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RESEARCH ARTICLE

Evaluation of completeness of package inserts in South India

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ABSTRACT

Background: A drug package insert (PI) is a document provided along with the drug. It provides information about the safe and effective use of the drug for the prescribers and also for the general population. The information provided in the PIs is sometimes suboptimal, which may lead to medical errors. Hence, this study was undertaken. **Aims and Objectives:** To study the completeness of PIs of allopathic medicines in South India. **Materials and Methods:** A total of 323 PIs were collected from SVS Hospital Pharmacy and from local pharmacy stores. They were analyzed for the completeness of information in accordance with the Drugs and Cosmetic Act (1940) and Rules (1945), Sections 6.2 and 6.3 of Schedule D (II). If the information was present under the relevant heading, it was scored as one otherwise a score of zero was assigned. A total score for each heading was calculated by adding the score from the individual PIs. The total scores were expressed as absolute numbers and also in percentages. **Results:** Out of 323 PIs, 60 duplicate inserts were excluded and the remaining 263 were used for further analysis. None of the reviewed inserts contained all the sections mentioned in the Drugs and Cosmetic Act (1940) and Rules (1945), Sections 6.2 and 6.3 of Schedule D (II). The indications and generic name were found in all the PIs (100%). The information given in Section 6.2 was present in 75-95% of PIs. Whereas, antidote for overdosing was mentioned in only 39% of PIs. A wide discrepancy of data was noted in Section 6.3 which mandates the pharmaceutical information. Special precautions for the storage were mentioned in 86% and the nature, and the specifications of the container were mentioned in 90% of PIs. **Conclusion:** From the study, it was concluded that none of the PIs were complete as per the Indian regulatory guidelines. Accurate drug product information is important for safe and effective use of medicines. Hence, the regulators should ensure that accurate and up to date product information is provided in PIs.

KEY WORDS: Drugs and Cosmetic Act; Package Inserts; Therapeutic Indications

INTRODUCTION

A drug package insert (PI) is a document which provides information about the safe and effective use of the drug primarily for the prescribers and also for the general population. The PIs are approved by DCGI in accordance with the Drugs and Cosmetic Act (1940) and Rules (1945), Sections 6.2 and 6.3 of Schedule D (II).[1]

Section 6.2 mandates that the PI should be in English and must include the following information, i.e. therapeutic indications, posology and method of administration, contraindications, special warnings and precautions if any, drug interaction, contraindications in pregnancy and lactation, effects on ability to drive and use machines, undesirable/side effects and antidote for overdosing (Table 1).

Section 6.3 mandates the pharmaceutical information which includes list of excipients, incompatibilities, shelf life as

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packaged, shelf life after dilution or reconstitution, shelf life after opening the container, special precaution for storage, nature and specification of the container, and instruction for use/handling (Table 1).

PIs by virtue of being amenable to strict regulations and being readily available with drug products can serve as precise sources of drug information. They serve as reliable and accurate sources of drug information for the health professionals. They can also produce an important impact on patients' compliance and thus on the ultimate effectiveness of drug use.[2]

The product information provided by pharmaceutical companies in India has been determined to be far from adequate and not conforming with the WHO recommendations and the requirements of DCGI.[3] Hence, this study was designed to assess the presentation and completeness of important clinical information in the available PIs in India.

MATERIALS AND METHODS

Collection of PIs

A total of 323 PIs in English were collected from SVS Hospital Pharmacy and from local pharmacy stores of Mahabubnagar.

Inclusion

This study included PIs only from an allopathic system of drugs. The selection included the drugs for different therapeutic indications.

Exclusion

The PIs from other systems of medicine such as Ayurveda, Homeopathy, Siddha, and Unani.

The study was approved by the Institutional Ethics Committee, SVS Medical College, Mahabubnagar (No. SVSMC/IEC/228/2015). The study was conducted over a period from February 2015 to August 2015.

Analysis

The PIs were analyzed according to the information as listed in Schedule D under Sections 6.2 and 6.3 of Drugs and Cosmetic Act (1940) (Table 1).[2] As per Section 6.2, it is mandatory that the PIs should be in English only. The same drug, same formulation, and the same company were identified as duplicate PIs and were excluded from the study. The remaining PIs were analyzed for the presentation of completeness of clinical information as per the Act. Each heading mentioned in Sections 6.2 and 6.3 was checked followed by the scrutiny of the information included under each heading. If the information was present under the relevant heading, it was scored as one otherwise a score of zero was assigned. A total score for each heading was calculated by adding the score from the individual PIs. The total scores were expressed as absolute numbers and also in percentages.

