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Article

Medication possession ratio in postmenopausal osteoporotic patients: a cross sectional study

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Osteoporosis is a chronic disease of bone that increases risk of low-trauma fracture. Chronic treatment may lead to lower adherence with medication. The current study aims are to determine adherence rate of antiosteoporotic medication by Medication Possession Ratio. Data has been collected from outpatient settings registering cases of postmenopausal osteoporotic women taking medications for an average duration of one year in Karachi. These patients were classified in lower, middle, and affluent socioeconomic classes. Collected data were analyzed by the standardized formula of Medication Possession Ratio and SPSS. Average Medication Possession Ratio ≥80% achieved by Risedronate Brands in the middle class (80.28%±4.41), the affluent class (82.50%±5.09), Raloxifen Brands in affluent class (93.62%±1.57), Gonadotropics in the middle class (81.36%±6.02), affluent class (91.09%±2.05), Alendronate Brands in affluent class (85.42%±5.46). Average Medication Possession Ratio is <80% with all antiosteoporotic medication in the lower class, while the average Medication Possession Ratio of Calcium and Vitamin D is ≥80% in all groups except lower class. Adherence rate was significantly higher among Alendronate group compare to Risedronate (p=0.044). Medication Possession Ratio is greater than 80% among all classes of low-cost antiosteoporotic medications. In addition, patients on once weekly oral medications are more adherent and compliant compare to oral daily or intranasal medications.

Keywords: Osteoporosis. Chronic. Medication. Adherence. Compliance.

INTRODUCTION

Osteoporosis is a disease pertaining to bone health in which bone mineral density decreases which results in the fragile bone. Osteoporosis is not a life-threatening disease, however, the major issue is hip fracture due to bone fragility.(Raisz 2005, Siris *et al.,* 2006) The 10 years' risk of osteoporotic fracture in women above 50 years is about 5% and this risk increase to 20% by the age of 65 years.(Raisz 2005) Due to such consequences adherence of patients to antiosteoporotic medications is imperative. In health care institutions, the main focus for the determination of adherence to drug therapy is through medication possession ratio (MPR). MPR is measured by dispensed quantity over a short period of time interval or overall length of the time interval.(Sperber *et al.,* 2017) Significantly contributing risk factors in Pakistani postmenopausal women for osteoporosis are; low BMI, personal history of osteoporotic fracture, family history of osteoporotic fracture, smoking, lack of exercise, calcium deficiency, vitamin D deficiency and long term use of corticosteroid.(Khaliq *et al.,* 2017)

The limiting factor for prevention and control of chronic disease is poor compliance with medications. (Cramer and Silverman 2006) Antiosteoporotic medications should be used chronically and may reduce the risk of fracture and indicated for the treatment and prevention of osteoporosis.(McCombs *et al.,* 2004, Cummings 2005)

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However, cost, side effects, and interference with daily life are major factors for poor compliance.(Gold and Silverman 2005, Reginster *et al.,* 2006) Compliance objectives cannot be achieved for asymptomatic diseases like osteoporosis where patients perceive that benefit is low and the cost is high. Bisphosphonate salts are used for the treatment and prevention of osteoporosis, however, 20% patients discontinue these salts within 6 months of prescription.(Segal *et al.,* 2003)

The main objective of the current study is to determine antiosteoporotic drug adherence among Pakistani postmenopausal women suffering from osteoporosis with the help of Medication Possession Ratio (MPR) during drug therapy. MPR is also referred to as adherence rate, it is expressed as a percent of days supply receive divided by period time. These periods may be fixed or variable depending upon the type of treatment and requirements.(Kozma *et al.,* 2013)

