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SHORT COMMUNICATION

Status quo of osteoporosis treatment in Japan disclosed by the National Database of Health Insurance Claims and Specific Health Checkups: too late in treatment initiation and too few in treated patients?

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Abstract

Summary For the first time ever, the details of osteoporotic treatment were unveiled through the big data published by the government of Japan. The number of patients being treated is low and treatment start is late, especially in men. Our data are useful for education to not only patients but also doctors.

Purpose To analyze the current status and trend of osteoporosis treatment in Japan by analyzing the data on main drugs for osteoporosis disclosed in the National Database open data.

Methods We used the National Database open data released by the Ministry of Health, Labour and Welfare in September 2018. Data on bisphosphonates, denosumab, and teriparatide were extracted to calculate the number of patients treated with these drugs based on the number of prescriptions filed. Using these prescription numbers, the proportion of patients treated with bisphosphonates, denosumab, or teriparatide among osteoporosis patients was calculated. Further, the data on the incidence of hip fractures were employed to validate the appropriateness of the timing of treatment initiation to osteoporosis patients in Japan.

Results The number of patients in men administered bisphosphonates, denosumab, or teriparatide was about one tenth of that in women. The proportion of osteoporosis patients in men treated with bisphosphonates, denosumab, or teriparatide was highest in age group over 80 years at 19.4%. The proportion of osteoporosis patients in women treated with bisphosphonates, denosumab, or teriparatide was highest in age group 70–79 years at 23.7%. The incidence of hip fractures increases sharply over 80 years of age in both genders.

Conclusion Our findings suggested that osteoporosis treatment should be initiated in younger age, especially in men, in order to avoid osteoporotic fractures in Japan.

Keywords Bisphosphonate · Denosumab · Teriparatide · National Database open data · Osteoporosis · Universal healthcare system

Introduction

In Japan, all citizens are covered by public health insurance under a universal healthcare system that was established in 1961. In October 2016, the Ministry of Health, Labour and Welfare released, for the first time on the World Wide Web (web), the National Database of Health Insurance Claims and Specific Health Checkups of Japan (NDB), which contain the big data on public health insurance claims.

Before the release of the NDB, the data on the treatment of osteoporosis (OP), such as types of drugs used, doses, gender, and age groups of patients where treatment is provided, had been available only at a hospital level. However, the data on the usage of drugs offered under the Japanese national healthcare system are now open to the public.

Osteoporosis has no subjective symptoms until fracture occurs. In particular, hip fractures significantly reduce the quality of life, and fracture prevention is therefore most

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important in osteoporosis clinic. To implement osteoporosis treatment nationwide at appropriate time and stage in Japan, it is inevitable to know the status quo of osteoporosis treatment using big data opened to public recently.

This study aimed to analyze patterns and trends in the usage of bisphosphonate (BP), denosumab (Dmab), and teriparatide (TPTD) for the treatment of OP patients according to gender and age groups, using the third NDB open data released in 2018 [1]. Earlier, we reported the regional difference of rheumatoid arthritis treatment in Japan using the NDB open data released in 2016 [2].

Methods

In the third NDB open data set released in 2018, the number of drug prescriptions issued by medical institutions throughout Japan as insurance claims between April 2016 and March 2017 (fiscal 2016 year) was disclosed according to age and gender. The number of tablets, vials, or syringes of each drug prescribed daily to a patient was multiplied by prescription days to enumerate the annual total number for each patient. The annual total number of a drug for the entire country was calculated by summing up the annual total number for each patient. Top 100 most frequently prescribed drugs were released in the NDB. Drugs with less than 1000 prescriptions a year were excluded from the database. Administration method was classified into two categories: oral or infusion/injection. The number of prescriptions of original and generic forms was also disclosed along with the unit price of each drug according to in-hospital prescription, prescription by out-of-hospital pharmacy, and prescription for inpatients.

From all the disclosed drugs approved for national health insurance reimbursement for OP, only BP, Dmab, and TPTD were selected in this study. These are "anchor drugs" for OP with evidence that the fracture prevention effect is high [3].

