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Utilization Pattern of Anti Dementia Drugs and Cost-Effective Analysis: Indian Scenario

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Research Article

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Abstract

Background: The population suffering from Alzheimer's disease (AD) and other dementias is estimated to increase every year in India, the reason being steady growth in the older population and stable increment in life expectancy.

Aim: To evaluate the trend of clinical practices in India as well as cost analysis of anti dementia drugs in an Indian scenario.

Material and Methods: Utilization pattern of anti dementia drugs studies was studied using literature survey and data mining of Prospective and Retrospective studies. Cost analysis was performed to evaluate wide variation in the prices of same anti dementia drug with different formulation in India.

Results: Alzheimer's disease is the most common subtype of dementia and Donepezil remains to be the most commonly prescribed drugs as indicated by Prospective and retrospective studies. Cost analysis of anti dementia drugs being manufactured by many companies across the different brands in India showed a very high variation in the minimum and maximum price. Cost ratio was highest for rivastigmine (1.5 mg capsule) and lowest for piracetam (**400 mg tablet**). It was observed that % cost variation of all the anti dementia drugs was above 100.

Conclusion: Thus, in India, a wide variation in the prices of same drug with different formulation has a severe economic impact. More effort is needed to understand and analyze in terms of its prescription, utilization pattern of anti dementia drugs as it has huge socioeconomic impact on patients and caregivers of mainly developing countries like India.

Keywords: Alzheimer's disease (AD); Dementia; Cost analysis; Cost ratio; % Cost variation

Introduction

Global estimates on Persons with Dementia (PwD) indicate that developing countries like China and India contributed to one-fourth (26.8%) of the global burden in 2001 and also there has been a 300% increase between 2001 and 2040 [1]. Rural studies reveal that the prevalence of dementia in South India and that in North India vary from 3.39 to 0.84%, respectively [2]. Similarly urban studies showed variation in prevalence of dementia in different regions-2.44 to 4.1% in West India, 1.83% in North India, 0.8-1.28% in East India, and 3.6% in South India [2]. Study has shown an association of higher odds for dementia and Alzheimer's disease (AD) with greater

age (≥75 years), lower education (≤8 years) and female gender based on population with Dementia in Kerala, South India [3]. The prevalence of dementia roughly doubles every five years over the age of 65 years [4]. As per The Dementia India Report 2010, number of people with AD and other dementias is estimated to increase every year in India, the reason being steady growth in the older population and stable increment in life expectancy. Recent study on 'cost of dementia care in India' showed that in 2010, nearly 37 lakh Indians have been estimated to be suffering from dementia [1]. In addition, some families in India often refuse to take dementia specific medications due to high cost and also fear of side effects [5].

In developing countries like India, pharmaco-economics plays an important role in clinical practices of medicines. Treatment of particular diseases which are critical and that take long term treatment is very much influenced by the cost of drugs. Hence, variation in the prices of the same drug manufactured by companies by different brands does affect the affordability especially the poor people. If costly brand is prescribed by a doctor, the person may not be able to complete the treatment. The present study describes utilization pattern of anti dementia drugs and cost-effective analysis of different commonly prescribed anti dementia drugs available in different brands in India.

Materials and Methods

MEDLINE, PUBMED and Web of Science were searched (from 2008-2016) for dementia prevalence, dementia assessment methods, utilization pattern of anti dementia drugs in an Indian Scenario. The literature survey included articles (prospective and retrospective studies) on dementia in an Indian Scenario. The key words used for search was dementia AND/OR Alzheimer's disease AND clinical studies in India.

Cost analysis

Cost of anti dementia drugs (cost per 10 tablets/capsules) in the same strength and dosage forms being manufactured by different companies were sorted out by referring latest Monthly Index of Medical Specialties [6,7]. This source was used to calculate the cost of 10 dosage forms (Tablets/capsules) in INR of each brand, Cost ratio and percentage cost variation of the anti dementia drugs. The calculation was done as follows:
Cost ratio = Maximum cost/Minimum cost

$$\% \text{ cost variation} = \frac{(\text{Max cost} - \text{Min cost}) \times 100}{\text{Min cost}}$$

Results

Cost-effective analysis

Cost ratio: The prices of commonly prescribed anti dementia drugs manufactured by different pharmaceutical companies were analyzed. Table 1 shows cost ratio and % cost variation of different anti dementia drugs. Rivastigmine (1.5 mg capsule) showed highest cost ratio (14.73) and piracetam (**400 mg tablet)** showed lowest cost ratio (2.07).