MATERIAL AND METHODS

Prospective observational study conducted in different outpatient departments of hospitals, clinics and primary care centers of Karachi city from October 2017 to December 2018. Data has been collected by primary method from 455 postmenopausal women aged 45 and older suffering from osteoporosis, their prescriptions were evaluated and interviewed about the frequency of usage by different brands of calcium, calcium & vitamin D and vitamin D along with different brands of antiosteoporotic medications. The antiosteoporotic medications included in the study are; Risedronate, Calcitonin, Raloxifen, Gonadotropics, and Alendronate. Population is classified as lower, middle and affluent socio-economic class. Medication possession ratio is calculated in percentage from different socioeconomic areas of Karachi. Sample size of study is determined by precision analysis technique by keeping level of significance 5%.(Aparasu 2016) October 01, 2018 was considered as first purchase of medication. Study period was defined on average one year from the date of first purchase. Compliance of these medication was evaluated by Medication Possession Ratio (MPR).(Downey *et al.,* 2006) MPR is also called adherence rate and can be determined by number of supply days per member in 365 days from the first purchase and is expressed in percentage of days within a year. Number of supply days = Number of purchases x Number of pills in packet and by frequency of dosing. For example, if women purchased Bisphosphonate once weekly tablets for one month duration, so she bought four pills. The MPR would be [4 packets x 4 pills x 7 days ÷ 365 days] x 100. Patients will be considered adherent for their medication if MPR is ≥80%. It is assumed that all tablets are taken on time as per physician's recommendations. Statistical analysis of collected data was done on SPSS 20 version software. Descriptive statistics and inferential statistics (t-test) applied.

RESULTS AND DISCUSSION

Medication possession ratio is a method to calculate medication adherence and is defined as being Adherent Patients if the amount of medication furnished to the patient is at least 80% based on days supply of medication divided by the number of days patients should be consuming the medication.(Kozma *et al.,* 2013)

The risk of osteoporotic fracture reduction is not appreciable if MPR is lower than 50%, similary, if MPR is 75-80%, the future risk of osteoporotic fracture is declined 50-75%.(Siris *et al.,* 2006) The study reveals that in lower socioeconomic class Brand C and Brand E of Risedronate salts(Harris *et al.,* 1999) have better adherence compare to Brand A, B, and D as their MPR is ≥80%. Similarly, in the same socioeconomic class Brand C and E of Calcium and Vitamin D has MPR ≥80%. In the middle class only Brand B of Risedronate has a better adherence rate (MPR≥80%) and for Calcium and Vitamin D Brand B and C has a high adherence rate. Similarly, in affluent socioeconomic class Brand C and E has a higher adherence rate of Risedronate salts, while for calcium and Vitamin D, except Brand A, all other brands have MPR ≥80% to prove a higher adherence rate (Table I). Compare to our findings 55% adherence was reported (MPR ≥80%) with weekly Bisphosphonate salts compare to daily i.e. 40%.(Cramer *et al.,* 2005b)

TABLE I - MPR of Riserdronate Brands, Calcium, Vitamin D in different Socioeconomic Classes

Groups (N=38)	Risedronate Brands	Lower Socioeconomic Class		Groups (N=24)	Risedronate Brands	Middle Socioeconomic Class		Groups (N=25)	Risedronate Brands	Affluent Socioeconomic Class	
		MPR* (Calcium, Vitamin D)	MPR* (Antiresoptive)			MPR* (Calcium, Vitamin D)	MPR* (Antiresoptive)			MPR* (Calcium, Vitamin D)	MPR* (Antiresoptive)
1	Brand A	54.79%	63.46%	1	Brand A	71.23%	76.92%	1	Brand A	75.34%	76.92%
2	Brand B	78.08%	76.92%	2	Brand B	87.67%	88.46%	2	Brand B	83.29%	78.85%
3	Brand C	83.29%	88.46%	3	Brand C	91.51%	78.85%	3	Brand C	91.51%	90.38%
4	Brand D	71.23%	73.08%	4	Brand D	72.60%	76.92%	4	Brand D	84.93%	79.85%
5	Brand E	93.15%	96.15%					5	Brand E	84.97%	86.54%
Average MPR*		76.10%	79.61%	Average MPR*		80.75%	80.28%	Average MPR*		84.00%	82.50%
Standard Deviation		12.83%	11.51%	Standard Deviation		8.95%	4.41%	Standard Deviation		5.17%	5.09%

