Efficacy of Aldren 70® Compared with Fosamax® in Terms of Bone Resorption Marker in Postmenopausal Osteoporosis

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Objective: *To compare the efficacy of Aldren 70® to Fosamax 70® once-a-week in term of bone resorption marker, along with their safety, adverse events and adherence.*

Material and Method: *With approval of the Ethical Committee, 74 postmenopausal osteoporosis were recruited in the randomized controlled trial. Each group has taken the drug every week for 24 weeks. The serum levels of bone resorption marker (CTX) were also collected at 12, and 24 weeks after taking medicine. The adverse events and evidence of osteoporotic fracture were interviewed and evaluated at regular intervals.*

Results: *The percentages of serum CTX reduction were not significantly different between both drugs at 12 weeks (66.3% in Aldren 70® group and 66.6% in Fosamax® group) and also at 24 weeks (71.1% in Aldren 70® group and 62.6% in Fosamax® group). Non drug response has been revealed 20% in Aldren 70® group and 23.5% in Fosamax® group. In relation to drug disintegration time, both drugs have resulted in same prevalence of side effects to gastrointestinal system. Although, Aldren 70® group had 10.8% of upper GI side effects and Fosamax® group had only 2.7%, but there is no statistical difference between both groups. Non-adherence rate was not significantly different in both groups. However, non-adherence with once a week bisphosphonate was 17.6% in 12 weeks and 26.2% in 24 weeks after starting treatment.*

Conclusion: *Aldren 70® was comparable to Fosamax® in terms of efficacy in reducing serum level of bone resorption maker (serum CTX) after 12 and 24 weeks of treatment. The adverse events in both groups were in an acceptable range and had no statistical difference.*

Keywords: *bisphosphonates, osteoporosis, post menopause, bone marker, adherence*

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Osteoporosis has been reported in one third of the postmenopausal women in Europe[1]. In Thailand, this problem also involves a large number of women. In 2001, 50 percent of Thai women older than 70 years old had osteoporosis[2]. Severe osteoporosis significantly increases risks of subsequent fractures, mortality, and decreases quality of life[1,3]. According to the high prevalence, severe complications and unwanted consequences, osteoporosis is a very important problem.

At present, there are many treatments and modalities proved to prevent osteoporosis and its consequences. The primary goal of treatment is to reduce the incidence of osteoporosis related fractures. Among the treatments, bisphosphonates has been established to be the first line drug for patients with postmenopausal osteoporosis since they have been proved to effectively reduce bone resorption and prevent osteoporotic fractures[4]. According to national policy and economic level of the country, cost, risks, and efficacy of the treatment should be considered carefully.

Alendronate is one of bisphosphonates that has evidence supports that it can increase bone density, decrease risk of vertebral and non-vertebral fractures. However, the price of the original drug is expensive. In recent years, the advent of generic bisphosphonates with a substantial decrease in price and the impact on cost-effectiveness of osteoporosis treatment. ALDREN 70® is one of the generic alendronate cost 60% cheaper. The generic formulation is expected to have the same clinical efficacy as branded formulation based on bioequivalence study. A bioequivalence study is a randomized clinical study in healthy volunteers, which compares the bioavailability between the test product and a reference product. This will include a comparison of absorption (area under the curve, AUC), the rate of absorption (Tmax) and peak concentration (Cmax) based on

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serum concentration or more usually with the bisphosphonates on cumulative urinary excretion (Ae)[5]. However, a high proportion of generic formulations of alendronate is associated with poorer tolerance and more adverse events than the branded compound. One of the probable mechanisms maybe the disintegration time which causes from the differences in the formulation of the excipients, rather than the content of active product[5,6]. Therefore, without a prospective randomized control study to evaluate its efficacy, compliance, and adverse events in the osteoporosis patients, the level of the evidence is limited.

The present study aimed to evaluate the potential differences in efficacy and tolerability of the generic drug (ALDREN 70®) compared with the original drug (Fosamax®), in terms of decrease in bone resorption marker, compliance, and side effects in postmenopausal women with osteoporosis.

