety and treatment outcomes. This issue was previously mentioned in an electronic letter, but no published study was found about it [14]. Therefore, to ascertain the presence of this problem and get some preliminary information, an exploratory survey was designed. The importance of this issue extends beyond Afghanistan and applies to any country where the reconstitution of pediatric oral suspensions is not carried out by healthcare professionals, particularly in relation to the availability of oversized bottles for such medications. There are reports indicating that in numerous countries, parents/caregivers are responsible for the reconstitution of pediatric oral suspensions [7,10].

Objective: To document the practice of parents/caregivers adding more than double the recommended volume of water to oversized bottles of oral Azithromycin or Cefixime suspensions.

2. Method

2.1 Study Design

Exploratory survey.

2.2 Study Population and Sampling

A non-probability sampling method was employed to select participants for the study. Pediatricians from Maiwand Teaching Hospital, an inner-city hospital in Kabul, were chosen. This hospital is particularly advantageous for conducting this study due to its central location within the city and its busy pediatric outpatient department. The participants from this hospital are likely to have meaningful insights related to the research topic, given that the hospital had a monthly pediatrics outpatient attendance of approximately 10,000. As the hospital supports such a large number of patients on an outpatient basis, the physicians there would have significant exposure and experience pertaining to the research question.

2.3 Study Tool: The Questionnaires

The focus of the study was to gather information on pediatricians' experiences related to the specific issue of interest. Short anonymous self-administered questionnaires were utilized. These questionnaires were specifically designed for this study and underwent subsequent revisions to enhance their appropriateness and effectiveness. Distribution of the questionnaires took place in person, allowing participants sufficient time to complete them at their convenience. Participants were provided with a clear explanation of the survey's objective. They had the option to return the questionnaire blank if they chose not to participate. The participants were inquired about instances they encountered during their practice where parents/caregivers added more than double the required amount of water to Azithromycin or Cefixime oral suspensions. These two specific antibiotic oral suspensions were chosen because they are packaged in bottles with larger empty spaces compared to the total dose volume. The total dose volumes for Azithromycin and Cefixime are 15 ml and 30 ml, respectively, while the bottles' capacities exceed 30 ml and 60 ml correspondingly. If the participants answered affirmatively to the aforementioned question, they were further prompted to provide details regarding the location of the encounter (outpatient/inpatient department or elsewhere), their course of action in that situation, and their estimation of the frequency of this problem.

3. Analysis

Since the study's objective was to confirm the problem's existence and get preliminary information, descriptive statistics were used.

4. Ethical Issues

Ethical considerations were considered during the study. It was designed as a non-interventional research, and participation by the pediatricians was voluntary. The questionnaires used in the study were both anonymous and concise. The purpose of the study was explained to the participants. It is important to note that all participants were medical doctors. Therefore, the act of filling out and returning the questionnaires was considered as implied consent to participate. Approval from the Research Committee of

Kabul University of Medical Science (Reference: 9-20/9/1401) was obtained.

5. Results

Data from a total of 32 questionnaires were analyzed, resulting in a response rate of 69.56%. The distribution of respondents across departments was as follows: 21 from general pediatrics, 6 from neonatology, and 5 from the pediatric surgery department. Among the 32 pediatricians, 25 (78.1%) reported encountering at least one instance where more than double the recommended amount of water was added to Azithromycin or Cefixime suspensions (Table 1). The majority of these cases (84%) were observed in the outpatient department (Table 2). Regarding their perception of the issue, 18 participants (72%) considered it to be rare or infrequent, while 7 participants (28%) believed it to be a frequent occurrence. When faced with such cases, approximately half of the respondents prescribed the same medication but emphasized the importance of correct reconstitution, while 5 participants (20.8%) opted to change the medication (Table 3).