ATC Classification	Unit (Tablet/capsule)	Quantity	Minimum Price INR	Maximum Price INR	Cost Ratio	%cost Variation
N06DA02-donepezil	5mg tablet	10	60	153	2.55	155
N06DA02-donepezil	10mg tablet	10	60	216	3.6	260
N06DA03 - rivastigmine	1.5mg capsule	10	45	663	14.73	1373.33
N06DA03 - rivastigmine	3mg capsule	10	65	611.66	9.41	841.01
N06DA03 - rivastigmine	4.5mg capsule	10	85	611.66	7.19	619.6
N06DA03 - rivastigmine	6mg capsule	10	105	611.66	5.82	482.53
N06BX03 - piracetam	400 mg tablet	10	26	54	2.07	107.69
N06BX03 - piracetam	800 mg tablet	10	51	300	5.88	488.23

Table 1: % Cost variation of most commonly prescribed anti dementia drugs.

Minimum and maximum price (INR) of most commonly prescribed anti dementia drugs are described in Figure 1. The cost ratio of these drugs is shown in Figure 2.

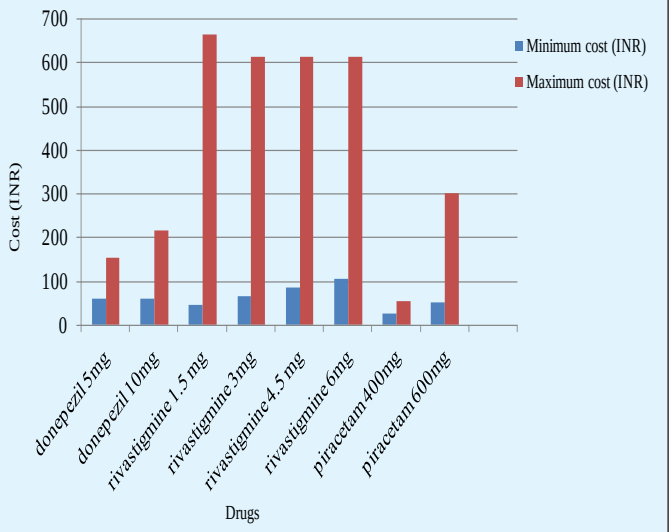

Figure 1: Cost difference [Min and Max] of commonly prescribed anti dementia drugs.

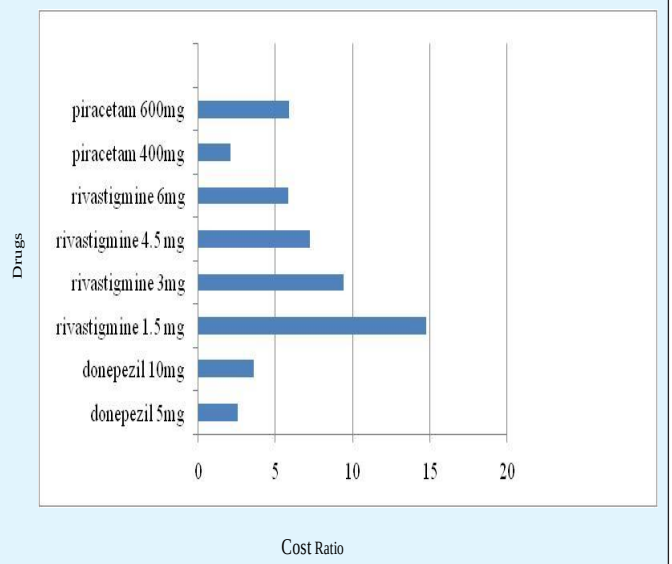

Figure 2: Cost ratio of commonly prescribed anti dementia drugs.

% cost variation: While Rivastigmine (1.5 mg capsule) showed highest % cost variation (1373.33), piracetam (**400 mg tablet) showed** lowest % cost variation (107.69) according to analysis of % cost variation of anti dementia drugs commonly prescribed. However, % cost variation of all the anti dementia drugs was observed to be above 100. % Cost variation of most commonly prescribed anti dementia drugs are shown in Figure 3.

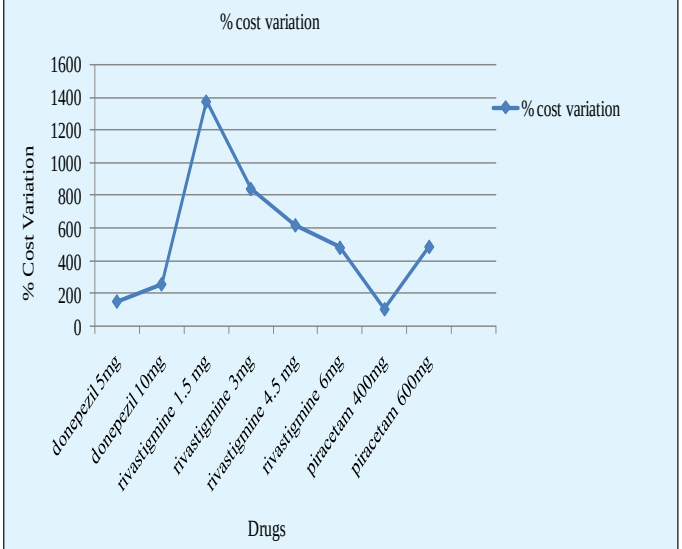

Figure 3: Cost variation of commonly prescribed anti dementia drugs.