Material and Method

With approval of the Ethical Committee, the authors conducted an open-labeled single-blinded prospective randomized controlled trial to compare efficacy of generic alendronate, ALDREN 70® with branded alendronate, Fosamax® in postmenopausal women with osteoporosis. Study population was postmenopausal women aged more than 60 years old visited the Orthopaedic out-patient clinic of Ramathibodi Hospital. The inclusion criteria were patients who had the BMD T-score of femoral neck or total hip lower than -2.5 or had T-score lower than -2.0 with high serum level of bone resorption marker (CTX or beta-CrossLaps was higher than 450 pg/ml or about +1 standard deviation of the average level of healthy pre-menopausal women)[7,8], normal complete blood count, liver function tests, normal kidney function, and normal levels of alkaline phosphatase, calcium, and phosphate, no history of peptic ulcer, gastrointestinal tract problems, diabetes, rheumatoid arthritis, or abnormal of genitourinary system, and willing to participate the study after informed consent. The authors excluded patients who had previous osteoporotic fracture, could not sit or stand upright for more than 30 minutes after taking the medicine, have had concurrent treatment of antiplatelet drugs or anticoagulants in the past 3 months and during the study periods.

The randomization was done under block of four technique using STATA 11.0 program (StataCorp, College Station, Texas) to imply the randomization numbers into either Fosamax® or Aldren 70® group. In Fosamax® group, the patients were given the original medicine (Fosamax® 70 mg, Merck & Co., Inc., Whitehouse station, NJ, USA.) and in Aldren 70® group, the patients were given the generic medicine (ALDREN 70®, Cadila Healthcare Limited, India).

The randomization number and assigned medicine were concealed in a sealed envelope by a pharmacist who did not involve in the evaluation of the study. The patients knew the medicine they took after open the envelope, since the shape and color of both drugs were different. However, the assessors were blinded and did not know the group assigned medication. All patients were informed that they had to take one pill weekly, early in the morning and they should stay upright for more than 30 minutes after taken medicine to prevent esophageal irritation or gastroesophageal reflux. All participants had assigned medicine for 24 consecutive weeks, along with daily 1,250 milligrams of calcium carbonate and 400 IU of vitamin D2 in a form of multivitamin tablet during the study. They were asked to be followed up at 12 and 24 weeks interval. Telephone calls by a clinical research associate were made in every 4 weeks to interview for adverse events and to reassure the patients' concerns.

All baseline characteristics were recorded, such as age, age at menopause, underlying diseases, BMD of the hip, liver function test, kidney function test, level of alkaline phosphatase, calcium, and inorganic phosphate. The bone resorption marker CTX in serum was also measured by electro-chemiluminescence immunoassay (ECLIA, Roche Diagnostics GmbH, Mannheim, Germany) at the beginning of the study. The total analytical CV (coefficient of variation) of ECLIA for CTX was <4.7% and intra-individual CV was 9.6%, so the least significant change (LSC) which can be considered statistically different was calculated as 30%[9,10]. Because of its low CV and large change with antiresorptive therapy, serum CTX has greater utility for assessing efficacy of bisphosphonate treatment than other markers.

At 12th and 24th week, the patients visited the Orthopaedic clinic for follow-up and all the pills left in their envelopes were counted to assess their compliances by a pharmacist.

The serum levels of bone resorption marker (CTX) were also collected at 12, and 24 weeks after taking medicine. The possible side-effects or adverse events such as nausea, vomiting, and heartburn and

also evidence of osteoporotic fracture of the wrist, the hip, and the spine were interviewed and evaluated by the clinical research associate who was well-trained and unawared of the randomized groups.

The results were analyzed based on intention-to-treat analysis. Continuous variables were reported using mean and standard deviation (mean+SD). Categorical variables were reported by the percentage. To compare continuous and categorical results between the 2 groups, the unpaired T-test and Fisher's exact test were employed, respectively. The significant level was defined at *p*-value less than 0.05. The statistical analysis was performed using STATA 11.0 (StataCorp, College Station, Texas, USA)

Sample size was calculated using Power and Sample Size Program (Vanderbilt), based on the hypothesis that Aldren 70® is effective in reducing the serum level of CTX after 12-24 weeks of medication. The level of clinical significant difference was 0.15 and standard deviation was 0.2[9,10]. The calculated sample size was 29 patients, plus 20% of loss to follow-up, lead to the total number of 35 in each group.

