



COST ANALYSIS OF DISEASE MODIFYING ANTI RHEUMATIC DRUGS: THE INDIAN SCENARIO

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ABSTRACT

BACKGROUND: Rheumatoid arthritis is a chronic, autoimmune and inflammatory disease affecting the joints and cartilages, eventually leading towards deformity and resultant disability. Today's rheumatologists have an armamentarium of Disease Modifying Anti Rheumatic Drugs (DMARDs) to choose from. The chronicity of the disease, resultant deformities and reduced work capacity adds to the socioeconomic burden of the disease. This study aims to compare the costs of various brands of DMARDs (both biological and non-biological agents), so as to give the readers an idea about the cost range and variation present amongst the available DMARDs. **MATERIALS AND METHODS:** Current Index of Medical Specialties (CIMS India) application was accessed in the month of August 2020 to note the cost of various brands of DMARDs. The information was tabulated. The cost difference and percentage cost variation was calculated and compared. **RESULTS:** The maximum number of brands was available for methotrexate amongst the biological as well as non-biological agents. Least and highest percentage cost variation was observed for 2.5 mg strength of methotrexate and 100 mg of cyclosporine, respectively. In general, biologicals had fewer brands in the market as the cost was considerably higher than the non-biological agents. **CONCLUSION:** There is a wide variation amongst the costs of various DMARDs. This has its own advantages. Conscious choice of economical brands can profoundly effect the socioeconomic burden of rheumatoid arthritis management.

KEYWORDS : DMARDs, Rheumatoid Arthritis, Cost Analysis, Percentage Cost Variation, Pharmacoeconomics, Cost-effectiveness

INTRODUCTION

Rheumatoid Arthritis (RA) is a chronic, autoimmune and inflammatory disease which affects the skeleton and cartilages, leading to significant disability and decreased quality of life. Swollen, stiff and painful joints are the common symptomatology of RA, eventually leading to deformity of joints and resulting disability [1]. According to a literature search study, the prevalence of RA in the Indian population ranges from 0.28% to 0.7% [2].

Rheumatoid arthritis has a profound socio-economic burden. Apart from the cost of medications, functional disability, reduced work capacity and decreased societal participation adds to the socio-economic burden [1]. Early diagnosis and treatment has led to significant reduction of inflammation and consequent damage [3].

The pharmacological management encompasses an armamentarium of disease modifying anti-rheumatic drugs (DMARDs) [1]. With the advent of biological drugs, the pharmacotherapy of RA has been revolutionized, however, at the cost of dramatic increase in the economic burden. The aim of the current study was to evaluate the cost variation of DMARDs amongst different brands in India.

MATERIALS AND METHODS:

Current Index of Medical Specialties (CIMS India) application, as accessed in the month of August 2020, was used to analyze the prices of DMARDs [4]. The search included both biologicals and non-biological agents. Data regarding the cost across various dosage form and strengths were collected. The cost of tablets was collected per 10 tablets (in one strip).

Differences between minimum and maximum cost were calculated for each agent. Percentage cost variation was calculated for each DMARD using the formula below.

$$\text{Percentage Price Variation (PPV)} = \frac{\text{Price of most expensive brand} - \text{Price of least expensive brand}}{\text{Price of least expensive brand}} \times 100$$

Biological DMARDs are available only in injectable form and their strengths are not uniform across different brands. Since the strengths of biological agents were not uniform, dosage requirement of each biological DMARD per month was calculated and compared. The formula for Percentage Price Variation for biological DMARDs was as below.

$$\text{PPV} = \frac{\text{Maximum Cost per Month} - \text{Minimum cost per month}}{\text{Minimum cost per month}} \times 100$$

DMARDs having only one manufacturer was also included. Their minimum and maximum cost were calculated as the same and cost difference and variation was noted as zero. As there was no involvement of patients or any intervention, the ethics committee approval was not required for this study.

RESULTS:

The entire cost-analysis of DMARDs results have been summarized in tables one and two. In general, the number of brands available for a given drug was higher amongst the non-biological drugs versus the biological drugs. Methotrexate had the highest number of brands (thirty-seven) amongst all medications. The lowest number of brands available was for sulfasalazine (six) amongst the non-biologicals and abatacept (one) amongst the biological DMARDs. The highest number of brands available amongst the biological DMARDs was for rituximab (ten).

Lowest percentage price variation was seen with the lowest strength of methotrexate (2.76% with 2.5 mg of methotrexate). This result excludes drugs with a single brand in the market. Highest percentage price variation was seen with the two strengths of cyclosporine (1387.1% with 50 mg and 1428.26% with 100 mg of cyclosporine). Cost analysis of cyclosporine oral solution demonstrated 128.9 percentage price variation.

Oral solutions were costlier than oral tablets.

