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Original Research Article

Awareness Regarding the Regulations Governing Fixed Drug Combinations (FDCs) among Clinicians: A Questionnaire-Based Study

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Abstract

Background: FDCs are combination of two or more actives in fixed proportions. They form a vital part in the treatment of certain diseases and offer advantages that single drug entities may not especially drug compliance. However, not all FDCs are rational. In view of curbing the surge of such irrational combinations, there was a ban imposed on 328 FDCs in 2018. This led us to conduct this study to evaluate the knowledge, perception and practice of practitioners regarding FDCs.

Methodology: A validated questionnaire containing 14 items covering the domains of knowledge, practice and perception was sent to clinicians practising across the state of Maharashtra. Responses were recorded and analysed using descriptive statistics.

Results: Of the 100 responses, which included clinicians from government and private set-up, it was found that 80% of them routinely prescribed FDCs and 46% were aware of the requirement of separate marketing approval for FDCs. Only 24% knew of the regulatory body that grants approval and only 14% knew the full form of SLA. Of the total, 46% knew of the ban imposed on certain FDCs in 2018 and 36% could enumerate a few. A quarter (25%) of the clinicians prescribed the drugs from the banned list of FDCs before the ban. A 12% of clinicians disagreed with the ban imposed, 11% were aware of such banned drugs still being marketed and 10% responded that they were aware of them still being prescribed. Only 9% of them knew of the website which provides updates on regulatory aspect. 94% opined that regular training is required in this regard; though making the training mandatory for registration was not agreed upon by 42%.

Conclusion: There exists a gap in the knowledge of clinicians regarding the regulatory aspect of FDCs and regular training would help overcome them.

Keywords: CDSCO, marketing approval, irrational FDC, training

Introduction

Drugs form an integral part of healthcare system. We often need more than one drug for effective management of a disease and for such conditions, fixed-dose combinations play an important role [1]. A fixed dose combination (FDC) consists of two or more active drugs in a single dosage form [2]. Of all the new drug products introduced worldwide in the last ten years, FDCs hold over one-third of the share [3]. Central Drug Standard Controller of India (CDSCO) defines an FDC as a combination of two or more actives in a fixed ratio of doses and uses this term generically to mean a particular combination of actives irrespective of the formulation or brand. It also states that FDC may be administered as single entity products given concurrently or as a finished pharmaceutical product [4].

Such combination products should offer advantages in terms of therapeutic efficacy, safety in comparison to the individual products and compliance, and only when such clear benefits are demonstrated, they can be considered rational and their use justified [5]. While such a cocktail of different active pharmaceutical components offer advantage, there have been scenarios of reduced therapeutic effect, medication errors, and detrimental effects on patient safety on their use [6].

WHO's 19th Essential List of Medicines released in 2015 contained a meagre 27 FDCs which increased to 42 in 22nd List that was released in 2021 and as per information available on National List of Essential Medicines, the latest version of 2021 is yet to surface in the public domain and the list published in 2015 has 24 FDCs. Indian pharmaceutical market is one of the biggest in terms of its size and has over 6000 FDCs. We have witnessed it time and again, as to how a lack of stringent licensing system can end up with bizarre FDCs entering the market [7]. YK Gupta *et al.* in their study mention how we, as a country are yet to have a database with exact details on use pattern and sales of FDCs. There is a disconnect between State Licensing Authorities and CDSCO regarding grant of approval that also poses a challenge regarding the marketing approval of FDCs [7], which makes it all the more important for practitioners to have a good understanding of the status of FDCs in the country. It is relevant for doctors in government as well as private set-up to have awareness about the prescribing medicines and their combinations. Hence it was of interest to evaluate their knowledge, perception and practice regarding FDCs.

Materials and Methods

This is a cross-sectional, questionnaire-based study conducted over a period of two years between 2019 and 2021. The study protocol was approved by the Institutional Ethics Committee (EC/OA-103/2018) of Seth GS Medical College and KEM Hospital, Mumbai. As the literature regarding regulatory changes of FDC in India is scarce, we carried out this pilot study in 100 clinicians. To widen the perspective and understand both academic and private sides of practice, we included 50 clinicians from the government-run Seth GS Medical College and KEM Hospital, Mumbai, and the other 50 practising privately across Maharashtra.