Results

From 210 postmenopausal women, 74 patients were met the inclusion criteria. The patients were randomly assigned into 2 groups, 37 patients in each group. Overall baseline characteristics of the patients were similar. Their mean age were 63.4±5.4 years in Fosamax® group and 62.4±7.7 years in Aldren 70® group. Average menopausal age were 50.2±4.4 years and 49.1±4.1 years in Fosamax® group and Aldren 70® group, respectively. History of underlying diseases were reported in 22 of 37 (59.5%) in Fosamax® group and 18 of 37 (48.7%) in Aldren 70® group, shown in Table 1. Means of bone mineral density (BMD) of femoral neck, and means of total hip BMD were not significantly difference between both groups. Means of T-score were also similar, -2.5±0.4 in Fosamax® group, and -2.6±0.5 in Aldren 70® group with *p*-value of 0.439. (Table 1).

In Fosamax® group, means of CTX at pre-treatment, 3 months, and 6 months were 536.8±194.6, 176.3±114.6, and 184.4±166.3 pg/ml., respectively. In Aldren 70® group, means of CTX were 602.4±364.4, 229.3±333.8, and 197.4±356.3 pg/ml. at pre-treatment, 3 months, and 6 months, respectively. The means of CTX at pre-treatment were not significantly different between groups, *p*-value = 0.234 (Table 2). However, the means of CTX were reduced significantly after treatments in both groups with *p*-value less than 0.001, (Fig.1). Percentage of CTX reduction by time were similar in patients who were treated with Fosamax® and Aldren70®, *p*-value was 0.299, (Fig.2).

Among the patients who took Fosamax®, 8 out of 37 patients (21.6%) reported side effects. Four of them had fever, two had myalgia, two had skin rash, and one of them had dry mouth and oral burn. Whereas the patients who took Aldren 70®, 8 out of 37 patients (21.6%) had side effects, three had fever, two had myalgia, two had gastritis, two had constipation, and two had dry mouth or oral burn. The comparison between both groups showed the overall adverse events were not significantly different with *p*-value of 1.000. Percentage of loss to follow-up were 8.1% in Fosamax® group and 5.4% in Aldren 70® group, *p*-value was 1.000. The percentage of patients who did not respond to bisphosphonate treatment, were similar in both groups. In Fosamax® group, 8 out of 34 patients (23.5%) were revealed less than 55% of the serum CTX reduction after treatment at 3 months and 8 out of 31 patients (25.8%) at 6 months. In Aldren 70® group, the serum CTX reduction was less than 55% in 7 out of 35 patients (20%) at 3 months and 5 out of 30 patients (16.7%) at 6 months. Regarding the serum level of bone turnover marker, the optimal suppression of CTX (less than 150 pg/ml) was reported in 18 of 34 patients (52.9%) at 3 months and 18 of 31 patients (58.1%) at 6 months in Fosamax® group. In Aldren 70® group, optimal CTX level was found in 19 out of 35 patients (54.3%) at 3 months and 22 of 30 patients (73.3%) at 6 months without statistical significance between both groups and both intervals, (Table 3).

Percentage of the patients, who had CTX level less than 100 pg/ml at 3 months and 6 months, were 26.5%, 48.4% respectively in Fosamax® group and were 34.3%, 43.3% respectively in Aldren 70® group. And percentage of participants with CTX level less than 100 pg/ml were also not significantly different, (Table 3).

Percentage of non-compliance were 10.8% in Fosamax® group and 24.3% in Aldren 70® group, which was not significantly different with *p*-value of 0.221. Non drug response rates were also not significantly different, 23.5% in Fosamax® group and 20.0% in Aldren 70® group, *p*-value was 0.777, (Table 3).

