

Present status of drug information regarding breastfeeding women -Evaluation based on expressions for the item "breastfeeding women" of package inserts-

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Some drugs administered to breastfeeding women not only act on the maternal body but are also transferred to infants via breast milk. Therefore, the selection of drugs with a consideration of their influences on infants is important. For the selection of drugs in a clinical setting, drug package inserts are an important source of information. Therefore, to determine whether the item "breastfeeding women" of drug package inserts can be effectively used in clinical practice, we performed an informatics-based study on the package inserts of products for ailments such as colds and coughs that are often used during the breastfeeding period. There were 152 products excluding generic drugs that could be classified according to their effect into antihistamines, antiallergic drugs, antitussives, expectorants, antitussive-expectorants, cold medicines (multipurpose), and antipyretic-analgesics. The percentage of products including a description regarding breastfeeding women markedly varied among these drug efficacy categories. Concerning the description of the item regarding breastfeeding women, expressions indicating that the drug itself should not be administered accounted for 18% of the products, and those indicating the need to restrict breastfeeding assuming drug administration accounted for 50%. In 32%, vague expressions were provided regarding the use of the drug. However, references as a basis for such expressions were included in package inserts in only 13% of the products, revealing the inadequacy of information on the appropriate use of drugs for breastfeeding women. These results highlight the necessity to organize and integrate information on drugs for breastfeeding women and information disclosure such as the description of references as a basis.

Key Words: Breastfeeding Women, Drug Information, Drug Package Inserts, Transfer to Breast Milk

Introduction

Breast milk is an optimal nutritional source for infants. Childcare with breastfeeding provides immunological protection and helps prevent infection, as well as promotes mother-child bonding and the mental health of the child. When drug administration to mothers during childcare with breastfeeding is necessary, the risks and benefits of the drug should be evaluated, and treatment based on evidence-based information is important. However, it is possible that cautions in the item "pregnant/breastfeeding women" of drug package inserts as drug information sources

provide insufficient information.

To clarify the present status of drug information regarding "breastfeeding women", we evaluated drug information in package inserts of drugs for ailments such as colds and coughs that are often used during the breastfeeding period.

Methods

1. Survey of descriptive contents regarding the item "breastfeeding women" of drug package inserts

Of drugs that are commercially available (as of November 2008), those classified into 7 drug effect

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categories commonly used for ailments such as coughs and colds were evaluated. For these products excluding generic drugs, the contents of the description regarding "breastfeeding women" in the "cautions for use" section of drug package inserts were evaluated.

(1) Classification of investigated drugs

- (1) Antihistamines
- (2) Antiallergic drugs
- (3) Antitussives
- (4) Expectorants
- (5) Antitussive-expectorants
- (6) Cold Medicines (multipurpose)
- (7) Antipyretic-analgesics

(2) Classification of descriptive expressions

For products with a description regarding "breastfeeding women", descriptive expressions were classified into the following 9 items including the former 8 items of the criteria on how to describe drugs in package inserts of the Ministry of Health, Labour and Welfare: "Do not administer.", "Administration is not advised.", "Administer only when therapeutic benefits outweigh risks.", "Reduce the dose, or suspend administration.", "Avoid high-dose administration.", "Avoid long-term administration.", "Avoid breastfeeding during administration of this drug.", "Discontinue breastfeeding.", and "Avoidance of breastfeeding is desirable.". "Administer carefully." and "Attention is

necessary." were included in "Administer only when therapeutic benefits outweigh risks." for analysis.

2. Analysis of reasons for description

In products with an item regarding breastfeeding women, the reason for the description was classified into 4: "Cases of transfer to human breast milk", "cases of transfer to breast milk in animal experiments", and "cases using similar drugs." and "others".

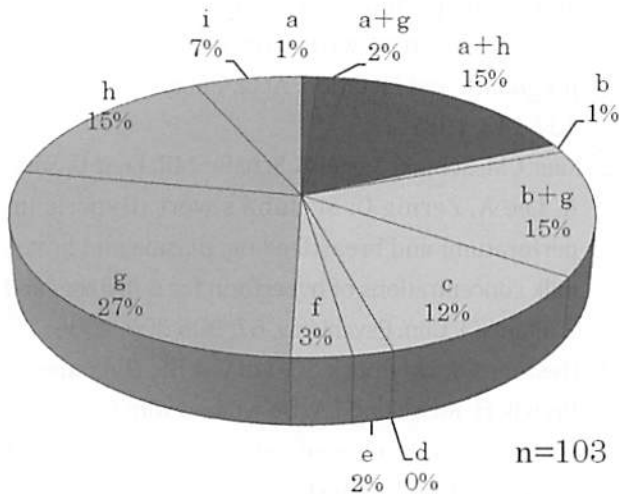
Results

1. Survey of description contents of the item "breastfeeding women" of drug package inserts

There were a total of 1,109 products in this survey, consisting of 100 histamines, 229 antiallergic drugs, 85 antitussives, 169 expectorants, 73 antitussive-expectorants, 18 cold medicines (multipurpose), and 435 antipyretic-analgesics. After excluding generic products, there were 152 products. The 152 products were classified according to the drug efficacy into 7 categories, and the percentage of products with an item regarding "breastfeeding women" and the numbers of products providing a reason for the description and those with references in each category are shown in Table 1. The package inserts included an item regarding "breastfeeding women" in 103 of the 152 products, a reason for the description in 94, but references in only 13 products.