Department	General pediatrics N=21(%)	Neonatology N=6(%)	Pediatric Surgery N=5(%)	Total N=32(%)
Encountered	16(76.19)	6(100)	3(60)	25(78.12)
Not Encountered	5(23.8)	0(0)	2(40)	7(21.87)

Table1: ***Reported Cases According to Departmentsa***

Place of encounter	N=25(%)
Outpatient department	20(80)
Inpatients department	1(4)
Outpatient and Inpatients department	1 (4)
Elsewhere	3(12)

Table 2: ***Places of Encountered Cases***

Actions taken	N=24 (%)
Prescribed same medication with emphasis on correct reconstitution	12(50)
Changed medication	5(20.8)
Other actions	4(16.6)
Not remembered	3(12.5)

Table 3: Actions taken by Pediatricians While Encountering Cases

6. Discussion

The sample consisted of pediatricians working in a busy pediatric hospital, enhancing the likelihood to offer relevant and valuable information concerning the research question. The response rate of 69.56% achieved in this study falls within an acceptable range [15]. The findings of the study indicate that the addition of more than double the recommended amount of water to oral suspensions of Azithromycin or Cefixime was observed. The majority of participants reported encountering these diluted suspensions in the outpatient department, as patients returning for follow-up visits often bring their current medications with them. It is important to note that this study focused solely on documenting the existence of the problem and did not investigate the prevalence, causes, or consequences of inappropriate reconstitution in detail. Additionally, it should be acknowledged that not all children who were prescribed these antibiotics were able to be monitored, and not all cases of inappropriate reconstitution revisited healthcare facilities. Based on the perceptions of the pediatricians involved in the study, the majority (72%) considered the issue to be rare or infrequent, while 28% believed it to be a frequent occurrence.

This study specifically examines the issue of oral suspension bottles that have a larger empty space than the total dose volume. When these bottles are filled nearly to their maximum capacity with water, it results in a significant decrease in the concentration of the active ingredient, which can have implications for treatment outcomes. In the context of antibiotics, excessive dilution can lead to underdosing, potentially contributing to an increased rate of antibiotic resistance [13,15]. Antibiotic resistance is a global concern that poses a significant threat to public health [16]. Its impact extends beyond individual patients and has negative economic consequences for society as a whole [18]. Previous studies have reported instances of adding extra water to oral suspensions, but the extent revealed by this study surpasses what has been previously documented [1]. The presence of oversized bottles with empty spaces that exceed the total dose volumes, and far exceed what is necessary for proper shaking, could not be justified Apart from other potential factors, the oversized bottles themselves appear to be a significant and distinct contributing factor to the over dilution of oral suspensions The central finding of this study, concerning the overdilution of antibiotic suspensions

due to the use of oversized bottles, extends beyond the context of Afghanistan. Considering that the two antibiotic suspensions investigated in this study are imported from other countries, and that the reconstitution of oral suspensions is performed by parents or caregivers in many countries, the implications of these findings have broader regional and international relevance [7,10].

The study suggests that this issue may have implications for medication safety and effectiveness in various settings, emphasizing the need for awareness and potential interventions at a broader scale. In order to enhance the appropriate reconstitution of oral suspensions, particularly in countries where reconstitution is typically performed by individuals who are not health professionals, it is recommended to implement educational interventions at various levels. Similar recommendations have been made in other studies to address this issue [6,10,17]. Additionally, it is important to establish standards for oversized bottles of oral suspensions to ensure appropriate dosing and minimize the risk of over dilution. Further comprehensive studies are warranted to investigate the causes, prevalence, and consequences of adding extra water to antibiotic suspensions in oversized bottles. These studies are necessary to provide a deeper understanding of the underlying factors contributing to this practice and its potential impact on patient outcomes. By understanding the underlying factors and potential impact, healthcare professionals, policymakers, and educators can implement evidence-based approaches to mitigate the problem and promote appropriate reconstitution practices. Ultimately, these efforts can improve medication safety, enhance treatment outcomes, and contribute to the overall well-being of patients.

7. Conclusion

The practice of adding extra water to oral suspensions was already known, but this study reports: Bottles of oversized oral antibiotic suspensions had been filled up with water to nearly their full volumes, which reduced the concentration of active substances to half or less, and may threaten the treatment outcome. This problem is not confined to any particular country but can arise in any situation where non-healthcare professionals reconstitute pediatric oral suspensions using oversized bottles. Improved reconstitution education, separate diluent bottles for oral suspension, and the establishment of standards and ceilings relative to total dose volume for oral suspension bottles are recommended.

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