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Research Article

COMPARATIVE STUDY OF PATIENT PACKAGE INSERT OF MARKETED BRANDS OF ANTIBIOTIC EYE DROPS

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ABSTRACT

Objective: In Indian scenario, there is a huge gap between the patient and health care workers leading to self-medication practices, antibiotic resistance, and adverse drug reactions. These emerging issues aggravate the need of providing a detailed package inserts (PI) in every drug formulations. Hence, this study was conducted with the objective to assess the completeness of a package insert and evaluate the content of information in PI among national and international pharmaceutical brands.

Methods: A prospective, cross-sectional, and observational study was conducted over 50 PI belonging to different class of antibiotic eye drops and same antibiotic from different pharmaceutical companies. Medication belonged to both international and national pharmaceutical companies and they were evaluated according to standards laid down by Drugs and Cosmetic Act (1940) and Rules (1945) covered under the section 6.2 and 6.3.

Results: The content of information was haphazard in both national and international PI but international PI was more valuable. International PI had clear information regarding warning and precautions and adverse effects. List of excipients, shelf life, storage indication, and handling were very well demarcated in both the level of pharmaceuticals.

Conclusions: The study revealed major lacunae in the context of package insert with reference to prevailing guidelines. The most of the brands did not have PI and the quality of information in package insert of international brand was more superior to national brands.

Keywords: Package insert, Drugs and cosmetic act, Antibiotic Eye drop.

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INTRODUCTION

A package inserts (PIs) are a valuable printed written information given to the patients or health care workers for a particular drug or an active pharmaceutical ingredient. These are primary source of information for the drugs which are sold primarily under the cover as OTC drugs [1]. The concept of package insert was initiated by Food and Drug Administration in 1960 for the use of medroxyprogestrone acetate as oral contraception to sensitize the adverse profile of this drug as thrombosis [2]. With increasing awareness to the prescribed medications and lack of communications with health care physicians, the concept of PI was widely accepted by regulatory bodies and, hence, pharmaceutical industries were enforced to provide all the necessary information about the drug.

In India, the concept of package insert is governed under the protocol of Drugs and Cosmetics Act (1940) and Rules (1945). The important details to be covered under a PI are mentioned in Section 6.2 and 6.3 of Schedule D, Drugs and Cosmetics Rules, 1945. Under section 6.2, a package insert should give relevant information about: Therapeutic indications; route of administration; drug interactions; contraindications; special indications in pregnancy and lactation; effects on ability to drive and use machinery; and antidote for overdosing. Under section 6.3, the relevant information includes list of excipients and there adverse effects, shelf life and storage precautions, specification of containers, and instructions for use and handling. All the information in a package insert should be written in English [3].

In the current Indian scenario, there is a huge gap between the patient and health care workers as a result of which several medication errors has come into existence such as self-medication practices, antibiotic resistance, adverse drug reactions, and drug-drug interactions. All these emerging issues aggravate the need of providing a detailed PI in every drug formulations. Several studies have demonstrated that a good PI with accurate reliable and approved information can provide a desirable better health outcome (Khafeel *et al.*) [4].

However, in spite of stringent laws and regulations, there is a gross deficiency of information in PI or if the information is accurate, the legibility of PI is inaccurate or inaccessible. Mahatme *et al.* [5], conducted a study to evaluate the adherence of drug PI to the recommended guidelines and found the information provided in most of PIs was not uniform and could not be accessed easily. They also noted that government supply inserts are of poorer information than that of non-government PI. Shivkar *et al.* [6] noted, after studying 92 inserts, that most PI contained information related to undesirable effects but none of the inserts highlighted the serious adverse events, including ones that could be life-threatening or fatal. Therefore, a regular review of PI is necessary by the regulatory bodies and the local agencies to ensure that the pharmaceutical companies comply with the regulatory guidelines.

Ophthalmic adverse drug reactions are increasing day by day and after careful analysis, it was noted that not much of the research has been conducted on PI of ophthalmic division especially on its antibiotic division. Hence, this study was conducted with the aim to critically assess the patient package insert of marketed brands of antibiotic eye drops sold in India according to the standards laid down by Indian drugs and cosmetics rules, 1945.

METHODS

Study design

It was a prospective, cross-sectional, and observational study conducted by Department of Pharmacology in collaboration with Department of Ophthalmology over a period of 1 month.

Methods

A total of 50 PI belonging to different class of antibiotic eye drops and same antibiotic from different pharmaceutical companies was selected from hospital pharmaceutical store and regional pharmacy shops. The medication chosen belonged to both international and national pharmaceutical companies. The scrutiny of these patient package insert was done according to the standards laid down by Drugs and Cosmetic Act (1940) and Rules (1945) covered under the section 6.2 and 6.3.

Following are the list of parameters included in study to assess the efficiency of patient package insert:

1. Legibility
2. Therapeutic information
3. Route of administration
4. Indication
5. Special warning and precaution
6. Drug-drug interactions
7. Undesirable effects
8. Pregnancy and lactation
9. Effect on ability to drive
10. Antidote for overdosing
11. Pharmaceutical information
12. List of excipients
13. Incompatibilities
14. Shelf life as package for sale
15. Shelf life after dilution
16. Storage specification
17. Handling instructions

Scoring

A scoring system was adopted to calculate the usefulness of the package insert. Each of the parameter mentioned above was taken into consideration and average amount of individual parameters present in national and international package insert was expressed in the form of percentage. Each of the parameter was also assessed for the completeness using simple grading scale very good: 100–96%, good: 91–95%, fair: 75–90%, average: 50–74%, and poor: ≤50% [7]., Both national and international pharmaceutical companies package insert were compared to each other by calculating the number of parameter present in a particular package insert and completeness of each package insert. All the data were recorded and analyzed by preparing a master chart using Microsoft Excel version 2007.