As the strengths of biological injectables was not uniform, the results for biological DMARDs was obtained after standardizing the readings to total monthly requirement of the medication. Amongst the biological DMARDs, the lowest percentage price variation was observed with adalimumab injection (13.64%) and the highest percentage price variation was observed for etanercept (318.04%).

DISCUSSION:

In India, the "Drug Price Control Order (DPCO), 2013" is referenced by the National Pharmaceutical Pricing Authority (NPPA) to decide the ceiling price of the available drugs [5,6]. Considering the currently increasing healthcare cost and limited healthcare resources, cost analysis is of utmost importance in the setting of chronic diseases including rheumatoid arthritis.

Pharmacoeconomics can be regarded as a branch of health economics which deals with identifying, measuring and comparing the cost of pharmaceutical products and services [7]. Such an analysis helps the physicians to make informed decisions regarding the selection of the most cost-effective management for the patients. Not only the physician but also the patient's preferences must be kept in mind while selecting the desired management, especially in chronic diseases [7].

Our current study focuses upon the cost variation prevailing amongst the different brands of various DMARDs, both biologicals as well as non-biologicals. As commonly known, the difference between the costs of biologicals and non-biologicals was very large, biologicals being very expensive.

Amongst the expensive biologicals, the highest number of brands available in the market was for rituximab. However, the highest percentage of cost variation was for the TNF alpha inhibitor, etanercept. This can be designated to the price reduction due to the availability of economically priced biosimilars by manufacturers.

Cyclosporine 50 and 100 mg demonstrated the highest percentage cost variation amongst the non-biologicals. Lowest cost was demonstrated for methotrexate 2.5 mg in the entire armamentarium of DMARDs, making it favorable choice as a first-line agent.

National List of Essential Medicine (NLEM) is a list of those medications which satisfy the priority health needs of the population. They are selected after meticulous analysis of the disease incidence, prevalence, efficacy, safety and cost-effectiveness. DMARDs viz. methotrexate (5 mg, 7.5 mg and 10 mg), azathioprine (50 mg), sulfasalazine (500 mg), leflunomide (200 mg) and hydroxychloroquine (10 mg and 20 mg) are listed under NLEM 2015 [8].

The limitations of this study is that it doesn't estimate the indirect cost in rheumatoid arthritis management. However, this study can help the treating physicians to estimate minimum and maximum cost estimate of drugs for rheumatoid arthritis. Also, it can encourage the physician to prescribe the generic names of drugs in order to reduce the burden of cost of therapy for the ailing patients. Manufacturers can be urged to venture into the making of more biosimilars in the near future. Reduction in the cost of biological DMARDs due to the advent of more biosimilars can potentially revolutionize the treatment scenario of RA in India.

Table 1: Cost-Analysis of various brands of non-biological DMARDs

Drug Name	ATC Code	Total brands	Dosage Form	Strength (number of brands)	Minimum Cost (INR)	Maximum Cost (INR)	Cost difference	Percentage Price Variation (%)
Methotrexate	L04AX03	37	Tablet	2.5 mg (25)	14.91	56	41.09	2.76
				5 mg (7)	67	89	22	32.84
				7.5 mg (8)	90	134	44	48.89
				10 mg (5)	119.65	187.5	67.85	56.71
Azathioprine	L04AX01	20	Tablet	50 mg (20)	55.12	179.4	124.28	225.48
Cyclosporine	L04AD01	15	Capsule	10 mg (1)	150	150	0	0
				25 mg (11)	221.8	2710.6	2488.8	1122.1
				50 mg (11)	337.3	5016	4678.7	1387.1
				100 mg (11)	639	9765.6	9126.6	1428.26
			Oral Solution	100 mg x 1 ml x 50 ml (8)	3050	6981.42	3931.42	128.9
Sulfasalazine	A07EC01	6	Tablet/Capsule	500 mg (6)	41.42	64.85	23.43	56.57
Hydroxychloroquine	P01BA02	20	Tablet	200 mg (20)	34	85	51	150
Leflunomide	L04AA13	11	Tablet	10 mg (11)	63.52	166.67	103.15	162.39
				20 mg (9)	135.15	316.1	180.95	133.89
				100 mg (1)	177	177	0	0

Table 2: Cost-Analysis of various brands of biological DMARDs

Drug Name	ATC Code	Total brands	Dosage Form	Approximate monthly dose	Minimum Cost per month	Maximum Cost per month	Cost Difference	Percentage cost variation (%)
Etanercept	L04AB01	4	Injection	200 mg	27500	114960	87460	318.04
Infliximab	L04AB02	2	Injection	600 mg	192000	246234	54234	28.25
Adalimumab	L04AB04	4	Injection	80 mg	44000	50000	6000	13.64
Abatacept	L04AA24	1	Injection	1500 mg	180000	180000	0	0
Rituximab	L01XC02	10	Injection	2000 mg	121140	320000	198860	164.16

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