The data on BP, Dmab, and TPTD extracted from the third NDB open data were classified by dosing interval (daily, weekly, monthly, and every 6 months). The number of prescriptions was divided, for daily formulations, by 365 (days/year); for weekly formulations, by 52 (weeks/year); for monthly formulations, by 12 (months/year); and for 6-month formulations, by 2 (half a year/year) to calculate the numbers of patients administered each drug which were stratified by gender and age group. The number of patients with osteoporosis in each age group and gender was obtained from the data previously published [4]. Japan's population data for 2016 were retrieved from the 2016 census data [5]. By using these data, we obtained the rough estimate of which percent of OP patients were receiving BP, Dmab, or TPTD according to age group and gender.

The data on the incidence of hip fractures were obtained from the previous publication [6] to analyze the appropriateness of the timing of treatment initiation for OP in Japan.

The statistical analysis of Fig. 2 was performed by a chi-square test.

Results

The number of individuals administered BP, Dmab, and TPTD in fiscal 2016 year was calculated to be 1,902,880, 309,999, and 131,569, respectively, assuming that all of them used these drugs throughout the whole year. When classified in gender, the number of individuals administered BP, Dmab, and TPTD in men was 176,152, 24,757, and 14,865, respectively. The number of individuals administered BP, Dmab, and TPTD in women was 1,722,969, 284,447, and 116,188, respectively. These numbers comprised 9% by men and 91% by women, showing that the number of patients in women was ten times higher than that in men (Fig. 1). The estimated number of patients treated with BP was 9.3% in men and 90.7% in women. The estimated number of patients treated with Dmab was 8.0% in men and 92.0% in women. The estimated number of patients treated with TPTD was 11.3% in men and 88.7% in women.

The estimated number of patients treated with BP, Dmab, or TPTD was less than 25% of those with osteoporosis in each age for both men and women (Fig. 2). Percentages of OP patients to the general population in men were 6.5%, 7.0%, 22.3%, and 13.0% at age groups 50–59, 60–69, 70–79, and over 80 years, respectively, whereas those in women were 4.8%, 22.2%, 42.9%, and 65.1% at age groups 50–59, 60–69, 70–79, and over 80 years, respectively. The ratios of OP patients treated to the whole OP patients in men were 2.2%, 5.2%, 4.8%, and 19.4% at age groups 50–59, 60–69, 70–79,

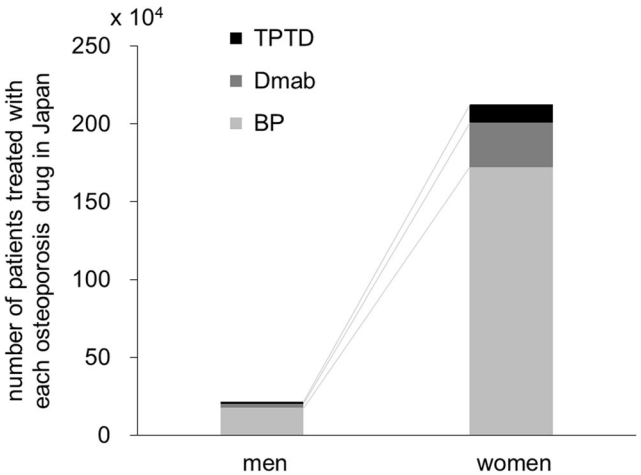

Fig. 1 The gender difference in the number of calculated patients receiving bisphosphonate, denosumab, or teriparatide. TPTD, teriparatide; Dmab, denosumab; BP, bisphosphonate

