**Cost Variation Analysis Study of Floroquinolones in India: Dilemma of the Prescribing Doctors “Which Brand To Choose?”**

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**Abstract**

**Background:** Prescriber plays a vital role of choosing the drug and its brand for the patient which affects the patient in terms of safety, efficacy as well as the cost. In India, the infectious diseases form the major burden. Floroquinolones are one of the most prescribed antibiotics which provide therapeutic cure. The study aimed to see the cost variation of oral flouroquinolones available in India. **Methods:** The costs of a particular oral flouroquinolones were obtained from CIMS and Drug Today for the same strength and dosage. **Results:** Of 25 drugs used as single drug therapy Levofloxacin (500 mg) showed highest price variation of 14526.87% and only 6 had less than 100% variation. Of the 10 types of combinations are available with 12 types of dosage forms. Maximum cost variation (390.63%) was seen with ofloxacin and ornidazole (200+500) combination. **Conclusion:** There is a wide cost variation among oral flouroquinolones which adds to the dilemma for the prescribing physician. There is a need to include pharmaco-economics in medical curriculum for sensitizing the doctors about cost of prescriptions and need for regulatory authorities to initiate measures to bring regularities in cost and monitor it.

**Keywords:** Floroquinolones, Cost variation, prescriber, brand selection, drug affordability, and prescription cost.

**INTRODUCTION**

Today the prescriber plays a vital role of choosing the right drug as well as its brand for the patient which affects the patient in terms of safety, efficacy as well as the cost. This choice by prescriber not only affects the patients pocket but also the pharmaceutical company whose turnover depends on the prescribers prescribing practices [1].

Rational use of medicines is described when the medication received by the patient is appropriate to the clinical need, at proper dose, for the proper duration and at the lowest cost which the patient can afford [2]. Hence, the cost consideration by the prescriber is important criteria along with others of rational prescription so that the patient is able to afford the medication and get his disease managed.

In September 2016, the Medical Council of India (MCI) brought an amendment in the Indian Medical Council Regulations (Professional Conduct, Etiquette and Ethics) in clause 1.5 which is related to the use of generic names of drugs by doctors. It is stated that ‘every physician should, as far as possible, prescribe drugs with generic names legibly and preferably in capital letters and he/she shall ensure that there is a rational prescription and use of drugs’[3]. Still the use of generic names of the drugs while writing prescription is still awaited [4]. Even after implementation the problem of affordability won’t be solved because the power of brand selection will merely shift from the doctor to the pharmacist who is dispensing the drug [5].

In India, the infectious diseases form the major burden and antibiotics play a major role in providing the therapeutic cure to the needy. Furoquinolones are one of the most prescribed antibiotics in India. They are synthetic, broad spectrum anti-bacterial agents whose appropriate utilization affects the therapeutic outcome of the patient. Ciprofloxacin and levofloxacin dominate the market in global sales taking a share of 65% ($3.3 billion) and furoquinolones in India forms 30% share of global pharmaceutical market counterparts. (REF)

Very few studies have been done to evaluate the cost variation of drugs of different brands in India [4-9]. A cost variation study on furoquinolones was
done 3 years back by Chawan et al. [10] in 2015 which showed wide variation and highlighted prompt need for actions. Hence, a study was planned to see the cost variation of different brands of oral fluoroquinolones and its combinations in India.

**Aims and Objective**

The study aimed to see the cost variation of brands of various oral fluoroquinolones available in India either as a single drug or in combination and to evaluate the difference in cost of various brands of same fluoroquinolone by calculating cost ratio and percentage variation in cost in Indian rupees.

**Material and Methods**

The costs of a particular oral fluoroquinolones (cost in INR per 10 tablets or capsules) of the same strength and dosage form being manufactured by different companies was obtained from latest “Current Index of Medical Specialties (CIMS) October 2018 – January 2019 and Drug Today January – March 2019.

The drug formulations manufactured by a single company were excluded. Also injections and pediatric syrups were excluded.

