



Survey of Availability, Use and Knowledge about Toxicity of Diphenhydramine for Children among Iranian Mothers

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Abstract

Diphenhydramine, as an antihistamine drug is widely used for the treatment of allergies. However, being classified as an over the counter medication and the general belief on the low adverse effect profile of this drug has made it widely accessible to the families. Recent reports of diphenhydramine intoxication and mortality, noticeably in children and infants have raised some serious concerns. In the present study, 241 mothers who referred to four different regional locations of mother and child health care service centers were asked to fill up a questionnaire on diphenhydramine. The results of our study showed that besides the lack of adequate information on the indications and safety of the drug, 97% of the mothers used this medication for different illness conditions of the children, with more than 20% misindications on respiratory infections, fever and pain conditions. More than 40% of mothers did not have specific idea about the age related restrictions of the medication and 81% had no information on the proper dose indication. Furthermore 86% of mothers had no information about its adverse effects and the rest of them knew only about drug induced drowsiness. The results of this study show that diphenhydramine usage should be more closely observed, the pharmacists should make consult families before providing them with diphenhydramine, the pharmaceutical companies should be obliged to provide a drug information sheet in the packaging, and the public media and various health care providers should also feel responsibility to forewarn mothers about the results of self-prescribed medication.

Keywords: Acknowledgments, Diphenhydramine, Infants, Mothers, Toxicity.

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1. Introduction

Diphenhydramine is an ethanolamine derivative antihistamine drug with both anticholinergic and sedative properties. This medicine is available in multiple formulation forms as an over the counter (OTC) antihistamine medication. Because of its

effectiveness and relatively low adverse effect profile, diphenhydramine has been extensively used for the treatment of allergies, respiratory infections and motion sickness, in addition to its use as a sedative or tranquilizer [1].

The FDA approval of diphenhydramine as an OTC drug increased its availability at homes and thus it can be found in most medicine cabinets. This might be a contributing factor to the rise of diphenhydramine poisoning. The American association of poison control centers annual report stated that among 6232 diphenhydramine poisoning in 2012, 3663 were younger than 5-year old children, three of which were ended in death [2].

Following the introduction of diphenhydramine hydrochloride in 1946, there were several case reports of accidental ingestions resulting in the death of children younger than five years old. The estimated dose varied from 100 to 500 mg, and the toxic symptoms were not necessarily dose-related [3-6].

In diphenhydramine overdose and poisoning, therapeutic effects are often exaggerated resulting in serious anticholinergic syndrome to which children are highly susceptible. Clinical presentation of subjects ingesting toxic amounts of diphenhydramine claims age-dependent effects. Depression of central nervous system (CNS) including drowsiness, lethargy, ataxia, and coma are more common in adults but children less than 5 years old are noticeably susceptible to the anticholinergic effects and often are presented with CNS

excitation symptoms including tremor, hyperpyrexia, and tonic-clonic seizures. The major complication in these patients are the development of status epilepticus seizures, which are continued for several hours despite appropriate therapy [7]. Cardiovascular changes, including hypertension, tachycardia, ventricular arrhythmias, and eventual cardiac arrest, have resulted following toxic ingestion of diphenhydramine. Temporary electrocardiogram changes, such as prolonged QT interval, nonspecific ST-T changes, wandering pacemaker, and left bundle branch block, may also be observed [8, 9]. Furthermore, some studies reported the development of hemorrhagic pulmonary edema and fatal respiratory distress syndrome following lethal ingestion of diphenhydramine [4, 10]. Recently, several reports have been presented about fatal diphenhydramine intoxication within therapeutic doses in children, causing paradoxical central nervous system stimulation, with effects ranging from excitation to seizures and death. Some delayed effects such as learning disorders, psychomotor disturbances, and impairment of cognitive and academic function have also been reported. Much concern has been raised about administration of diphenhydramine for young children and infants (especially infants <6 months) and most references recommend that diphenhydramine not be prescribed for these groups of patients [1, 11-14].

In recent years, Iran has been ranked as the first drug user in Asia, with drug consumption

per capita of three times higher than the global standard. On the other hand self-medication in this country is very common and in this regard, Iran has the first rank in Asia [15]. According to these information and some local investigations, several types of drugs, especially OTC drugs, are found in Iranian homes and are administered without enough medical consult. Diphenhydramine is amongst these drugs and is found in many Iranian homes. With regard to the mentioned toxic effects about diphenhydramine, specifically for children, the present study was conducted to investigate the availability of this drug in Iranian homes, its usage for children and the knowledge about its toxicity among Iranian mothers, by designing a suitable questioner, which was completed by mothers.

