Pharmacoeconomics of Oral Antidiabetic Drugs

Abstract

Aim: To study the pharmacoeconomic aspect of oral antidiabetic drugs available in India.

Method: We analyzed 326 oral antidiabetic formulations mentioned in CIMS Jan 2003 issue for: (1) Percentage price variation for each dose; (2) price variation in relation to number of companies marketing a formulation and (3) cost of drug therapy per patient per year.

Results: 19.23% single drugs and 20% fixed dose combinations showed a high price variation (more than 250% for single drugs and more than 100% for drug combinations). There is no relation between number of companies manufacturing a drug and price variation in case of single drugs. The cost of drug per patient per year varies from Rs 94.90 for glibenclamide to Rs 3285.00 for acarbose and nateglinide. The combination of glimepiride and metformin (Rs 1204.50) and rosiglitazone and gliclazide (Rs 1596.88) cost much more than if the drugs are taken separately (Rs 653.35 and Rs 1168.00, respectively).

Conclusion: The cost of oral hypoglycemic drugs should be considered before prescribing, especially for newer products.

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Introduction

The number of oral hypoglycemic agents available for the treatment of type 2 diabetes mellitus has increased over the past few years. The physician can now opt for new drugs like meglitinide analogs, thiazolidinediones, alpha glucosidase inhibitors and newer sulfonylureas. However, he should also consider the cost of the drugs to ensure that the patient can afford them. The present study aims at providing information to the physician about the most cost-effective oral antidiabetic drug.

Methods

Drugs under the heading of "oral antidiabetic and related drugs" in *CIMS* Jan.-Mar. 2003 issue[1] were considered for analysis. Glucomannan, chromium picolinate and guar gum were ignored since they are not used as single drugs in treatment of type 2 diabetes mellitus. Sustained release formulations were also not considered in our analysis

Price analysis

Price analysis was done for individual drugs as well as available fixed dose combinations. Minimum and maximum price for the same dosage forms and number of companies marketing drug were recorded. This data was analyzed for number of formulations having high price

variation and relation between price variation and number of companies manufacturing a drug.

Cost analysis

For cost analysis, the usual initial daily dose of a drug was obtained from Martindale's The Complete Drug Reference[2]. The minimum price for the drug was recorded from CIMS[1]. The yearly cost of the drug for the patient was calculated using the formula:

Cost/year in rupees = cost of usual initial daily dose (Rs) × 365 days

Results

We analyzed 326 products manufactured by 57 companies, of which 256 products were single drugs and 70 were fixed dose ratio combinations. 57.69% single agents showed a price variation of less than 100%. However, 19.23% single drugs had a high price variation of more than 250%. Among the combinations, 80% of drugs had a less than 100% price variation. Drugs having a high price variation are listed in Table 1.

Table 2 shows the relation between number of companies manufacturing a drug and the price variation. It was observed that price variation is not related to the number of companies manufacturing a drug. However, for drug combinations, the price variation is wider if more companies manufacture the combination.

Table 3 shows the cost of initial drug therapy per patient for a year assuming that the patient treatment is started with a single drug and the patient receives the same dose for the year. The cost per patient per year varies from Rs 94.90 for glibenclamide to Rs 3285.00 for acarbose and nateglinide. Most drugs cost less than Rs 500 per year. The newer drugs acarbose, repaglinide, nateglinide and rosiglitazone cost the patient more than twice the other drug therapies. Among the insulin secretagogues, nateglinide is almost 7 times costlier than the costliest sulfonylureas. Among the insulin sensitizers, rosiglitazone is priced nearly 4 times more than pioglitazone. Table 4 compares the cost of fixed dose combinations per patient per year to the cost of the same dose of drugs taken singly. The difference in costs was less than Rs 220 except for glimepiride and metformin (Rs 551.15) and rosiglitazone and gliclazide (Rs 428.87) where the cost of the combinations is much more than the same drugs taken separately in the same doses. Glipizide and metformin is the only combination which is less expensive than individual drugs.

Discussion

Pharmacoeconomics is a branch of health economics dealing with costs and benefits of treatment. Costs of treatment include direct medical costs, direct non-medical costs, indirect costs and intangible costs[3]. In this study, we observed that 19.23% single drugs and 20% fixed dose combinations have a high price variation. The physician should be

Table 1

Drugs with high percentage price variation (>250% for single drugs and >100% for fixed dose combination)

	Generic drugs	Formulation and strength	Number of manufacturing companies	Price range in rupees per 10 units	% Difference in price
Single drugs	Gliclazide	Tab. 80 mg	29	14.00–62.00	342.86
	Glimepiride	Tab. 1 mg	10	11.90–53.00	345.37
		Tab. 2 mg	10	21.80–103.40	374.31
	Pioglitazone	Tab. 15 mg	14	9.00–51.20	468.89
		Tab. 30 mg	14	17.50–83.20	375.43
Fixed dose ratio combinations	Glibenclamide + metformin	Tab. 2.5 mg/ 400 mg	6	8.25–21.00	154.55
	Gliclazide + metformin	Tab. 80 mg/ 500 mg	23	17.00–40.00	135.29