The difference in the maximum and minimum prices of drugs formulation manufactured by different pharmaceutical companies was calculated along with cost ratio and percentage of cost variation.

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\text{Cost ratio} = \frac{\text{Maximum cost}}{\text{Minimum cost}}
\]

\[
\% \text{ cost variation} = \frac{\text{Maximum cost} - \text{Minimum cost} \times 100}{\text{Minimum cost}}
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**Results**

Table 1 shows percentage cost variation, cost ratio with minimum and maximum cost per 10 tablets of 11 fluoroquinolones with their various dosages. So in total 25 drug dosages as single drug therapy are depicted. Levofoxacin (500 mg) shows highest price variation of 14526.87 % which is the most commonly used fluoroquinolone and most frequently prescribed dose. As sparfloxacin 300 mg was marketed by single manufacturer hence it showed 0 % variation while minimum price variation was shown by sparfloxacin 400 mg which was 15.6 %. Out of 25, only 6 had less than 100 % variation.

| Drug          | Formulations (n) | Dose (mg) | Minimum cost/ 10 tab (INR) | Maximum cost/ 10 tab (INR) | Cost ratio | % Variation in cost |
|---------------|------------------|-----------|---------------------------|---------------------------|------------|---------------------|
| 1. Ciprofloxacin | 5                | 100       | 12.52                     | 25.20                     | 2.01       | 101.28              |
|               |                  | 250       | 12.50                     | 69.85                     | 5.59       | 458.80              |
|               |                  | 500       | 16.67                     | 137.50                    | 8.25       | 724.84              |
|               |                  | 750       | 59.51                     | 308.65                    | 5.19       | 418.65              |
|               |                  | 1000      | 85.06                     | 169.30                    | 1.99       | 99.04               |
| 2. Gemifloxacin | 1                | 320       | 178.00                    | 749.00                    | 4.21       | 320.79              |
| 3. Levofloxacin | 3                | 250       | 19.00                     | 75.00                     | 3.95       | 294.74              |
|               |                  | 500       | 6.70                      | 980.00                    | 146.27     | 14526.87            |
|               |                  | 750       | 55.53                     | 143.00                    | 2.58       | 157.52              |
| 4. Lomefloxacin | 1                | 400       | 90.00                     | 185.00                    | 2.06       | 105.56              |
| 5. Moxifloxacin | 1                | 400       | 27.00                     | 800.00                    | 29.63      | 2862.96             |
| 6. Norfloxacin  | 3                | 100       | 13.50                     | 20.80                     | 1.54       | 54.07               |
|               |                  | 200       | 13.60                     | 39.00                     | 2.87       | 186.76              |
|               |                  | 400       | 10.71                     | 68.00                     | 6.35       | 534.92              |
| 7. Ofloxacin | 4                | 100       | 20.00                     | 48.00                     | 2.40       | 140.00              |
|               |                  | 200       | 16.00                     | 310.64                    | 19.42      | 1841.50             |
|               |                  | 300       | 60.00                     | 75.00                     | 1.25       | 25.00               |
|               |                  | 400       | 20.62                     | 594.28                    | 28.82      | 2782.06             |
| 8. Pefloxacin | 1                | 400       | 24.06                     | 49.50                     | 2.06       | 105.74              |
| 9. Sparfloxacin | 4                | 100       | 28.70                     | 99.50                     | 3.47       | 246.69              |
|               |                  | 200       | 8.90                      | 250.00                    | 28.09      | 2708.99             |
|               |                  | 300       | 150.00                    | 150.00                    | 1.00       | 0.00                |
|               |                  | 400       | 150.00                    | 173.40                    | 1.16       | 15.60               |
| 10. Balofloxacin | 1              | 100       | 83.50                     | 140.00                    | 1.68       | 67.66               |
| 11. Prulifloxacin | 1              | 600       | 240.00                    | 990.00                    | 4.13       | 312.50              |

Figure 1 shows the cost difference of various formulations used as single drug therapy, figure 2 shows its cost ratio and Figure 3 shows its percentage variation.
Table 2 shows percentage cost variation, cost ratio with minimum and maximum cost per 10 tablets of combinations with fluoroquinolones available in market. 10 types of combinations are available with 12 types of dosage forms. Maximum cost variation (390.63%) is seen with ofloxacin and ornidazole (200+500) combination. Figure 4 shows the cost difference of various formulations of fluoroquinolones available as combination drug therapy, Figure 5 shows its cost ratio and Figure 6 shows its percentage variation.

