

Original research article

Assessment of rationality of calcium formulations available in market

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Abstract

Indian drug market is flooded with more than 70000 drug formulations, the majority of which are proprietary multi-drug combinations. The prescribing and buying of drugs is an issue of unparalleled peculiarity because the prescriber (the doctor) decides what to buy, but he is not the one who pays for the drug; the one who pays and benefits (the patient) has no say in what he/she buys. The law comes into the picture for the price control of only a limited number of drugs and formulations

Keywords: Acceptable, Elemental Calcium, Irrational.

Introduction

Calcium is essential for a variety of micro molecular and macroscopic biological functions. It is found mostly in the bones and teeth. It is critical for mediating vascular contraction and vasodilatation, muscle function, nerve transmission, intracellular signalling and hormonal secretion.² Oral calcium supplements are used to treat conditions caused by low calcium levels such as bone loss (osteoporosis), weak bones (osteomalacia/rickets), decreased activity of the parathyroid gland (hypoparathyroidism) and a certain muscle disease (latent tetany). It may also be used in certain patients to make sure that they are getting enough calcium (e.g. women who are pregnant, nursing or postmenopausal), people taking certain medications such as phenytoin, phenobarbitone or prednisolone.³ Most of the calcium formulations marketed in India contain not only calcium, but also other substances like vitamins, minerals, amino acids and other chemicals. So rationality of such combinations is questionable. The objective of the study was to analyze the formulation available in Indian market for varieties of dosage forms, calcium salts, content of elemental calcium, frequency of administration required, additional nutrients and cost.

Materials and Methods:

Detailed information about calcium containing formulations was obtained from the Indian Drug Review (IDR) 2012, issue 2. The formulations were classified into the following categories: (A) solid formulation, (B) liquid formulation, and (C) parenteral formulation. Each category was further subdivided into formulation containing: (i) Calcium only, (ii) Calcium+Vitamin D only (iii) Calcium + Vitamin D+ others. If information about the elemental calcium content of calcium salt, type of calcium salt, quantity or cost were not available, such formulations were not included for cost analysis. For comparison of cost, instead of dose of calcium salts, elemental calcium content was taken into consideration because elemental calcium content of different salts differs significantly and the response depends on the elemental calcium available. For cost analysis we consider the supplemental dose and the recommended supplemental dose of calcium is 0.8-1.5 gm daily.⁴ Data entry

was done in Microsoft Excel 2007. Thus, cost of 1.5 gm (1500 mg) of elemental calcium available from each formulations containing only calcium salts were very few. Vitamin D, amino acids like arginine, lysine and minerals like potassium, magnesium and zinc increases the absorption of calcium.⁵ The formulations containing vitamin D and these amino acids and minerals were considered as irrational. To find out whether difference between minimum and maximum cost value was due to different calcium salt, we classified acceptable oral solid formulations containing calcium and vitamin D according to the various calcium salts. To provide 1500 mg elemental calcium per day in not more than three doses, the formulation should deliver 500 mg elemental calcium per dose. So Hence we also separated out those formulations which contained less than 500 mg elemental calcium per dose. The median cost value of acceptable calcium formulations was calculated and compared with that of irrational ones.

Results:

Out of 680 calcium formulations, 572 were oral solid formulations, 92 were oral liquid and 16 were parenteral formulation. Several dosage forms are available for oral solid calcium formulations like tablets (269), powder (85), capsules (74) sg-cap (64), fc-tab (44), chw.tab (118), sachet (6), kit (4), sc-tab(2), filco,tab (1), softcap (1), captab (1), gran (1), and biscuit (1). Among oral liquids, syrup (48) was the most common followed by suspension (35) and liquid (6). As shown in table- 1, there were 32 oral solid formulations containing calcium only. Among the liquid and parental formulations, situation was 3 and 13 options respectively. Even after allowing for inclusion of vitamin D, arginine, lysine, potassium, magnesium and zinc as a compromise, 8% oral solid, 15% oral liquid and 18% parenteral calcium formulations were irrational. Information about the elemental calcium content of calcium salt, the type of calcium salt, its amount or the price was not mentioned in the IDR for certain formulations, and they were not considered for cost analysis. Thus from category- A (oral solid), 213 formulations were dropped and from category- B (oral liquid) and category- C (parenteral) 57 and 12 respectively were not included for cost analysis. As shown in Table 2, median cost value of irrational formulations among oral solid, oral liquid and parental group were Rs. 53.8, Rs. 47.1 and Rs. 369.9 subsequently as compared to acceptable formulations among oral solid and oral liquid which were Rs. 45.7 and Rs. 16.35.