Evaluation of four brands of another antiosteoporotic agent Calcitonin (Intranasal)(Mehta *et al.,* 2003) demonstrated that in lower, middle, and affluent socioeconomic classes, the higher adherence rates are reported by MPR ≥80% of Brand B, Brand C, and D and Brand B respectively. As far as concerned with Calcium and Vitamin D, Brand B and D, Brand C and D, Brand A and B have MPR ≥80% in lower, middle, and affluent socioeconomic classes respectively, so these brands have better adherence (Table II). Raloxifen, an agent used for the treatment and prevention of osteoporosis(Brixen *et al.,* 2005) was also evaluated with two available brands. The MPR is ≥80% of Brand A in the lower class, Both Brand A and B in affluent class, while in middle socioeconomic class, none of the brands are reported to have MPR ≥80%, just Brand A reaches the figure of 79.72%. All brands of Calcium and Vitamin D are having MPR ≥80% with the treatment of Raloxifen among all socioeconomic classes (Table III).

TABLE II - MPR of Calcitonin Brands, Calcium, Vitamin D in different Socioeconomic Classes

Groups (N=38)	Calcitonin Brands	Lower Socioeconomic Class		Groups (N=24)	Calcitonin Brands	Middle Socioeconomic Class		Groups (N=25)	Calcitonin Brands	Affluent Socioeconomic Class	
		MPR* (Calcium, Vitamin D)	MPR* (Antiresoptive)			MPR* (Calcium, Vitamin D)	MPR* (Antiresoptive)			MPR* (Calcium, Vitamin D)	MPR* (Antiresoptive)
1	Brand A	60.27%	58.33%	1	Brand A	68.49%	58.33%	1	Brand A	83.56%	75.00%
2	Brand B	83.29%	83.33%	2	Brand B	77.81%	66.67%	2	Brand B	93.15%	91.67%
3	Brand C	49.32%	33.33%	3	Brand C	94.52%	83.33%	3	Brand C	76.71%	58.33%
4	Brand D	83.56%	50.00%	4	Brand D	91.67%	83.33%	4	Brand D	69.86%	66.67%
Average MPR*		69.11%	56.24%	Average MPR*		83.12%	72.91%	Average MPR*		80.82%	72.91%
Standard Deviation		14.82%	18.04%	Standard Deviation		10.55%	10.82%	Standard Deviation		8.61%	12.32%

TABLE III - MPR of Raloxifen Brands, Calcium, Vitamin D in different Socioeconomic Classes

Groups (N=38)	Raloxifen HCl Brands	Lower Socioeconomic Class		Groups (N=24)	Raloxifen HCl Brands	Middle Socioeconomic Class		Groups (N=25)	Raloxifen HCl Brands	Affluent Socioeconomic Class	
		MPR* (Calcium, Vitamin D)	MPR* (Antiresoptive)			MPR* (Calcium, Vitamin D)	MPR* (Antiresoptive)			MPR* (Calcium, Vitamin D)	MPR* (Antiresoptive)
1	Brand A	88.35%	81.64%	1	Brand A	83.28%	79.72%	1	Brand A	97.26%	95.20%
2	Brand B	86.30%	77.80%	2	Brand B	80.82%	75.61%	2	Brand B	96.43%	92.05%
Average MPR*		87.32%	79.72%	Average MPR*		82.05%	77.66%	Average MPR*		96.84%	93.62%
Standard Deviation		1.025%	1.92%	Standard Deviation		1.23%	2.055%	Standard Deviation		0.415%	1.575%