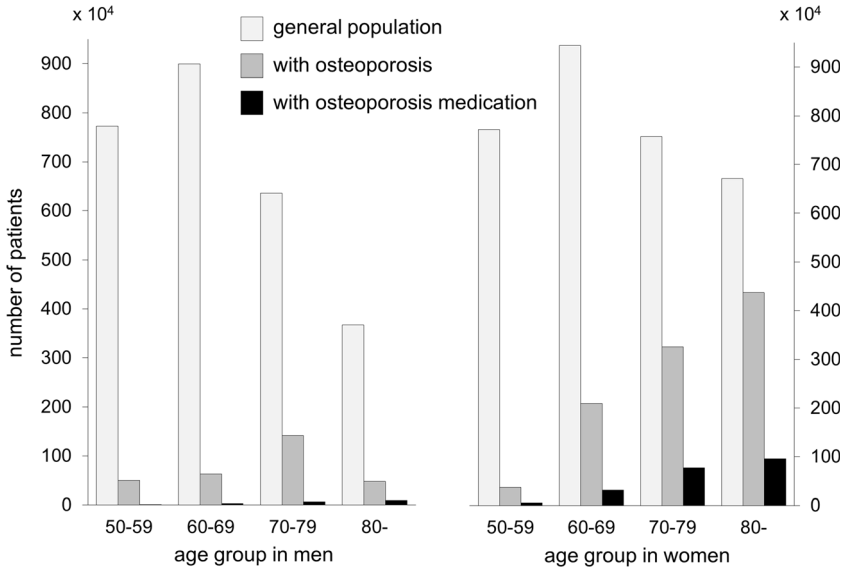

Fig. 2 The stratified number by age groups of the number of general population, patients with osteoporosis, and osteoporosis patients being treated with bisphosphonate, denosumab, or teriparatide in men and women

and over 80 years, respectively, whereas those in women was 15.6%, 14.9%, 23.7%, and 21.9% at age groups 50–59, 60–69, 70–79, and over 80 years, respectively. The rate of treatment with bisphosphonates, denosumab, or teriparatides was significantly lower in men than women in all age groups at 50s, 60s, 70s, and over 80 years of age ($P < 0.01$).

Discussion

There is an estimation that 3 million men and 9.8 million women have OP in Japan [4]; the prevalence is three times higher in women than in men. However, the man-to-woman ratio in patients who received BP, Dmab, or TPTD was 1:10, which was substantially different from the man-to-woman OP ratio. Considered from these figures, OP treatment might be inadequate in men in Japan.

The ratio of OP patients to the general population in men was the highest in the age group 70–79 years. However, the ratio of OP patients treated to OP patients in general in this age group was actually lower than that in the age group 60–69 years. There was a sharp increase in this ratio in men in the age group over 80, compared to that in the age group 70–79. This might imply that OP patients in men under 80 years of age were considerably undertreated. OP patients in men aged 80 years or older decreased greatly in number, and this might suggest that patients without OP drugs had a poorer prognosis than those with OP drugs.

The ratio of OP patients to general population in women increased with each age group by approximately 20%, whereas the ratio of OP patients with OP drugs to OP patients was approximately 15% in both 50–59 years and 60–69 years groups and increased by approximately 10%, reaching a peak in the 70–79 years group. Many patients in women have menopause in their 50s, which may be a chance to initiate OP treatment. This may explain why ~ 15% of patients in this age group receive OP treatment, compared to men of the similar ages with very little OP treatment. The incidence of OP increases with age and the older people should preferably receive more frequently OP treatment in order to prevent osteoporotic fractures. However, in reality, the frequency of OP treatment was not increasing with the patients' age.

The annual incidence of hip fractures per 10,000 population is higher among older individuals, particularly showing a sharp increase among those aged 70 years or older in Japan [6, 7]. According to Tamaki et al., the patients included were those who received any osteoporosis treatment agent [7]. On the other hand, in our report, only patients who were treated with major osteoporosis treatment agents such as bisphosphonates, denosumab, or teriparatides were included. Treatment rate in the present paper is about half of that from Tamaki et al.'s. Many OP patients might not have received OP treatment until a bone fracture develops in Japan. There is evidence that vertebral fracture risk decreases among women who receive alendronate. Alendronate is effective in reducing the risk of symptomatic osteoporotic fractures in patients of 55–85 years of age [8, 9]. Alendronate reduces vertebral body fracture risk 1 year after initiation and the fracture risk decreases by 48% after 5 years of alendronate continuation [10].

In consideration of a sharp increase of hip fractures in patients of 70 years or older, OP treatment should be started at least before 70 years in order to prevent osteoporotic hip fractures.

This study is based on data from Japanese health insurance records under universal insurance system. Although we did not know from those data which patient received which drug vis-à-vis, the analysis from an unprecedented scale of big data was closer to the real world than that from institution-based small data.

Conclusion

OP treatment may be better if introduced earlier at the stage when patients have no symptom and should be implemented more widely in Japan, especially in men.

Compliance with ethical standards

Conflicts of interest None.

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