2. Material and Methods

Based on the required information, a one-page, 14-item questionnaire was designed. This questionnaire included both multiple choice and open ended questions relating to: a) demographic data, b) therapeutic values of diphenhydramine [3] availability at home and usage for children, [4] side effects, [5] potential for harm or lethality in overdose, and [6] quantity of drug to cause harm or death. This questionnaire is translated to English and is presented as the supplementary document.

The questionnaire was distributed among the mothers who referred to the mother and child health care center in different geographical areas (north, west, south, east and center) of Tehran, Iran and completed by them. All subjects

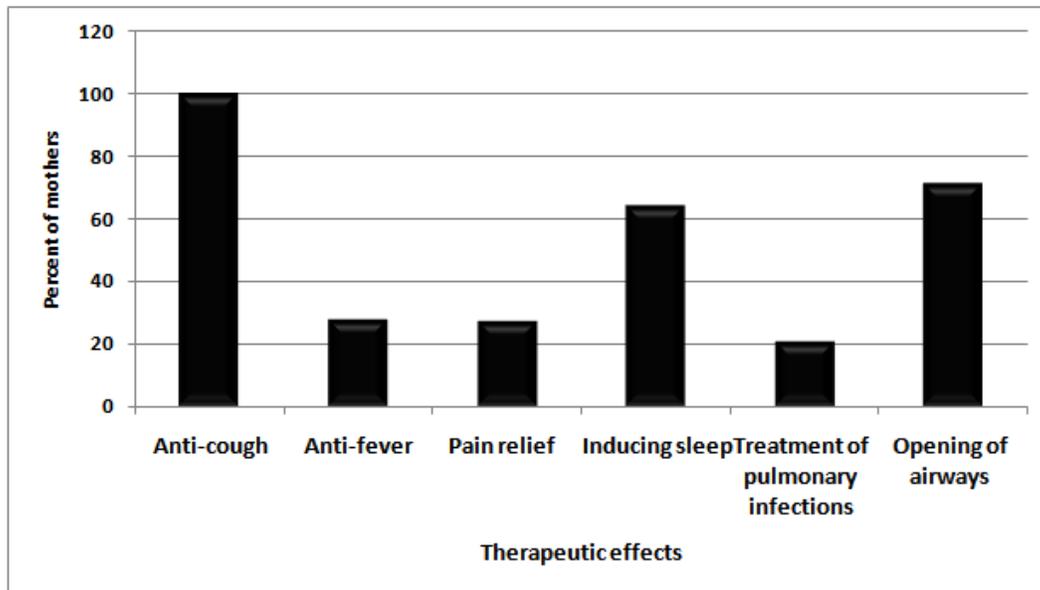


Figure 1. Mothers’ opinion regarding the therapeutic effects of diphenhydramine. The percent of mothers who considered diphenhydramine as either anti-cough agent, anti-fever agent, pain reliever, sleep inducer, airway dilator agent or medication for pulmonary infections is illustrated.

provided written informed consent before participation.

3. Results and Discussion

Four different mother and child health care service centers in four different regional locations (north, south, east and west of Tehran) were visited in random days of the week, and 241 mothers had interest to attend the study and fill the questionnaire. The overall results of this study indicate that out of 241 participants in this study, 234 mothers (97%) were acquaintance with diphenhydramine and had used it in several sickness occasions of their children. Out of these 234 mothers, 162 (68%) were sure to have this medication at home at the time of the study. More importantly are the answers to questions 5 and 6, indicating that almost all of the mothers

were not asked for any prescription by the pharmacist and no one was informed about the drug indication, dosage and adverse effects. Unfortunately, most mothers had insufficient information about the therapeutic effects of diphenhydramine; for example, 21% of the mothers supposed that diphenhydramine is indicated for respiratory infections and 28% strongly believed that this drug has anti-fever and pain relief effects. The detailed responses of mothers to the aforementioned questionnaire are illustrated in figure 1.