The clinicians were contacted via email or in person and Informed Consent Document was shared by either of the two methods. Once the clinician agreed to participate in the study, questionnaire was administered via email or in person. A reminder was sent on the email once a week for 4 weeks to respond to the questionnaire.

Questionnaire (attached) administered was designed specifically for this study and validated (CVR =0.76) by experts for face and content. It was a 14-item questionnaire (refer to Table 1) of which 7 (Question nos. 2,3,4,5,6,11 and 12) pertain to the domain of knowledge, 4 (Question nos. 1,7,9,10) to practice and 4 (Question nos.

8,13,15) to perception domain. For questions numbered (1,2,3,4,5,7,10,11,13, 14) in the questionnaire, the responses were recorded as 'Yes' or 'No'; for questions numbered (8,9), in addition to 'Yes' and 'No' responses, an option of 'Don't Know' was also provided to choose from. Also, in questions (1,6,7) they were asked to enlist the names of drugs, where the respondents were asked to name few examples. The responses were recorded as 'Yes' only if the respondent gave correct examples.

Data were analysed using SPSS software, version 22.0 and given as descriptive statistics. Parametric quantitative variables are expressed as mean ± Standard deviation (SD), whereas non-parametric quantitative data are expressed as proportion. Qualitative variables are expressed as absolute and relative frequencies.

Results

All the results are depicted in Table 1. Data analysis revealed that in the domain of knowledge, 54% of the total number of clinicians did not know that a separate marketing approval is needed for FDCs, other than what is obtained for its individual constituents. Only 24% of them could name the government body as CDSCO that grants approval for marketing of FDCs in India, while the rest could not. Only 14 out of 100 clinicians were aware of the full-form of SLA in regard to FDC approval, the remaining 86 were not. There was a ban issued against 328 FDCs in September 2018 in India, about which only 46% were aware. Mere 36% of them could enlist up to 5 banned FDCs.

91% of them had no knowledge of the website which regularly provides updates on drugs-related regulatory changes in the country, only 9 were aware and were able to name it. News updates (13%) stand as the most common sources of information to keep them updated followed by journals (9%), CMEs (8%) and internet (8%). Information exchange with colleagues, Google, Medical representatives and social media are few other sources.

Pertaining to the domain of practice, we found that 80% of the clinicians (n=100) prescribed FDCs in their practice. Only 25% of the clinicians used to prescribe the FDCs from the list of those banned and were able to name a few of them. 11% were aware about FDCs on that list still being marketed and were able to name them. 81% were unaware and 8% unsure about the existence of banned FDCs in the market. Only 10% of them still knew of the practice of prescribing the banned FDCs.

Regarding the perception, 77% of them were in agreement with the ban issued, whereas 12 % disagreed and the remaining 11% were not sure. 94% agreed to the fact that regular training would be needed to stay up-to-date with regulatory aspects of drugs approved for use in our country. However, the need for mandatory training session in the area and that being necessary for renewal of registration in medical council was agreed upon by 58% of the clinicians while denied by the remaining 42%.

Table 1: Response to the questionnaire by the clinicians

Sl. no	Question	Response (%)	
		Yes	No
1	Do you prescribe FDCs in your practice? If yes, can you name a few? (max. 5)	80	20
2	Do you know that a separate marketing approval is needed for FDCs other than the one obtained for individual components of FDCs?	46	54
3	Can you name the Govt body which gives approval for	24	76

	marketing the FDCs?		
4	Do you know the full-form of SLA in regard to FDC approval?	14	86
5	Are you aware about the ban on marketing of 328 FDCs issued in September 2018?	46	54
6	Can you enumerate a few FDCs banned (max 5)	36	64
7	Before the FDCs were banned did you prescribe any of those? If yes, can you name a few?	25	75
8	Do you disagree with the decision to ban any particular FDC/s? If yes, can you state the name/s of FDC/s and your reason/s for disagreement?	12	77, Don't know - 11
9	Are you aware if any of the banned FDCs are still marketed? If yes, can you name them?	11	81, Don't know – 8
10	Are you aware whether any of the banned FDCs are still prescribed?	10	90
11	Are you aware of any website/s which gives regular updates about the regulatory changes in our country? If yes, please name.	9	91
12	What is/are your source/s of information to remain updated about the regulatory changes?	100	0
13	Do you think regular training/session is needed to remain updated with the regulatory changes?	94	6
14	Do you think regulatory training should be made mandatory and is necessary for renewal of registration of RMPs?	58	42