RESULTS

A total of 323 PIs were collected during the study period. Out of these, 60 duplicate inserts were excluded and the remaining 263 were used for further analysis. The PIs were categorized according to the system (Table 2) and route of administration (Table 3). Out of 263 PIs, the majority were from oral formulations followed by parenteral dosage formulation. The data regarding the presence of important information as per the Section 6.2 and of Section 6.3 was presented in Table 4.

The information given in Section 6.2 was nearly mentioned in all the PIs (Table 4). The indications and generic name were found in all the PIs collected for analysis. Posology and method of administration was incomplete in 5% of PIs. Contraindication to the drug use, which forms a very important part for drug prescription, was mentioned in 93% PIs. It was

Table 1: Drugs and Cosmetic Act 1940 and rules 1945, Section 6.2 and 6.3 of Schedule D (II)

Section 6.2	Section 6.3
Indications	List of excipients
Method of administration and posology	Incompatibilities
Contraindications	Shelf life in the medical product as packed for sale
Special precautions/ warnings for use if any	Shelf life after dilution or reconstitution according to direction
Interactions with other drugs and type of indication	Shelf life after first opening of the container
Effects on vulnerable population: pregnancy/ lactation, if CI	Special precaution for storage
Effects on ability to drive and use machines if contraindicated	Nature and specification of the container
Undesirable side effects	Instructions for use/handling
Antidote for overdosing	

Table 2: Classification of drug package inserts according to formulation

Routes	*N* (%)
Oral	137 (52)
Parenteral	61 (23)
Topical	35 (13)
Inhalational	21 (8)
Miscellaneous	09 (4)

found that much stress was given to the interactions with other medicaments. Interactions with other drugs and type of indication were mentioned in 76% of PIs. Effects on pregnancy/lactation were mentioned in 75% of PIs. Effects on ability to drive and work with machines if contraindicated were not mentioned in 81% of PIs. Undesirable side effects were mentioned in 89% and antidote for overdosing was mentioned in only 39% of PIs.

A wide discrepancy of data was noted in Section 6.3 (Table 4). The pharmaceutical information had several deficiencies. The list of excipients was mentioned in only 35% of PIs. The incompatibilities were mentioned in 28% of total collected information leaflets. Shelf life was mentioned in 29% of a total number of PIs analyzed. However, the shelf life after dilution was 13% and shelf life after first opening of the container was 10%. Special precautions for the storage in this study were mentioned as 86%. Nature and the specifications of the container were mentioned in 90% of PIs. Additional information supplied in the PIs is presented in Table 5.

Table 3: Classification of drug package inserts according to system

Class	*N* (%)
Autonomic nervous system	18 (7)
Cardiovascular system	18 (7)
Gastrointestinal system	11 (4)
Autacoids	24 (9)
Endocrines system	38 (15)
Central nervous system	28 (11)
Chemotherapy	72 (27)
Blood	21 (8)
Local anesthetics+skeletal muscle relaxants	3 (1)
Respiratory system	6 (2)
Miscellaneous	13 (5)
Combinations	11 (4)

DISCUSSION

A PI is a document provided along with a prescription medication. They are approved by the administrative licensing authority and serve as reliable and accurate sources of drug information for the prescribers and the patients.

From the study, it was clear that none of the PIs were complete as per regulatory guidelines. It was found that presentation of information was not uniform and it was difficult to locate and retrieve the information easily due to lack of common layout and heading. Moreover, the PIs were of different shapes and sizes with variation in font size, which made it very inconvenient for analyzing. The study was compared with various other studies done in different parts of India (Tables 6 and 7).[4-10]

In our study, under Section 6.2 therapeutic indication was present in all PIs (100%). Similar results were reported by Shivkar,[4] Mahatme et al.,[5] Solanki et al.,[6] and Sowmya et al.[7]

Other headings such as method of administration, contraindication, special precautions/warnings for use if any and undesirable side effects were present in 95%, 93%, 85% and 89% of the PIs, respectively. Other studies also reported similar results between 80% and 100%.[4-11]

Interactions with other drugs and type of indication, effects on vulnerable population: Pregnancy/lactation, if CI were present in only 76% and 75% of PIs. The results were comparable with other studies except the study done by Lal and Sethi[8] who reported only 42%. The information like effects on ability to drive and use machines if contraindicated and antidote for overdosing were present in only 19% and 39% of PIs. Even Lal and Sethi,[8] Shivkar,[4] Mahatme et al.,[5] Solanki et al.,[6] and Sowmya et al.,[7] observed similar poor results under these headings of Section 6.2.[4-7] Other studies from South India by Sudhamadhuri and Vishal[11] and Deepak et al.,[12] reported better outcomes. Most of the headings of Section 6.2 were present (90-100%) in their studies.