The results of this study showed that 38% of the mothers had no specific information about age-related restrictions of this medication, while 31% believed that there are no age restrictions for diphenhydramine (figure. 2). In addition, about 81% of the mothers had no knowledge about the proper dose indication, believing that

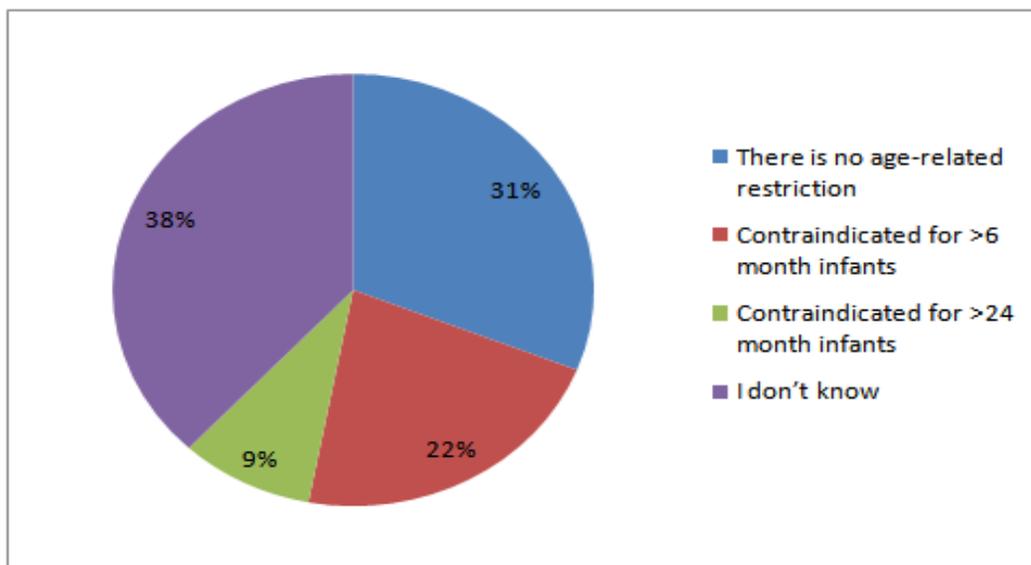


Figure 2. Mothers' opinion regarding the age-related limitations of diphenhydramine indication in children. The percent of mothers who considered diphenhydramine without any age-related restrictions, contraindicated for children younger than 6 months old, contraindicated for children younger than 24 months old, or had no idea on age-related restrictions of this drug is illustrated.

diphenhydramine can be used in children depending on the severity of the disease and worsening of certain symptoms such as coughs and fever. Furthermore, about 86% of the mothers had no information about the adverse effects of the drug and the rest of the mothers only knew about diphenhydramine induced drowsiness. None of the mothers had information about this drug's contraindications and interactions. About 73% of the mothers considered emesis as the solution for diphenhydramine overdose and toxicity. All mothers kept the medication in refrigerator. It is worth mentioning that background factors such as education or the residence location did not lead to any significant changes in any of the replies to the questions.

Diphenhydramine, as an OTC medication, is easily obtained from pharmacies without requiring a physician prescription. In recent years, there have been various reports on adverse effects of diphenhydramine, which seemed hard to neglect especially in infants younger than 6 months old [11-14]. Considering the current extra self-medication prevalent in this country, disastrous complications can be anticipated. The results of the current study shows that, unfortunately, most mothers are able to procure this drug, despite their ignorable knowledge about its therapeutic properties, adverse effects, indications and contraindications, interactions and the proper dose, while this inadequate knowledge cannot be ignored. On the other hand, it seems that

pharmacies also are not obliged to consult the patient on OTC drugs such as diphenhydramine. Other contributing factors are high rate of production and the general belief on the safety of this medication, which results in the lack of any information sheet inside the drug package.

On the other hand, most of the mothers have no adequate information about the therapeutic effects and some use it as a fever and pain reliever, and thus not viewing any expected effect might increase the possibility of using additional doses and enhanced adverse effects and toxicity. The possibility of intoxication is further increased considering the existence of diphenhydramine in 97% of homes with children. This is along with the high possibility of induction of emesis following accidental intoxication, since about 75% of mothers consider emesis as first line solution to the poisoning.

4. Conclusion

The results of this study indicate that diphenhydramine, if still has to be considered as an OTC drug, should be more closely observed regarding its production, prescription and presentation. The pharmaceutical companies should be obliged to provide a drug information sheet in the packaging to inform families about the indication, dosage, adverse effects, cautions and warnings about this drug. It is also suggested that the pharmacists also be more alert and conservative about providing this

medication to mothers and make sure to notify them about the necessary information. In addition, the public media, family physicians and various health care providers should also feel responsibility to forewarn mothers about the results of self-prescribed medication and forbid such irrational drug use.

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