Hormone replacement therapy (HRT) also termed as gonadomimetics are also indicated in postmenopausal osteoporosis.(Gambacciani and Levancini 2014) Two commercial brands of these agents demonstrated that Brand B in the lower class and Brand A and B in affluent class has a higher adherence rate (MPR ≥80%), while in lower socioeconomic classes, these agents are having poor compliance. Calcium and Vitamin D demonstrated higher compliance in these groups of patients in all socioeconomic classes (MPR ≥80%) (Table IV). Another very commonly prescribed antiosteoporotic medication is Alendronate.(Bone *et al.,* 2004) Data of overall

eight brands of Alendronate confirmed that in lower socioeconomic class Brand A and E have MPR ≥80% and these groups of patients have an acceptable adherence rate. Similarly, for middle-class Brand C, D and F are having MPR ≥80%, while in affluent class Brand B, C, D, E, F, and H have MPR ≥80%. In these groups of patients, calcium and vitamin D compliance were better (MPR ≥80%) of Brand C and E in lower socioeconomic class, Brand A, D, and E in the middle-class while Brand C, D, E and G in affluent class (Table V). Among new users of Bisphosphonate salts, the one-year adherence rate (MPR ≥80%) is about 43%.(Penning-van Beest *et al.,* 2006)

TABLE IV - MPR of Gonadomimetics Brands, Calcium, Vitamin D in different Socioeconomic Classes

Groups (N=38)	Gonadomimetic Agents (HRT**) Brands	Lower Socioeconomic Class		Groups (N=24)	Gonadomimetic Agents (HRT**) Brands	Middle Socioeconomic Class		Groups (N=25)	Gonadomimetic Agents (HRT**) Brands	Affluent Socioeconomic Class	
		MPR* (Calcium, Vitamin D)	MPR* (Antiresoptive)			MPR* (Calcium, Vitamin D)	MPR* (Antiresoptive)			MPR* (Calcium, Vitamin D)	MPR* (Antiresoptive)
1	Brand A	84.10%	73.97%	1	Brand A	92.46%	75.34%	1	Brand A	95.89%	93.15%
2	Brand B	80.82%	59.17%	2	Brand B	82.46%	87.39%	2	Brand B	96.43%	89.04%
Average MPR*		82.46%	66.57%	Average MPR*		87.46%	81.36%	Average MPR*		96.16%	91.09%
Standard Deviation		1.64%	7.40%	Standard Deviation		5.00%	6.025%	Standard Deviation		0.270%	2.055%

TABLE V - MPR of Alendronate Brands, Calcium, Vitamin D in different Socioeconomic Classes

Groups (N=38)	Alendronate Brands	Lower Socioeconomic Class		Groups (N=24)	Alendronate Brands	Middle Socioeconomic Class		Groups (N=25)	Alendronate Brands	Affluent Socioeconomic Class	
		MPR* (Calcium, Vitamin D)	MPR* (Antiresoptive)			MPR* (Calcium, Vitamin D)	MPR* (Antiresoptive)			MPR* (Calcium, Vitamin D)	MPR* (Antiresoptive)
1	Brand A	78.08%	80.77%	1	Brand A	89.04%	78.85%	1	Brand A	68.49%	78.85%
2	Brand B	69.86%	73.08%	2	Brand B	79.45%	78.85%	2	Brand B	76.71%	84.62%
3	Brand C	83.29%	78.85%	3	Brand C	76.71%	80.77%	3	Brand C	87.67%	88.46%
4	Brand D	63.01%	65.38%	4	Brand D	94.52%	90.38%	4	Brand D	100.00%	92.31%
5	Brand E	90.41%	84.62%	5	Brand E	84.93%	76.92%	5	Brand E	87.67%	93.00%
				6	Brand F	78.36%	84.62%	6	Brand F	65.75%	82.69%

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TABLE V - MPR of Alendronate Brands, Calcium, Vitamin D in different Socioeconomic Classes