**Fig.1:** Cost difference (minimum and maximum) of fluoroquinolones formulations used as single drug therapy

**Fig.2:** Cost ratio of fluoroquinolones formulations used as single drug used as a single drug therapy
Fig-3: Percentage variation of fluoroquinolones formulations used as single drug used as a single drug therapy

Table-2: Variation in cost of combination therapy

| Drug combination               | Formulations (n) | Dose (mg)       | Minimum cost (INR) / 10 tablets | Maximum cost (INR) / 10 tablets | cost ratio | % Variation in cost |
|-------------------------------|------------------|----------------|--------------------------------|--------------------------------|------------|--------------------|
| Ciprofloxacin + Ornidazole   | 1                | 500 500 +      | 79.00                          | 92.40                          | 1.17       | 16.96              |
|                              |                  | 250 500 +      | 80.00                          | 125.00                         | 1.56       | 56.25              |
| Levofoxacin + Azitromycin    | 2                | 250 500 +      | 128.70                         | 169.40                         | 1.32       | 31.62              |
|                              |                  | 250 250        | 128.70                         | 169.40                         | 1.32       | 31.62              |
|                              |                  | 500 500        | 228.50                         | 290.00                         | 1.27       | 26.91              |
|                              |                  | 500 250        | 228.50                         | 290.00                         | 1.27       | 26.91              |
| Ofloxacin + Ornidazole       | 1                | 200 500 +      | 32.00                          | 157.00                         | 4.91       | 390.63             |
| Ofloxacin + Tinidazole       | 1                | 200 600 +      | 39.00                          | 105.41                         | 2.70       | 170.28             |
| Ofloxacin + Metronidazole    | 1                | 200 500 +      | 11.37                          | 11.37                          | 1.00       | 0.00               |
| Ofloxacin + Nitazoxanide     | 1                | 200 500 +      | 66.00                          | 100.00                         | 1.52       | 51.52              |
| Ofloxacin + Serratiopeptidase| 1                | 200 10         | 89.00                          | 89.00                          | 1.00       | 0.00               |
|                              |                  | 200 varies     | 42.00                          | 110.00                         | 2.62       | 161.90             |
| Ofloxacin + prebiotics       | 1                | 200 200 +      | 77.00                          | 132.00                         | 1.00       | 0.00               |
| Ofloxacin + cefixime         | 2                | 100 100 +      | 77.00                          | 77.00                          | 1.00       | 0.00               |
|                              |                  | 200 200        | 132.00                         | 132.00                         | 1.00       | 0.00               |
Fig-4: Cost difference (minimum and maximum) of flouroquinolones formulations available in market

Fig-5: Cost ratio of flouroquinolones formulations used as single drug used as a single drug therapy
DISCUSSION

A large number of formulations for the same drug are available at different prices in India as more than one pharmaceutical company is selling a particular drug or a combination. Very few studies have been done in India evaluating cost variation of a drug. Hence, a study was planned to evaluate the cost variation of fluoroquinolones which have a good demand and market availability.

The findings in our study show a percentage variation in cost above 100% for the available oral fluoroquinolones in India. The same situation was prevalent 3 years back when Chawan et al. [10] had done a similar study. The situation has actually worsened with higher percentage variation today. These percentage variations in cost cannot be accepted in a developing country like India which leads to an unnecessary economic burden over the population. Studies have suggested that price variation was directly related to the number of companies manufacturing a particular drug. So it can be concluded that the price variation increases because of the increase in competition among the manufacturing companies.