Table 2

Price variation with relation to number of companies making a drug

	No. of manufacturing companies	No. of formulations	Percentage price difference	
			Min %	Max %
Single drugs	2–4	27	1.01	161.60
	5–9	37	26.67	119.40
	10–14	40	111.11	468.89
	>20	53	81.67	342.86
Fixed dose combinations	2–4	15	12.00	71.43
	5–9	22	65.56	154.55
	>20	23	—	135.29

Table 3

Cost of drugs per patient per year

Sl. no.	Drug	Usual initial daily dose	Minimum cost/day (Rs)	Total cost/year (Rs)
1	Acarbose	75 mg (25 mg t.d.s.)	9.00	3285.00
2	Tolbutamide	1 g (500 mg b.d.)	1.30	474.50
3	Glibenclamide	2.5 mg	0.26	94.90
4	Gliclazide	40 mg	1.20	438.00
5	Glimepiride	1 mg	1.19	434.35
6	Glipizide	2.5 mg	0.384	140.16
7	Repaglinide	1500 mg (500 mg t.d.s.)	5.97	2179.05
8	Metformin	1 g (500 mg b.d.)	1.20	438.00
9	Phenformin	25 mg	0.786	286.89
10	Pioglitazone	15 mg	0.90	328.50
11	Rosiglitazone	4 mg	3.50	1277.50
12	Nateglinide	180 mg (60 mg t.d.s.)	9.00	3285.00

careful in selecting brands for these drugs, since a wrong choice may result in an unnecessary financial burden on the patient. The price variation for single drugs is not related to the number of companies manufacturing the drug. Ideally, it would be expected that if more companies manufacture a drug, the price variation would be less due to competition. We also calculated the minimum cost of oral hypoglycemic drugs per patient per year. We did not consider the efficacy aspect since most drugs have similar efficacy i.e., they reduce HbA_{1c} by 1-2%. The only exception is acarbose, which reduces HbA_{1c} by 0.5-1%.[4] In spite of this, acarbose is one of the costliest drug. In the UKPDS study[5], 32% patients discontinued acarbose at the end of a 3-year period. The high cost of this drug together with its low efficacy and gastrointestinal side effects make its use as initial drug questionable.

Among the insulin secretors, the costs of repaglinide (Rs 2179.05) and nateglinide (Rs 3285.00) are much more than that of sulfonylureas. However, the meglitinide analogues are useful in controlling the postprandial blood glucose levels[6] and allow flexibility in meal timings[7].

Among the sulfonylureas, tolbutamide is the costliest, probably due to its multiple daily dosing and the fact that it is manufactured by only one company. The use of the

Table 4

Cost of fixed dose combination/patient/year compared to that of individual drugs

Sr. no.	Drugs	Dose (mg)	Cost/year for combinations (Rs)	Total cost/year (Rs) for both drugs taken separately
1	Glimepiride + metformin	1/400	1204.50	653.35
2	Rosiglitazone + gliclazide	2/80	1596.88	1168.00
3	Rosiglitazone + metformin	2/500	1095.00	876.00
4	Gliclazide + metformin	40/400	839.50	657.00
5	Glibenclamide + metformin	1.25/250	361.35	245.28
6	Glipizide + metformin	2.5/250	288.35	304.41

drug however, is quite low[8]. Glibenclamide is the cheapest, but it does carry the risk of dangerous hypoglycemia due to its long half-life[9]. Glipizide is cheaper than both glimepiride and gliclazide and is less likely to cause serious hypoglycemia as glibenclamide[9]. Thus, glipizide should probably be the first insulin secretagogue to be considered while treating a diabetic patient.

Among the insulin sensitizers, phenformin is the cheapest. However, it has been banned in several countries due to risk of lactic acidosis. Metformin is cheap, has low incidence of lactic acidosis[10] and in the UKPDS study has been shown to be the only agent to reduce macrovascular complications in overweight patients[11]. Among the thiazolidinediones, pioglitazone is nearly 4 times cheaper than rosiglitazone. Their efficacy appears to be equal and in addition, pioglitazone appears to have a beneficial effect on the lipid profile[12]. The daily cost of pioglitazone is comparable to that of metformin. However, treatment with pioglitazone will incur additional cost of doing regular liver function tests every 2 months[13].

Fixed dose ratio combinations help to improve patient compliance[14]. However, if the cost difference of a combination and of individual drugs is large, as for glimepiride and metformin (Rs 551.15) and rosiglitazone and gliclazide (Rs 428.87), it may itself be a reason for non-compliance.

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