Table 1: Calcium formulations: Acceptable V/s Irrational

Formulations	Contents	%
Oral-solid (n=572)	Calcium salts only (n=32)	5.59
	Calcium salts+Vitamin D (n=154)	26.92
	Calcium salts+Vitamin D+ Amino acids (arginine, lysine) +Minerals (potassium+magnesium+zinc+ (n=338)	59.09
	Calcium salts+Vitamin D+Others (n=48)	8.39
Oral-Liquid (n=92)	Calcium salts only (n=2)	3.26
	Calcium salts+Vitamin D (n=30)	32.61
	Calcium salts+Vitamin D+Amino acids (arginine, lysine) +Minerals (potassium+magnesium+zinc (n=45)	48.91
	Calcium salts+Vitamin D+Others (n=14)	15.22
Parenteral (n=16)	Calcium salts only (n=12)	81.25
	Calcium salts+Vitamin D (n=0)	0
	Calcium salts+Vitamin D+Amino Acids (arginine, lysine)+Minerals (potassium+magnesium+zinc (n=0)	0
	Calcium salts+Vitamin D+Others (n=3)	18.75

Table 2: Median Cost Value of Irrational and Acceptable Calcium Formulations:

Formulations	Irrational	Acceptable
Oral-Solid	Rs. 53.8 (n=34)	Rs. 45.7 (n=322)
Oral-Liquid	Rs. 47.1 (n=6)	Rs. 16.35 (n=27)
Parenteral	Rs. 369.9 (n=6)	Rs. 0

Discussion:

As mentioned earlier, for comparison of cost instead of dose of calcium salts, elemental calcium content was considered since the element calcium available from different calcium salts differs significantly. List of other nutrients added in the calcium formulations was quite long: (a) Vitamins like beta carotene, Vit. C, Vit. B₁₂, Vit. E acetate, Vit. B₆, Vit. A, Vit. B₁, Vit. E etc. (b) Minerals like zinc, magnesium, phosphorus, manganese, copper, selenium etc.) Amino acids like 1-lysine, 1-leucine, arginine, histidine, tyrosine etc. (d) Miscellaneous substances like creosote, protein, fat, carbohydrate, moisture, fibre, DHA etc. What would be his daily cost of treatment and total cost of nutritional supplement and treating calcium deficiency condition Calcitriol promotes intestinal calcium absorption by increasing the expression of epithelial calcium channel, protein, which increases transport of calcium across the membrane.² Amino acids like arginine, lysine and minerals like potassium, magnesium and zinc also increase absorption of calcium.⁵ When we allowed for addition of Vitamin D, arginine, lysine, potassium, magnesium and zinc as compromise formula, and excluded all other 'irrational' formulations, the cost range of acceptable formulations containing Calcium only Calcium with Vitamin D was narrowed down and Calcium with Vitamin D and others (containing arginine, lysine, potassium, magnesium, and zinc) was not changed, which was shocking. Based upon bioavailability, cost and clinical efficacy, calcium carbonate, in the form of Os-Cal^R, would appear to be a good choice for calcium supplementation in a US population at risk for both low bone mineral density and hip fracture.⁶ We also analysed the information to see if type of calcium salt has any bearing on the cost of the formulations. From results we can say that formulations containing calcium salts like calcium carbonate and tribasic calcium phosphate are cheaper than other salts like calcium phosphate are cheaper than other salts like calcium citrate and calcium citrate maleate containing formulations. Form-ulations containing less than 500 mg elemental calcium, require more than three administrations per day, and this can affect the patient compliance. Prices of 'acceptable' calcium preparations were compared with that of 'irrational' formulation. We found that the acceptable products were cheaper than the irrational ones to a significant extent except the parenteral preparations (Table- 4).

Conclusion:

One of the major principles of rational use of drugs is to prescribe only those drugs which are really indicated. In other words, unnecessary drugs should NOT be prescribed. 86% of calcium formulations fit in the definition of acceptable. Acceptable oral calcium formulations are preferred over irrational once because they are cheaper.

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