Discussion

Branded alendronate has been reported in randomized control trials that it can significantly increasing bone mineral density and lowering risks

of vertebral fracture, hip fracture, and non-vertebral fracture[11,12]. Bone turnover markers or biochemical markers for bone turnover have the ability to detect changes in bone turnover rate as early as two weeks of starting treatment, and usually between 1 and 6 months[13]. They are relatively cheap and non-invasive, which can be measured from the fasting blood ampling in the early morning. Bone resorption marker, especially carboxy-terminal telopeptide cross-linked type 1 collagen (CTX), is highly sensitive in monitoring the efficacy of bisphosphonate treatment and is also useful to confirm compliance with oral bisphosphonate therapy.

From this randomized controlled trial, Aldren 70® was comparable to Fosamax® in terms of efficacy in reducing serum level of bone resorption maker (serum CTX) after 3 and 6 months of treatment. The percentages of serum CTX reduction were not significantly different between both drugs at 3 months (66.3% in Aldren 70® group and 66.6% in Fosamax® group) and also at 6 months (71.1% in Aldren 70® group and 62.6% in Fosamax® group). The significant decrease in bone resorption marker (CTX) determines the response to oral bisphosphonate therapy. Usually 40-70% reduction from baseline was found in these anti-resorptive drugs[9,14] and a decrease in CTX concentration of more than 50% from the baseline correlates with a reduction in fracture risk[15,16]. Regarding the recommendation of the International Osteoporosis Foundation (IOF) for monitoring osteoporosis treatment, a reduction of CTX of more than 55% is a cut-off point to indicate the individual response to bisphosphonate therapy[17,18]. So we defined the participants who had CTX reduction less than 55% as non-responders to bisphosphonate. Non drug response has been revealed 20% in Aldren 70® group and 23.5% in Fosamax® group after 3 months of treatment, and no more patients in either group had further responded to treatment at 6 months. This delineates that the percentage of non-responder to oral alendronate, particularly Thai participants in the present trial, was rather high by monitoring the change of bone resorption marker. On the contrary, Alendronate and other bisphosphonates are potent anti-resoptive agents, and all of them have to administer to patients in the fixed dose as recommended by the manufacturers. An over-suppression of bone turnover may occur and lead to frozen bone with a very slow rate of remodeling cycle. The consequences of this condition are highly morbid, including atypical femoral fracture and osteonecrosis of the jaw. Therefore, the ideal objective of post-menopausal osteoporosis treatment is to decrease the bone turnover rate to the optimal level. That is to control bone turnover rate within the normal range of pre-menopausal period or maintain the serum level of CTX between 100 to 300 pg/ml[8]. From the data, the participants who had over-suppression of bone turnover CTX less than 100 pg/ml at any interval of treatment were similar in both groups, 48.4% in Fosamax® group and 43.3% in Aldren 70® group. The present study had confirmed by bone turnover marker monitoring that alendronate, either branded or generic in a fixed dose of 70 mg once a week, had a high potency to inhibit resorption phase in bone remodeling cycle. The long-

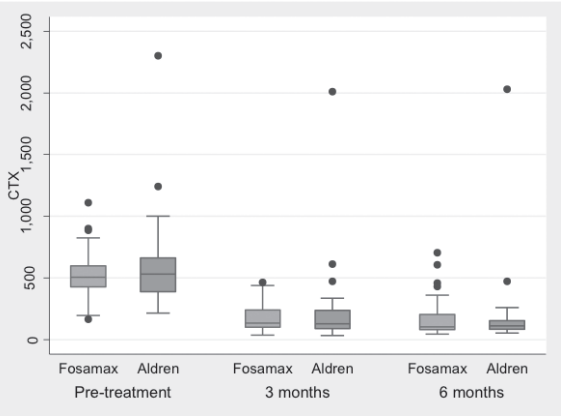

Fig. 1 The comparisons of bone resorption marker (serum CTX) between treatment groups according to time, from the baseline until the end of treatment. The means of CTX in both groups were clinically significant reduction.