We could find various combinations available with fluoroquinolones which are completely irrational. Surprisingly the infamous Tab Norflox-Tinidazole combination was not available in the market as it was 3 years back but it looks like oflox-ornidazole combination has taken over the previous famous irrational combination with highest cost variation ratio. Only education and awareness might be able to control the misuse of this combination.

Drug price control order (DPCO) is an order issued by the government to fix prices of drug. Once medicine is brought under DPCO, it cannot be sold at a price higher than that fixed by the government (DPCO). Out of 509 drugs under price control DPCO list released in March 2019 has levofloxacin (250 mg with max price per tab as Rs. 4.32, 500 mg with max price per tab as Rs. 7.89 750mg with max price per tab as Rs. 10.70) moxifloxacin 400mg with max price per tab as Rs.24.79 and ciprofloxacin (500mg with max price per tab as Rs.3.57) are covered in this list [11]. Further studies are needed to be done to monitor this situation.

Patient compliance is poor for the expensive brands [12]; they buy only a few tablets because of the high cost of medicine. Inadequate prescription coverage and out of pocket expenses is one of the strongest predictors of their medication adherence problems and with antibiotics this might further add to the resistance problem. Many poor people frequently face a choice between buying medicines or buying food or other necessities due to limited resources and high pricing of drug and do spend out-of-pocket [13]. So medicine prices do matter. The excess profit margins which are being shared by pharmaceutical traders must be passed on to consumers which are a feasible and economically viable.
Over the counter access to antibiotics is a problem, but regulations to restrict access have to be balanced against the need to maintain access for the significant proportion of the population that lack access to doctors. Indeed lack of access to effective and affordable antibiotics still kills more [14].

Many physicians are not very conscious about the drug price variation and it is always been felt that physicians could provide better services and reduce costs of drugs only if information about drug prices and manual of comparative drug prices annotated with prescribing advices are readily available for the physicians[15]. This might help physicians prescribe better and reduced their patients’ drug expense. Pharmaco-economics could also be introduced as a practical lesson to undergraduate medical curriculum, wherein students could be taught to calculate the cost of their prescription by using CIMS or MIMS. This will also sensitize students about the enormous differences in prices of the drugs[8].

Superiority of any particular brand over the others has never been proved scientifically but doctors do feel that the costlier and specific brands might be having better quality which might give better therapeutic outcome for the patient[7]. Also the fact that there is a presence of counterfeit and substandard drugs in the market adds to complexities [16, 17]. Hence, the doctors are in a dilemma of which drug to prescribe. In the absence of information on comparative drug prices and its quality, it becomes difficult for doctors to prescribe the most economical prescription. Hence, there is a need to provide updated and complete information regarding bioequivalence, quality and cost of the pharmaceutical preparation to the doctors. There is a strong need to create awareness about this huge price variation among the general public, health care providers, health care payers, government agencies, policy makers, pharmacists for appropriate intervention and concerted actions.

Measures must be taken by the government to bring about the uniformity in the price. Currently, very few medicines are under drug prices control order. Hence, it is desired that the Government should bring all lifesaving and essential medicines under price control especially antimicrobials. Government of India has opened few generic drug stores in some states that sell generic medicines manufactured by public sector companies. The quality of generic medicines available on these stores at cheaper rates should be tested and compared with popular branded drugs and results should be widely published.

**CONCLUSION**

Our study highlights that there is a wide cost variation among oral fluoroquinolones manufactured by different pharmaceautical companies which creates a dilemma for the prescribing physician. There is a need to add pharmaco-economics in medical curriculum for sensitizing the doctors about cost of prescriptions. There is a need for regulatory authorities to initiate measures to bring regularities in cost and monitor it. Also there is a need to control irrational combinations with antimicrobials in the market. It is recommended that the marketing of drugs to be appraised and directed to provide maximum benefit of therapy toward patients and minimum negative economic impact.

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