Discussion

This questionnaire-based study focusses on the triad of knowledge, practice and perception of practitioners on FDCs. Such studies are very insightful in the field of healthcare as they survey the representative population and help in eliciting what is known, perceived and practiced in the topic of interest [8,9]. We were able to get a better picture of the understanding among doctors regarding the scenario after banning of FDCs in 2019 through this study.

To understand the depth of knowledge one has on FDCs, most of the studies have focussed on their rationality, their presence in the Essential List of Medicines, their advantages and disadvantages on resident doctors, dental students and clinicians [10-12]. Through this study, we tried to gather information on the knowledge of clinicians on the regulatory aspect of FDCs in India, where we assessed whether they know if a separate marketing approval is required for FDCs, if they know of the regulatory body that grants approval for the marketing of FDCs, full form of SLA, and banning of certain combinations. As observed in the analysis, questions around the regulatory body, the need for separate marketing approval, full-form of SLA, were not a part of other studies carried out on similar lines. The responses to them are reflective of the poor awareness regarding the regulatory aspects of FDCs. While other studies had percentages ranging from 13 – 42% regarding the awareness of banned FDCs, 46% of the clinicians in our study were aware of the ban, but only 25% of all the clinicians who could name a few of them and also wrote them in their prescriptions [11,13].

In contrast to a study by Singh *et al*, where only 52% of the doctors prescribed FDCs in their practice, we found 80% of the doctors prescribing them. However, in a study on the use of FDCs in a city in Western India, 80.2% of 1170 prescriptions contained FDCs, which is reflective of the practice among doctors [14]. We could not find data from

literature as to how many were prescribing from the banned FDCs nor could we find details regarding the awareness about these FDCs being marketed or in use. However, we found 25% of them agreeing to be using them in practice and only 10% of the clinicians still knew of the practice of prescribing such banned FDCs.

There is varied attitude of clinicians towards FDCs as per Gupta *et al*, where about 63% of the participants opined that FDCs should be allowed to be marketed, with only 47% having an idea about rationality of these combination products, we had 77% of them agreeing to the ban imposed [3]. We had all the clinicians referring to the CDSCO website. News updates were the most common source of information regarding FDCs as per the responses in our study whereas; textbooks (66%) and medical representatives (71%) were the most common sources of information in other studies. Other studies had CMEs (Continued Medical Education) as the source of information for about 40-42% of the practitioners whereas only 8% in our study relied on CMEs for the updates [3,11,15].

94% of the clinicians in our study felt the need for regular training to stay up-to-date with regulatory aspects of drugs approved for use in our country in contrast to 42% as seen in a study by Sharma *et al* [15]. It was one of our study's finding alone that though many opined for the need for mandatory training session in the area and that being necessary for renewal of registration in medical council was agreed upon by only 58% of the clinicians. With a cross-sectional study like this, we were able to gain the information by striking a good balance between practitioners of both government and private sectors, focussing on regulatory perspective as well.

Though the study was initiated in the pre-COVID era, because of the COVID pandemic, the response rate decreased. Hence, to achieve response from minimum number of respondents, we took more than two years. We are also of the opinion that administering the questionnaire by email or providing a hard copy of it left the respondents free to reach out to internet to gather information. However, the results still display a poor knowledge of clinicians with regard to regulatory aspect of FDCs.

Conclusion

A few of the clinicians admit to prescribing FDCs currently on the list of banned FDCs before the ban was imposed and a few opine them being still in use. Lacunae do exist in the knowledge of clinicians regarding FDCs and their approval process. The clinicians do feel the need for regular training of clinicians so that they stay up-to-date in this area.

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