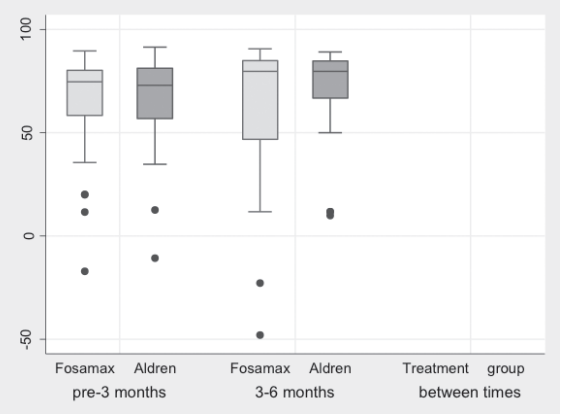

Fig. 2 The comparisons of % CTX reduction between treatment groups according to time.
Note: significant improvement with means >55% reduction from the baseline.

Table 1. Baseline characteristics between treatment groups

Variables	Treatment		*p*-value
	Fosamax	Aldren70	
Age (years), mean(SD)	63.4 (5.4)	62.4 (7.7)	0.542
Menopausal age (years),mean (SD)	50.2 (4.4)	49.1 (4.1)	0.277
Underlying disease (%)	22 (59.5)	18 (48.7)	0.484
Thyroid (%)	2 (5.4)	0 (0)	0.493
Dyslipidemia (%)	8 (21.6)	7 (18.9)	1.000
Asthma (%)	2 (5.4)	0 (0)	0.493
Heart (%)	3 (8.1)	1 (2.7)	0.615
Knee osteoarthritis (%)	1 (2.7)	0 (0)	1.000
Hypertension (%)	6 (16.2)	9 (24.3)	0.564
Meniere (%)	1 (2.7)	0 (0)	1.000
Allergy (%)	1 (2.7)	3 (8.1)	0.615
BMD			
Femoral neck BMD (g/cm2), mean (SD)	0.53 (0.05)	0.51 (0.05)	0.209
Femoral neck T-score, mean (SD)	-2.5 (0.4)	-2.6 (0.5)	0.439
Total hip BMD (g/cm2), mean (SD)	0.71 (0.09)	0.69 (0.7)	0.312

Table 2. The comparison of outcomes between treatment groups

Variables	Treatment		*p*-value
	Fosamax	Aldren70	
CTX (pg/ml), mean (SD)			
Pre-treatment	536.8 (194.6)	602.4 (364.4)	0.234
3 months	176.3 (114.6)	229.3 (333.8)	
6 months	184.4 (166.3)	197.4 (356.3)	
p-value according to time	<0.001	<0.001	
%CTX reduction, mean (SD)	63.3 (29.8)	71.2 (18.2)	0.299
3 months	66.6 (25.1)	66.3 (21.8)	
6 months	62.6 (34.8)	71.1 (22.7)	
p-value according to time	0.791	0.402	

term use of alendronate for post-menopausal osteoporosis treatment should beware of the serious consequences from the over-suppression of bone remodeling. Therefore, regular monitoring and closed follow up with thorough clinical examination are mandatory.

In a term of drug disintegration time, both drugs resulted in same prevalence of side effects to gastrointestinal system, such as dry mouth, oral burn, and gastritis. In Aldren 70® group revealed 10.8%, whereas in Fosamax® group had 2.7% of upper GI side effects but there is no statistical difference between both groups. One patient in Aldren 70® group complained of dyspepsia but was not correlate to the time of drug intake. She was reassured and willing to continue the trial to complete the protocol. No participant in either group had a serious adverse event of gastrointestinal system. Therefore, it could be assumed that the disintegration time of Aldren 70® is not different to Fosamax® and the GI side effects in both groups are in an acceptable range unless the patient takes medicine improperly.