Table 4: Results of analysis of drug package inserts (*N*=263)

Section 6.2	*N* (%)	Section 6.3	*N* (%)
Indications	263 (100)	List of excipients	91 (35)
Method of administration and posology	249 (95)	Incompatibilities	73 (28)
Contraindications	245 (93)	Shelf life in the medical product as packed for sale	75 (29)
Special precautions/warnings for use if any	233 (85)	Shelf life after dilution or reconstitution according to direction	33 (13)
Interactions with other drugs and type of indication	201 (76)	Shelf life after first opening of the container	26 (10)
Effects on vulnerable population: pregnancy/lactation, if CI	198 (75)	Special precaution for storage	227 (86)
Effects on ability to drive and use machines if contraindicated	49 (19)	Nature and specification of the container	238 (90)
Undesirable side effects	235 (89)	Instructions for use/handling	76 (29)
Antidote for overdosing	103 (39)		

Whereas the information like effects on ability to drive and use machines if contraindicated was present in only 20% and 37% of PIs. The antidote for overdosing was present in only 20% of PIs.[11,12] The better results in these South Indian studies may be due to their small sample size ($N = 120$ and $N = 70$).[11,12]

In Section 6.3 under the heading pharmaceutical information, many deficiencies were observed. A list of excipients, incompatibilities, shelf life after package for sale, shelf life after dilution and after opening the container and instructions for use were present in only 35%, 28%, 29%, 13%, 10% and 29% of PIs. This is comparable with the other studies done by Mahatme et al.,[5] Solanki et al.,[6] and Sowmya et al.[7] Only the headings like special precautions for storage and nature and specification of the container were present in 86% and 90%, respectively, which is in accordance with the earlier studies.[5-7] Sudhamadhuri and Vishal[11] and Deepak et al.[12] reported similar outcomes on Sudhamadhuri and Vishal[11] and Deepak et al.[12] reported better outcomes.

Table 5: Additional information in package inserts

Contents	*N* (%)
Clinical pharmacology	192 (73)
Pharmacokinetics	180 (68)
Information update date	121 (46)
Pediatric use	165 (63)
Geriatric use	187 (71)
Clinical trail	32 (12)
Mechanism of action	190 (72)
Effects on vulnerable population	215 (82)
Food drug interaction	17 (6)

CONCLUSION

From the study, it was concluded that none of the PIs were complete as per the Indian regulatory guidelines. They provide the information about the safe and effective use of the drug to the prescribers and also for the general population. Accurate drug product information is important for safe and effective use of medicines. Hence, the regulators should ensure that accurate and up to date product information is provided in PIs.

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Table 6: Comparison with other studies (Section 6.2)

Section 6.2	Shivkar[4]	Mahatme et al.[5]	Solanki et al.[6]	Sowmya et al.[7]	Lal A and Sethi[8]	Current study
Indications	80 (100)	205 (100)	70 (100)	188 (100)	311 (98)	263 (100)
Method of administration and posology	80 (100)	199 (97)	58 (83)	179 (95)	316 (100)	249 (95)
Contraindication	79 (99)	190 (93)	56 (80)	172 (91)	285 (90)	245 (93)
Special precautions/warnings for use if any	76 (95)	194 (95)	60 (85)	172 (91)	275 (87)	233 (85)
Interactions with other drugs and type of indication	61 (76)	162 (79)	51 (73)	138 (73)	134 (42)	201 (76)
Effects on vulnerable population: pregnancy/lactation, if CI	69 (86)	182 (81)	56 (80)	138 (73)	NR	198 (75)
Effects on ability to drive and use machines if contraindicated	13 (16)	43 (21)	5 (7)	138 (73)	NR	49 (19)
Undesirable side effects	77 (96)	190 (93)	60 (85)	171 (90)	282 (89)	235 (89)
Antidote for overdosing	55 (69)	9135 (66)	4 (6)	70 (37)	124 (39)	103 (39)

NR: Not reported, All values are in *N* (%)

Table 7: Comparison with other studies (Section 6.3)

Section 6.3	Mahatme et al.[5]	Sowmya et al.[6]	Solanki et al.[7]	Currentstudy
List of excipients	90 (44)	117 (63)	60 (85)	91 (35)
Incompatibilities	77 (38)	43 (23)	23 (33)	73 (28)
Shelf life in the medical product as packed for sale	59 (29)	36 (19)	17 (24)	75 (29)
Shelf life after dilution or reconstitution according to direction	25 (12)	19 (10)	NR	33 (13)
Shelf life after first opening of the container	44 (21)	15 (8)	NR	26 (10)
Special precaution for storage	171 (83)	159 (85)	62 (89)	227 (86)
Nature and specification of the container	181 (88)	17 (9)	56 (80)	238 (90)
Instructions for use	145 (71)	7 (39)	58 (83)	76 (29)

All values are in ***N*** (%), NR: Not reported

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