Dementia prevalence

The most common subtype of dementia include Alzheimer's disease (45%) followed by Frontotemporal dementia (25%), Vascular dementia (12%), Mixed dementia (6%), Diffuse Lewy body disease (4%) [8]. Others specified 'Unspecified Dementia with Psychoses' to be the most common followed with Vascular dementia, Alzheimer's disease, Unspecified dementia with depression and lastly dementia in Parkinson's disease [9].

A study based on the drug utilization patterns with different types of dementia in Western India indicated Alzheimer's dementia to be the most common (65.6%) followed by vascular dementia (21.6%), and frontotemporal dementia (10.4%), with rarest being Lewy body dementia (2.4%) [10]. Dementia is prevalent in aged people.

Utilization pattern of anti dementia drugs

Dementia Drugs approved for marketing in India is shown in Table 2.

Name of Drug	Pharmacological Classification	Year of approval
Donepezil HCl	For Alzheimer's Dementia	20.03.2001
Memantine HCl	For dementia of Alzheimer's type	19-07-2004
Memantine 5mg /10mg + Donepezil 5mg Tablets	Alzheimer's disease	31-01-2008
Donepezil Hydrochloride Orodispersible Tablet 5mg/10mg	For the treatment of mild to moderate severe Alzheimer's Dementia	15-10-2009
Memantine HCl ER Tablet 28mg	treatment of moderate to severe Alzheimer's disease	6/9/2010
Donepezil Sustained Release Tablet 23mg (Modified Dosage Form)	For the Treatment of Mild to Moderate Severe Alzheimer's Dementia	3/6/2011
Rivastigmine transdermal patch.	for the treatment of patients with severe dementia of the Alzheimer's type	28-10-2014
Rivastigmine capsules 0.5mg/1.0mg/1.5mg/3mg/4mg/5mg/6mg	treatment of patients with mild to moderate dementia of Alzheimer type	31-07-1998

Table 2: Dementia Drugs approved for marketing in India.

Among anti dementia drugs, donepezil (52%) is most commonly prescribed drug followed by memantine (18%) and others. This is followed by prescription of Quetiapine which is atypical antipsychotics given to the patients to manage behavioral and psychological symptoms of dementia (BPSD) [8]. Donepezil hydrochloride is a potent, reversible, and highly selective inhibitor of acetyl cholinesterase (AChE). Other investigators have also described that Donepezil remains the most effective in the treatment of Alzheimer's disease [11]. It has also been observed that transdermal patch extends the release of donepezil for many hours and also ensure enhanced bioavailability [11]. On the basis of safety and efficacy of donepezil hydrochloride therapy, it has been found that donepezil is well tolerated in Indian patients with mild to moderate AD with significant improvement in cognition and function [12].

Other anti dementia drugs such as Galantamine, Rivastigmine is used to a lesser extent. Antipsychotic like Olanzapine and Risperidone is also prescribed but not widely used. Combination of these drugs is prescribed rarely. Serotonin uptake inhibitors such as benzodiazepines are given to patients with frontotemporal dementia. However, due to risks such as falls and amnesia, this drug is often avoided [8]. The description of co-prescribed drug is shown in Table 3.

Study Type	No. of patients (N)	Mean Age	Anti Dementia Drugs prescribed	Co-prescribed drugs	Study Duration	Study Conducted at	Reference
Retrospective chart review	51	65.72	Donepezil (52%)	Atypical Antipsychotics-Quetiapine (47%)	January - December, 2007 (11months)	Geriatric Clinic Outpatient Department of a tertiary center (NIMHANS, Bangalore, India)	[8]
			Memantine (18%)	Resperidone (4%)			
			Galantamine (6%)	Olanzapine (2%)			
			Rivastigmine (2%)				
Prospective, cross	100	64.04	Donepezil (76%)	Antioxidants Antipsychotics	July-August 2011	Neurology and Psychiatry	[9]

sectional study			Memantine (34%)	Antihypersensitives		outpatient department of tertiary care hospitals in Mumbai	
			Piracetam (8%)	Antiemetic			
			Rivastigmine (6%)	Antacids			
				Hypolipedemics			
				Antidepressants and others			
Prospective and Retrospective study-cross sectional study	125	72 ± 2.01	Donepezil (58.4%)	Antipsychotics-	July - December 2013	Tertiary	[10]
			Rivastigmine (13.63%)	Quetiapine (38.46%)		care hospital (ShriKrishna Hospital, H.M.Patel Centre	
			Donepezil + Memantine (6.43%)	Lorazepam (23.07%)		Medical Care & Education, Gokalnagar, Karamsad, Gujarat.)	
			Galantamine (12.83%)	Escitalopram (10.25%)		western India	
				Zolpidem (2.56%)			
				Sertraline (2.56%)			
				Clozapine (11.53%)			
				Nitrazepam (1.28%)			
				Olanzepine (2.56%)			
				Lamotrigine (1.28%)			
				Haloperidol (3.84%)			
				Fluoxetine (1.28%)			
				Tianeptine (1.28%)			

Table 3: Utilization pattern of anti dementia drugs and Co-prescribed drugs.