For acute phase reaction and allergy to amino-bisphosphonate, fever was found 8.1% in the Aldren® group and 10.8% in the Fosamax® group, complaint of myalgia was 5.4% in both groups and there was no significant difference between groups. Two patients in the Fosamax® group had skin rash but

Table 3. Side effects and non-compliance rate between treatment groups

Variables	Treatment		*p*-value
	Fosamax	Aldren70	
Side effect (%)	8 (21.6)	8 (21.6)	1.000
Fever	4 (10.8)	3 (8.1)	1.000
Myalgia	2 (5.40)	2 (5.4)	1.000
Rash	2 (5.4)	0 (0)	0.493
Stress	0 (0)	2 (5.4)	0.493
Gastritis	0 (0)	2 (5.4)	0.493
Constipation	2 (5.4)	0 (0)	0.493
Dry mouth/oral burn	1 (2.7)	2 (5.4)	1.000
Loss to follow-up (%)	3 (8.1)	2 (5.4)	1.000
Non-compliance (%)	4 (10.8)	9 (24.3)	0.221
Non drug response (%)			
CTX reduction <55%			
- 3 months	8 (23.5)	7 (20.0)	0.777
- 6 months	8 (25.8)	5 (16.7)	0.534
CTX < 150 pg/ml			
- 3 months	18 (52.9)	19 (54.3)	1.000
- 6 months	18 (58.1)	22 (73.3)	0.283
CTX < 100 pg/ml			
- 3 months	9 (26.5)	12 (34.3)	0.603
- 6 months	15 (48.4)	13 (43.3)	0.799

none was found in the Aldren® group. One patient also had perioral vesicular rash with itching after taking the first tablet of Fosamax®. These two patients in the Fosamax® group were withdrawn from the study and had been treated with other anti-osteoporotic drugs. The acute phase reaction usually subsides within a few days and rarely occurs on the next dose. But allergy to bisphosphonate and ingredients may cause serious sequelae and patients should be informed to observe the allergic reactions and discontinue the treatment whenever drug allergy was suspected. Although two cases were suspicious of allergy to Fosamax®, but no allergic reaction was detected in the Aldren® group. However, there was no statistical difference between both groups.

Non-adherence rate was not significantly different in both groups. Since both medicines are on weekly basis, compliance with once a week therapy should be better than with daily dosing. Total 74 patients from starting treatment, non-adherence with once a week bisphosphonate was 17.6% at 3 months and 26.2% at 6 months. However, doctor-patient relationship is important to improve the drug adherence. Doctors can provide feedback to osteoporosis patients using bone turnover marker to illustrate the improvement of treatment which can be used as motivation. Telephone interview periodically by health care providers is another factor to maintain the adherence and persistence to treatment.

The strength of the present study is a single-blinded randomized controlled trial that strongly deals with a selection bias, and confounding factors. Limitations of the study were an open-labeled trial affecting an outcome measurement bias; and short-term followed up of 24 weeks that could not evaluate rate of fracture prevention which was the direct result, so we had to employ bone resorption marker as a surrogate outcome.

Conclusion

Aldren 70® has a comparable efficacy with Fosamax® in terms of serum CTX reduction, high potency of inhibit bone resorption, adverse drug reaction, non-adherence rate, and non drug-response rate after 6 months of treatment. With lower cost, and acceptable competency, Aldren 70® may be another choice of anti-osteoporotic treatment in developing countries. However, further study of this generic drug is mandatory to evaluate long-term osteoporotic fracture prevention in postmenopausal women.

What is already known on this topic?

The first line therapy for the treatment of osteoporosis is bisphosphonates which are the most

widely used and have demonstrated significant anti-fracture efficacy of vertebral, non-vertebral and hip sites. Their anti-fracture benefits increase with increasing compliance and a minimum of six to twelve months of persistence is required in order to obtain the anti-fracture benefits. Due to their poor absorption and adverse events of gastrointestinal tract, poor adherence to the treatment is usually occurred.

Regarding the cost-effectiveness of treatment, NICE guidance recommends to treat elderly postmenopausal women with a fragility fracture by generic alendronate as a first line option.

Alendronate was the first commercially-marketed amino-bisphosphonate for the treatment of osteoporosis and then the first to lose its patent and be provided to the market as a generic drug. Differences in the excipient composition between the branded and generic formulations of alendronate may alter the bioavailability of the generic alendronate to bone. So, the users still concerns about the efficacy of each generic alendronate.

What this study adds?

The development of the generic equivalent requires only the demonstration of its bioequivalence with the branded product in healthy subjects. While generic substitutions may lead to equivalent outcomes to the branded formulation in other drugs, but not the case with alendronate. The efficacy and tolerance ascribed to branded alendronate should not be extrapolated to the untested generic alendronates. The formulation of expedients and drug disintegration time should also be concerned and may determine the side effects or the bioavailability to bone.