RESULTS

A total of 50 PI of various topical antibiotic eye drops belonging to different class and same antibiotic from different pharmaceutical industries were collected. The comparison was carried out among the national and international pharmaceutical companies. Out of the 50 package insert, 10 were excluded due to fixed dose combinations of antibiotics with steroidal or NSAIDs preparations. Rest of the 40 PI were initially assessed for written English language as per section 6.2 of drugs and cosmetic act. Out of these 20 packages insert belonged to national pharmaceutical companies and rest 20 belonged to international companies.

The percentage of individual parameters present in a national and international pharmaceutical PI can be very well assessed from Table 1. Although the content of information in PI of both national and international companies was a bit haphazard, the extent of organization of information was more valuable in international pharmaceuticals PIs. Due to smaller font size, the legibility in national PI was less than international PI. The accurate therapeutic information was missing in few of the national PI in contrast to international PI. The PI of international brands had very clear cut information regarding special warning and precautions, drug-drug interaction, and undesirable effects. Both the level of pharmaceutical showed very less information regarding the effect of medication on driving and use of machinery. List of excipients, shelf life, storage indication, and handling were very well demarcated in both the level of pharmaceuticals.

The extent of completeness of each parameter was also assessed and is tabulated in Table 2. International PI has most of the information very well covered and complete under individual headings as compared to national PI. Comprehension to the matter in international PI was also more as compared to national PI.

DISCUSSION

With increasing complexity of modern medicine and its efficient use, PIs serve as a valuable source of information to health care workers and patients. Therefore, these PI should be self-explanatory and should continuously undergo revision especially in developing countries like India where self-medication practice is very prevalent. Several studies have been conducted on PI of allopathic medications sold in India and the revealed outcome is always the same with deficiency of information regarding list of excipients, incompatibilities, effect on the ability to drive and overdose information [8-11]. Shivkar and Kalam *et al*. [6,9] in separate studies, reported that most PIs did contain information on therapeutic indications, contraindications, undesirable effects, etc., but there were also important gaps in clinically important information.

In our study, only ophthalmic topical antibiotics were taken into consideration and there was very scarce information regarding its use under therapeutic information, drug-drug interaction, use in

Table 1: Percentage of individual parameters present in PI of national and international pharmaceutical companies

Serial No.	National PI (n=20) (%)	International PI (n=20) (%)
Legibility	94	98
Therapeutic information	93.3	97
Route of administration	98	100
Indication	96	98.9
Special warning and precaution	91	96.8
Drug-drug interactions	85	91
Undesirable effects	88	93.45
Pregnancy and lactation	61.3	88.71
Effect on ability to drive	65.53	78.65
Antidote for overdosing	88.91	94.36
Pharmaceutical information	96	99.8
List of excipients	93.43	96.81
Incompatibilities	78	89.36
Shelf life as package for sale	96	97.84
Shelf life after dilution	98.56	99.4
Storage specification	94.63	97.47
Handling instructions	97.13	98.56

PI: Package inserts

Table 2: Completeness of individual parameters

Serial No.	National PI	International PI
Legibility	Good	Very good
Therapeutic information	Good	Very Good
Route of administration	Very good	Very good
Indication	Very good	Very good
Special warning and precaution	Good	Very good
Drug-drug interactions	Fair	Good
Undesirable effects	Fair	Good
Pregnancy and lactation	Average	Fair
Effect on ability to drive	Average	Fair
Antidote for overdosing	Fair	Good
Pharmaceutical information	Very good	Very good
List of excipients	Good	Very good
Incompatibilities	Fair	Fair
Shelf life as package for sale	Very good	Very good
Shelf life after dilution	Very good	Very good
Storage specification	Good	Very good
Handling instructions	Very good	Very good

special population, etc. The most of the drugs under study did not have package insert at all and, hence, they were discarded from sample size. The legibility was also an issue in some of the brands. The most of the PI did not contain additional information such as mechanism of actions, pharmacokinetics profile, and safety dose range.

From our study and other studies quoted so far, it can be concluded that there is a big lacunae in post-marketing surveillance by regulatory bodies and lack of stringent laws which gives empowerment to pharmaceutical companies to diverge away from the guidelines. Pharmaceutical companies try to smartly hide the valuable information which can seriously affect branding and marketing value such as adverse effects, contraindications or drug interactions, and promote beneficial effects of drug like therapeutic indications. It is very important that PIs must be regular scrutinized by regulatory bodies before marketing approval as well as during defined periodic intervals for better treatment outcome.

Limitations of our study

Our study also had certain limitations. Our study included very limited amount of therapeutic segments. There were several brands of same product and this is a known feature of the Indian pharmaceutical market, and we selected only certain brands. The possibility of biased selection of PIs, therefore, remains.

CONCLUSIONS

Our study revealed major loop hole in the context of package insert with reference to prevalence guidelines. The most of the brands of a particular antibiotic did not have package insert and those who had package insert contained insufficient information. Moreover, the quality of package insert of international brand was more superior to national brands. Hence, reinforcement of guidelines and periodic surveillance is required for better outcomes.

AUTHORS' CONTRIBUTIONS

1. Vaibhav Kumar Gupta: Research investigator, data and statistical analysis, and manuscript preparation
2. Anand Deshpande: Research investigator and Data Collection
3. Kartik Nayak: Research investigator, data and statistical analysis, and manuscript preparation
4. Nitesh Jain: Research investigator and Data Collection.

CONFLICT OF INTEREST

There was no conflict of interest in the study.

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