	Number of products	Products with a description	Percentage (%) of products with a description	Number of products given a reason for the description	Number of products with references
Antipyretic-analgesics	55	45	81.8	40	7
Antiallergic drugs	27	25	92.6	25	5
Antitussives	21	13	61.9	11	0
Antihistamines	21	6	28.6	5	0
Antitussive-expectorants	13	8	61.5	7	0
Expectorants	11	4	36.4	4	0
Cold Medicines (multipurpose)	4	2	50.0	2	1
Total	152	103	67.8	94	13

Table 1 Percentage of products with a description regarding "breastfeeding women" in the package inserts according to drug effect categories

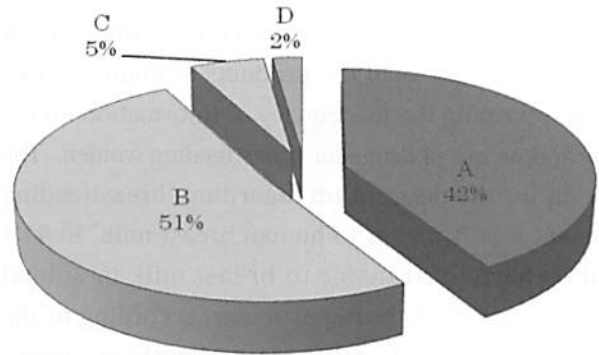


- a. Do not administer, avoid administration to breastfeeding women
- b. Administration is not advised
- c. Administer when therapeutic benefits outweigh risks
- d. Reduce the dose, or suspend administration
- e. Avoid high-dose administration
- f. Avoid long-term administration
- g. Avoid breastfeeding during administration of this drug
- h. Discontinue breastfeeding
- i. Avoidance of breastfeeding is desirable

Fig.1 Classification of descriptive expressions for the item "breastfeeding women"

The expressions of the description in the 103 products with an item regarding "breastfeeding women" are classified in Fig. 1. Products with expressions indicating that the drug itself should not be administered ("Do not administer," alone or in combination with "Discontinue breastfeeding during administration of this drug," or "Avoid breastfeeding during administration of this drug") accounted for 18%.

Products with expressions causing difficulty in determining drug administration ("Administration is not advised," "Administer when therapeutic benefits outweigh risks," "Reduce the dose or suspend administration," "Avoid high-dose administration," "Avoid long-term administration", and the combination of "Administration is not advised," and "Avoid breastfeeding during administration of this drug.") accounted for 32%. In addition, products with expressions advising restriction of breastfeeding assuming drug administration ("Avoid breastfeeding during administration of this drug," "Discontinue breastfeeding," and "Avoidance of breastfeeding is desirable") accounting for 50%.



- A. Transfer to human breast milk
- B. Transfer to breast milk in animals
- C. Cases involving similar drugs
- D. Others

Fig.2 Reason for the description

2. Analysis of reason for the description

The reason for the description was evaluated in 94 products. "Transfer to human breast milk" was observed in 41.5% and "Reports of transfer to breast milk in animal experiments" in 51.1%; Transfer of the product itself to breast milk accounted for 92.6% (Fig. 2).

Discussion

In this study, we evaluated the description of the item "breastfeeding women" of package inserts in 152 products obtained after excluding generic drugs from 1,109 products used for ailments such as colds and coughs. These products were classified according to their effects into 7 categories. Products with a description regarding "breastfeeding women" accounted for 67.8% (mean). The percentage widely varied among the categories, being 92.6% in antiallergic drugs and 28.6% in antihistamines. Products with expressions indicating that the drug itself should not be administered accounted for 18%, and those with expressions advising a restriction of breastfeeding assuming drug administration accounted for 50%. In the other 32% of the products, vague expressions were included regarding the use of the drug, which may delay decisions in the clinical setting. In addition, expressions advising a restriction of breastfeeding may be due to a consideration of the influences on infants, while those indicating that the drug itself should not be administered may be due to a consideration of its influences on both infants and breastfeeding mothers. It is also possible that drugs unfavorably affect the mammary gland and drug

kinetics of breastfeeding women. References as the basis for such decisions were observed in only 13% of the package inserts of the products evaluated in this study, revealing the inadequacy of information on the appropriate use of drugs for breastfeeding women. The reason for the description regarding "breastfeeding women" was "transfer to human breast milk" in 41% and "reports of transfer to breast milk in animal experiments" in 51%. In particular, according to the criteria on how to describe drugs in package inserts, the reason "transfer to human breast milk" should be given "when there are data that the drug is transferred to human breast milk and adversely affects the infant". However, "transfer to human breast milk" was given as a reason for not only "Do not administer.", "Discontinue breastfeeding.", and "Avoid breastfeeding." but also all expression categories including vague expressions. On the other hand, as a reason for expressions indicating that the drug itself should not be administered, "reports of transfer to breast milk in animal experiments" was also included. Thus, in the present criteria on how to describe drugs in package inserts for breastfeeding women, the criteria are unclear regarding expressions indicating that the drug itself should not be administered, or breastfeeding should be restricted. Therefore, standardized information disclosure such as the description of references as a basis and description methods are necessary in order to make an informed decision regarding the use of drugs that have been confirmed to be "transferred to breast milk".

At present, concerning the use of drugs for pregnant women, there are established criteria such as the FDA Pregnancy Category in the U.S., Prescribing Medicines in Pregnancy by the Australian Drug Evaluation Committee, and Swedish Classification System, in which drugs are classified according to the risk level into risk categories. However, for breastfeeding women, the criteria for drug use by the American Academy of Pediatrics (AAP) and some books are used as references, but clear data are insufficient compared with data for pregnant women. In Japan, the use of sulfonamides¹⁾, antidepressants²⁾, and opioids³⁾ is restricted in breastfeeding women. However, some studies have shown their weak influences on infants. Therefore, regarding drug use in breastfeeding women, the available information should be organized and integrated.

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