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Editorial OMICS International

Effect of Adherence in Osteoporosis Treatment Drugs

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Editorial

Several drugs have in the past decade demonstrated to be safe and effective in reducing fractures in patients with postmenopausal osteoporosis. Despite this use of relative effective drugs for the treatment of osteoporosis, these diseases still represent an important problem for the clinical and public health services.

Hip fractures, clinical vertebral fractures and distal forearm fractures (estimated worldwide numbers in 1.6, 1,4 and 1.7 millions) have a great impact in mortality and morbidity [1].

Prior observational studies on osteoporosis, have shown association between the pharmacotherapy adherence and persistence and the effect upon the disease. Drugs most used for treatment and prevention of osteoporosis in postmenopausal include second generation of aminobisphosphonates (alendronate, risedronate, ibandronate and zolendronate), selective estrogens receptor modulator (raloxifen), teriparatide (recombinant 1-34 human parathyroid hormone) and estrogens/hormone replacement therapy (HRT) and recently denosumab.

Therefore we have to refer to some concepts used in this publication regarding adherence [2,3]. Compliance is a latin word, meaning to complete an action and fulfil a promised, in few words it means to act in accordance with his advice.

Patient and the prescriber should agree about the regimen the patient will take for this purpose. Adherence also comes from latin and means to remain constant, to cling to. This is why strict adherence can severely modify the habits and way of life of patients to an impose regimen, and could have negative effect to accept adherences. In general medicine, it has been claim that adherence to beneficial drug therapy is associated with lower mortality than poor adherence, while an increase in mortality can in the inverse be associated to good adherence to harmful drugs [4].

In the other hand, it has been estimated that only a 50% of patients with chronic diseases have a good adherence to treatments recommendations. This has been the case of different therapies for asthma, diabetes and hypertension, and not only with antiosteoporotics drugs [5]. The purpose of this review is to comment the consequence of poor adherence with osteoporosis therapy, including the effects of transition of bisphosphonates to the new drug denosumab in these parameters.

State of the art

Therefore, we can admit a clear benefit of the use of bisphosphonate for the treatment of postmenopausal osteoporosis. But we have to recognize that drug adherence to anti-osteoporotic drugs can limit their effectiveness. Bisphosphonates are still the most commonly initially treatment used, with different regimens and multiple side effects that can influence patient acceptance. The efficacy of the drugs used for osteoporosis treatment, has been well demonstrated for increasing bone mineral density and reducing the risk of fractures in randomized controlled trials. But in many cases, in the setting of real practice, it is found a group of patients with sub optimally efficacy, in which, poor adherence to the drug is claim to be due to patients acceptance, drug dosing and side effects. An approach to this problem has been to change treatment, for example, from alendronate (most widely used) to other oral or intravenous bisphosphonates. Recently, it has been proposed that the transition to other drug with different mechanism could potentiate the effect of the first.

Although the transition of therapy with alendronate to denosumab has been associated with greater gains in bone mineral density, it was not known whether this fact could be also the case with risedronate or others bisphosphonates well prescribed for this therapy [6].

Recently denosumab, a human monoclonal antibody directed against RANKL, that is involved the formation, function and survival of osteoclast, has been introduced for the treatment of postmenopausal osteoporosis in women with high risk for fracture [7]. In a previous study in which our center participated, it was demonstrated that the administration of 60 mg subcutaneously of denosumab every 6 months, had a marked increased bone mineral density and reduction of vertebral, hip and non vertebral fractures, during a 36 months study. In the followed open label extension of this study, denosumab therapy at the third years was associated with a further reduction in nonvertebral fracture rate, and was associated with a continued low vertebral fracture rate that persisted through 8 years of continuous administration [8].

Adherence of persistence

It has to be considered that therapy should include evaluation of these two conditions. Adherence to osteoporosis drugs is a problem, given the dosing, adverse effects, and costs. It is well known the persistence and compliance with osteoporosis therapy is sub optimally with marked reductions in ant fracture efficacy. It has been estimated that 30-50% of oral bisphosphonate treatment are not adherent, that persistence is lower than 6 months with a great proportion discontinue the bisphosphonate at one year [9]. Although persistence is somewhat higher with the intravenous bisphosphonates, the adverse effects (post infusion syndrome) still limit this procedure.

Denosumab and adherence

In the paper of Roux et al. [10] a total of 870 postmenopausal women were randomized to risedronate and denosumab, Patients were

treatment naïve or previously treated with alendronate. Patients with any prior therapy for osteoporosis different from alendronate were excluded. Using the OS-MMAS, an osteoporosis specific version of the Morisky Meication Adherence Scale, In this scale high adherence mean a score of 8, medium ≤ 6 to 8 and low adhernce <6. At month 12, denosumab increased BMD significantly more than risedronate at the hip (2.0% vs. 0.5%) femoral neck (1.4% vs. 0%) and lumbar spine (3.4% vs. 1.1%).

The authors concluded that transitioning to denosumab was more effective than to risedronate as measured by BMD in postmenopausal women previously suboptimally adherent to alendronate therapy. The transitioning to denosumb has a better outcome as demonstrated in this study, while in subjects change from alendronate to a single infusion of zoledronic acid, BMD values did not change significantly a year of treatment. In the DECIDE trial (Determining efficacy: Comparison of initiating denosumab versus alendronate) a preference and satisfaction questionary was completed by patients after 12 months of treatment or upon study discontinuation; there were more significantly patients that preferred the injection (denosumab) that the pill (alendronate) after the year of therapy [11].

In this context the DAPs study is interesting. This was a 2 years crossover trail (Denosumab adherence preference satisfaction study) in which naïve postmenopausal women were randomized to denosumab every 6 months for one year followed by alendronate orally once weekly for one year or the inverse. Lower score of preference were reported for alendronate, regarding satisfaction, dosing frequency, route of administration and convenience [12]. Finally, recently using the Treatment Satisfaction Questionary form Medication used for evaluation of different chronic diseases, it was show the postmenopausal women with osteoporosis, suboptimally adherent with oral daily or weekly bisphosphonate therapy, who transitioned to denosumab or monthly bisphosphonates, were more satisfy with this two latter therapies, but that positive changes were more significantly greater in the denosumab treated [13].

Adherence specifically to denosumab

It has been confirm a high adherence to denosumab, in the 12 months study of Hadji et al. [14], which showed that 82.7% to 89.3% of patients involved this study, received a second injection of this drug at six months, a proportion significantly greater that that observed with bisphophonates. Also the application of the MMAS-8 questionnaire for adherence shows that adherence to denosumbad was high, independently of having low or medium score adherence to previous therapies.

Summary

The interpretation of adherence studies in well controlled trials can be different in the real life setting, due to modifications in life conditions and behaviour of patients that can modify the effort or randomized clinical trials, were patients are regularly followed. Inclusion criteria's in the trails, can limit the generalization of adherence. Finally, longer period of time of follow up therapy can also modify adherence, although in our experience with Denosumab this does not seems to be a significative problem.

Available experience shows that there is a better adherence to denosumb compared to common bisphophonates. The safety of the drugs has been demonstrated, as also a better increased in BMD and reduction in fracture with denosumab. There are require more studies taking in consideration patients preference and self-involvement in the process, as taking in account longer periods and cost-effectiveness of the drugs used for osteoporosis therapy in observational studies.

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