Donepezil, Galantamine, Rivastigmine are recommended for managing mild to moderate Alzheimer's disease and memantine for moderate to severe Alzheimer's disease [9]. Co-prescribed drugs include antioxidants, antipsychotics, antihypertensives, antiemetic, antacids, hypolipedemics, antidepressants, NSAIDS, anti Parkinson's, anti diabetics [9]. Drug utilization patterns with different types of dementia in Western India showed Donepezil (58.4%) to be most prescribed drug in patients with mild to moderate dementia and Rivastigmine (13.63%) was the second most choice for dementia patients [10]. Other prescribed drugs included Donepezil + Memantine (6.43%), Galantamine (12.83%). It has been observed that vitamin B9, that is folic acid and vitamin B12 is highly prescribed to dementia patients without checking their serum levels [10]. These patients are also co-prescribed with drugs in addition to ant-dementia drugs and this include Antipsychotics such as Quetiapine (38.46%), Lorazepam (23.07%) Escitalopram (10.25%) Zolpidem (2.56%), Sertraline (2.56%) Clozapine (11.53%), Nitrazepam (1.28%) Olanzepine (2.56%), Lamotrigine (1.28%), Haloperidol (3.84%), Fluoxetine (1.28%), Tianeptine (1.28%).

Socioeconomic classification of dementia cases

A study based on Drug utilization pattern with different types of dementia in Western India noted that most dementia cases were found in patients belonging to low socioeconomic class [10]. They observed that almost 8.0% of the patients were illiterate, 56.0% patients were high school graduate. Advanced age, poor literacy level, low socioeconomic status is the risk factors for dementia occurrence.

Discussion

Alzheimer's dementia is the most common dementia prevalent in India followed with vascular dementia. Prospective, cross sectional and retrospective studies reveal that mean age for dementia prevalence is in the range of 64-72 years [8-10]. It means that it is mainly prevalent in aged population. Rivastigmine was approved for marketing in India in the year 1998 before Donepezil drug which was introduced in the year 2001. Interestingly, Donepezil remains to be the most commonly prescribed drugs; however, prescription pattern of other anti-dementia drugs varied in patients visiting different hospitals in India [8]. There is no clear cut reason why donepezil and memantine are most commonly prescribed drugs. However, Donepezil is known to be less expensive than Rivastigmine. Even combination of anti dementia drugs such as Donepezil + Memantine was given to patients in few cases [8]. Evidences based on the prospective, cross sectional and retrospective studies reveal that in addition to anti dementia drugs, most patients were also co-prescribed with atypical antipsychotics, antioxidants, anti hypersensitives, antiemetic, antacids, hypolipedemics, antidepressants etc [8-10]. However, rational use of these co-prescribed drugs is not very evident. Over prescription of drugs to dementia patients in India has been commonly observed, that too without investigating whether it is essential to the patients. This leads to an economic burden to the patients. Hence, this problem needs to be addressed [10].

Cost analysis of anti dementia drugs that are commonly prescribed showed a very high variation in the minimum and maximum price of these drugs being manufactured by many companies across the different brands. The cost ratio for anti dementia drugs was found to be very high. In addition, the % variation in the cost of these drugs was above 100%. Now, India is known to export medicines to various countries at low price, but unfortunately, faces challenges of access to affordable and quality medicine on its own. Since a single drug is being sold under different brand names, therefore, there occurs a large price variation. In India, a wide variation in the prices of same drug with different formulation has a severe economic impact. This affects the affordability of buying a particular drug for poor people. Unawareness about the cost difference of different brands of the same drugs among doctors in India is not uncommon. Thus, if a costly brand is prescribed to the poor people in case of long term treatment such as dementia, they may no longer take the treatment. It is important that Government need to focus on this issue, so that drugs for lifelong diseases are under price control. Also, adverse drug effects and cost effectiveness of the treatments given to these patients need to be addressed.

Conclusion

It is important to create awareness about huge price variation in the drugs not only among general public but also health care providers, government agencies, policy makers so as to reduce economic burden on patients and healthcare system. This will improve affordable healthcare system in India. Overall, more effort is needed to understand and analyze in terms of its prescription, utilization pattern as it has huge socioeconomic impact on patients and caregivers of mainly developing countries like India.

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