Groups (N=38)	Alendronate Brands	Lower Socioeconomic Class		Groups (N=24)	Alendronate Brands	Middle Socioeconomic Class		Groups (N=25)	Alendronate Brands	Affluent Socioeconomic Class	
		MPR* (Calcium, Vitamin D)	MPR* (Antiresoptive)			MPR* (Calcium, Vitamin D)	MPR* (Antiresoptive)			MPR* (Calcium, Vitamin D)	MPR* (Antiresoptive)
				7	Brand G	71.23%	71.15%	7	Brand G	93.15%	76.92%
				8	Brand H	75.34%	76.92%	8	Brand H	71.23%	86.54%
Average MPR*		76.93%	76.54%	Average MPR*		81.19%	79.80%	Average MPR*		81.33%	85.42%
Standard Deviation		9.66%	6.70%	Standard Deviation		7.22%	5.35%	Standard Deviation		11.72%	5.46%

In the descriptive statistical analysis of data, it has been found that mean MPR of Risedronate in lower, middle, and affluent socioeconomic classes are 79.61%, 80.28%, and 82.50%, which is fairly logical that lower class in developing countries have low buying power of many medications.(Tanimura *et al.,* 2014) A similar analysis of Calcitonin reveals that regardless of socioeconomic classes MPR is <80%, the probable reason is its intranasal mode of administration.(Combe *et al.,* 1997) Mean MPR ≥80% of Raloxifen is only reported in affluent socioeconomic class despite the cost effectiveness of this medication. (Sheehy *et al.,* 2009) HRT (Gonadomimetics) treatments are costly compare to other antiosteoporotic medications,(Zethraeus *et al.,* 2002) because of this probable reason mean MPR of HRT is ≥80% only in middle and affluent socioeconomic classes. Despite the reasonable cost of Alendroante, mean MPR ≥80% was only found in affluent class.

Alendronate sodium and Risedronate sodium are very commonly prescribed bispohosphonate salts in the treatment and prevention of Osteoporitic fractures. (Silverman *et al.,* 2007) These medications are oral agents, their comparative evaluation of adherence rate among different socioeconomic classes establish that Alendronate adherence rate is significantly higher among all classes compare to Risedronate, alike overall adherence rate is better significantly with Alendronate in the whole population compare to Risedronate (t = -2.537, p=0.044) (Table VI). J. Kertes et al. (2008) reported that 53% of women 45 years and above are compliant with Bisphosphonate salts and on average women discontinue these salts in seven months.(Kertes *et al.,* 2008) In another comparison, the average persistence was 196 days compared to 216 days of Bispohosphonate salts.(Cramer *et al.,* 2005a) In general, compliance is poor for the dosages require daily administration compare to weekly doses.

TABLE VI - Medication Adherence with Riserdronate, Alendronate, Calcium, Vitamin D in different Socioeconomic Classes

Alendronate, Calcium, Vitamin D			Risedronate, Calcium, Vitamin D		t-test Significance (p<0.05)
Class	**Medication**	**Adherence %**	**Medication**	**Adherence %**	
Lower Socioeconomic	Calcium, Vitamin D	49.67% (N=75)	Calcium, Vitamin D	39.47% (N=15)	t = - 2.537 (p=0.044)
	Alendronate sodium 70mg	42.38% (N=64)	Risedronate sodium 35mg	39.47% (N=15)	
Middle Socioeconomic	Calcium, Vitamin D	50% (N=76)	Calcium, Vitamin D	50% (N=12)	
	Alendronate sodium 70mg	46.71% (N=71)	Risedronate sodium 35mg	25% (N=06)	
Affluent Socioeconomic	Calcium, Vitamin D	62.20% (N=51)	Calcium, Vitamin D	56% (N=14)	
	Alendronate sodium 70mg	67.07% (N=55)	Risedronate sodium 35mg	40% (N=10)	
All Socioeconomic	Calcium, Vitamin D	52.46% (N=202)	Calcium, Vitamin D	47.13% (N=41)	
	Alendronate sodium 70mg	49.35% (N=190)	Risedronate sodium 35mg	35.63% (N=31)	

CONCLUSION

MPR is greater than 80% regardless of socioeconomic class of low-cost antiosteoporotic medications. In addition to this finding, patients on once weekly oral medications are more adherent and compliant compare to oral daily or intranasal medications.

CONFLICT OF INTEREST

All authors declare no conflict of interest.

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