The authors had arranged a head-to-head comparison between generic and branded alendronate in post-menopausal osteoporosis using randomized controlled trial. The outcomes delineated that Aldren 70® once-a-week, one of the generic alendronate, has comparable efficacy with Fosamax® in terms of serum CTX reduction, adverse drug reaction, non-adherence rate, and non drug response rate.

Potential conflicts of interest

None.

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การเปรียบเทียบประสิทธิผลระหว่างยาAldren 70® กับยา Fosamax® ถึงผลต่อการสลายกระดูกในสตรีวัยหมดประจำเดือนที่เป็นโรคกระดูกพรุน

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วัตถุประสงค์: *เพื่อทำการเปรียบเทียบประสิทธิผลของยา Aldren 70® กับยา Fosamax® ในการลดค่าการสลายกระดูก (bone resorption marker) และเปรียบเทียบความปลอดภัยในการใช้ยา ผลข้างเคียงที่เกิดขึ้น และความร่วมมือของผู้ป่วยในการรับประทานยา*

วัสดุและวิธีการ: *ผู้วิจัยได้รวบรวมข้อมูลจากผู้เข้าร่วมวิจัยที่เป็นสตรีวัยหมดประจำเดือนที่เป็นโรคกระดูกพรุนจำนวน 74 คน จากนั้นทำการสุ่มแบ่งเป็น 2 กลุ่ม เพื่อรับยา Aldren 70® หรือ Fosamax® โดยรับประทานยาสัปดาห์ละ 1 ครั้ง ติดต่อกันนาน 24 สัปดาห์ และได้ทำการตรวจ bone resorption marker (carboxy-terminal telopeptide cross-linked type1 collagen: CTX) ที่ 12 และ 24 สัปดาห์หลังรับประทานยา โดยได้มีการนัดผู้ร่วมวิจัยมาติดตามความร่วมมือในการรับประทานยา อาการข้างเคียง ปัญหาจากการบริหารยา และภาวะแทรกซ้อนอื่น ๆ เป็นระยะ*

ผลการศึกษา: *ค่าเฉลี่ยร้อยละของ CTX ทั้ง 2 กลุ่มลดลงได้ดีในระดับที่น่าพอใจที่เวลา 12 สัปดาห์ (ร้อยละ 66.3 ในกลุ่ม Aldren 70® และร้อยละ 66.6 ใน Fosamax®) และที่ 24 สัปดาห์ (ร้อยละ 71.1 ในกลุ่ม Aldren 70® และร้อยละ 62.6 ในกลุ่ม Fosamax®) และไม่แตกต่างกันอย่างมีนัยสำคัญทางสถิติ แต่พบผู้ร่วมวิจัยที่ไม่ตอบสนองต่อยาถึงร้อยละ 20 ในกลุ่ม Aldren 70® และร้อยละ 23.5 ในกลุ่ม Fosamax® ส่วนอาการข้างเคียงต่อระบบทางเดินอาหาร แม้ว่ากลุ่ม Aldren 70® จะมีผลข้างเคียงต่อระบบทางเดินอาหารส่วนต้นถึงร้อยละ 10.8 ส่วนกลุ่ม Fosamax 70® พบเพียง 2.7 แต่ไม่แตกต่างกันอย่างมีนัยสำคัญทางสถิติ และความร่วมมือในการรับประทานยาอย่างสม่ำเสมอ ไม่แตกต่างกันอย่างมีนัยสำคัญทางสถิติระหว่าง 2 กลุ่ม*

สรุป: *Aldren 70® มีประสิทธิผลเท่าเทียมกับ Fosamax® ในการลดระดับ CTX ในเลือด ที่ 12 และ 24 สัปดาห์หลังรับประทานยา โดยมีความปลอดภัยในการใช้ยา ผลข้างเคียงที่เกิดขึ้น และความร่วมมือของผู้ป่วยในการรับประทานยาไม่แตกต่างกัน*
