EFFECTS OF RISEDRONATE ON BONE TURNOVER MARKERS IN OSTEOPOROTIC POSTMENOPAUSAL WOMEN: COMPARISON OF TWO PROTOCOLS OF TREATMENT.

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EFFET DU RISÉDRONATE SUR LES MARQUEURS DU REMODELAGE OSSEUX CHEZ LES FEMMES OSTÉOPOROTIQUES MÉNOPAUSÉES: COMPARAISON DE DEUX PROTOCOLES DE TRAITEMENT.

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RÉSUMÉ

But : Les bisphosphonates permettent la prévention de la perte osseuse. L'objectif de cette étude est d'évaluer l'efficacité et la tolérance du risédronate 35 mg en une prise hebdomadaire en comparaison avec la prise journalière de 5 mg chez les femmes ostéoporotiques.

Méthodes: Une étude randomisée, en double-aveugle a enrôlé 102 femmes ménopausées âgées de 66.5+7.5 ans avec fractures ostéoporotiques. Toutes les femmes ont reçu du risédronate pendant 6 mois. Groupe 1 (G1, n=51) a reçu la dose de 5 mg/jour et groupe 2 (G2, n=51) la dose de 35 mg/semaine. Les phosphatases alcalines totales (PAL) et osseuses (PALo), le C-terminal télopeptide du type I du collagène (CTX) ont été mesuré à To, 3 mois et 6 mois après traitement dans les deux groupes.

Résultats: Aucune différence significative n'a été notée pour les marqueurs entre les 2 groupes. Après 3 mois, PALo et CTX ont baissé (respectivement -22.1% et -47.6%) dans les 2 groupes sans différence significative. Après 6 mois, PALo et CTX ont baissé respectivement de -46.5% et -62.9% sans différence statistiquement significative entre les 2 groupes pour les marqueurs osseux.

Conclusion: Notre étude a trouvé que le traitement avec risédronate à la dose de 35 mg par semaine pourrait faire baisser CTX et PALo en comparaison avec la prise quotidienne de 5 mg chez les femmes ménopausées avec fractures ostéoporotiques. Nous n'avons pas trouvé d'effets indésirables avec la dose hebdomadaire de 35 mg en comparaison avec la dose quotidienne de 5 mg. Ainsi, l'effet du risédronate 35 mg/semaine est similaire en efficacité à la dose journalière de 5 mg et pourrait donner moins d'effets indésirables qu'une prise mensuelle. Ce protocole thérapeutique pourrait être une alternative pour les patients qui préfèrent une prise hebdomadaire unique.

MOTS-CLÉS

Risédronate- Bone markers- menopause- ostéoporose- fracture essai thérapeutique - tirage au sort

SUMMARY

Aim : Bisphosphonates are powerful agents able to prevent bone loss. The objective of the study was to evaluate the efficacy and tolerability of risedronate once a week (35 mg) compared with risedronate 5 mg once daily in women with osteoporosis.

Methods: A randomized, double-blind, active-controlled study enrolled 102 postmenopausal women aged 66.5+7.5 years with osteoporotic fractures. All women received risedronate during 6 months. Group 1 (G1, n=51) received risedronate 5 mg once daily and group 2 (G2, n=51) received 35 mg once a week. Serum alkaline phosphatase (ALP), bone alkaline phosphatase (bone ALP), serum C-terminal telopeptide of type I collagen (CTX) were measured at baseline, 3 months and 6 months after treatment in the two groups.

Results: We noted no significant difference in markers between women of the 2 groups. After 3 months, bone ALP and CTX decreased (respectively -22.1% and -47.6%) in the 2 groups with no significant difference between them. After 6 months study, bone ALP and CTX decreased respectively by -46.5% and -62.9% with no statistically significant difference between study groups for bone markers.

Conclusion: Our study found that treatment with once weekly risedronate 35 mg is able to decrease CTX and bone ALP compared with risedronate 5 mg once daily, in postmenopausal women with osteoporotic fractures. We didn't find adverse events with the 35 mg once-a-week dose group compared to the once-daily dose group. Based on these results, the effects of risedronate 35 mg once a week are similar in efficacy to daily dosing and may lead less adverse events than once-a-month dose. This therapeutic protocol may provide an alternative for patients who prefer once-a-week oral dosing.

KEY-WORDS

Risedronate- bone markers- menopause- osteoporosis- fracture controlled trial - randomized trial

تأثر الريزيدرونات على وسمة إعادة تكون العظم عند النساء المصابات بهشاشة العظام في سن اليأس

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الهدف من هذه الدراسة هو تقييم نجاعة تناول الريزيدرونات 35 مغ مرة في الأسبوع مقارنة بتناول الريزيدرونات 5 مغ يوميا عند النساء المصابات بهشاشة العظام أشتملت دراستنا على 12 امرأة وقع توزيعهن على مجموعتين الأولى 51 (امرأة) تناولن الدواء مرة في الأسبوع والثانية 51 (امرأة) تناولن الدواء يوميا أستنتجنا أنه ليس هناك فرق على مستوى النجاعة بالنسبة للطريقتين مما يجعل منه علاجا مناسبا للمريضات الآتي يفضلن تناول الدواء.

الكلمات الأساسية : ريزيدرونات - وسمة العظام - سن اليأس - هشاشة العظام - كبد

In postmenopausal osteoporosis, inhibition of bone resorption is a rational approach for prevention of bone loss. Bisphosphonates are powerful agents able to achieve this goal [1]. The objective of the current study was to evaluate the efficacy and tolerability of risedronate (oral bisphosphonate) once a week (35 mg) compared with risedronate 5 mg once daily in women with osteoporosis.

MATERIAL AND METHODS

Hundred and two postmenopausal women aged 66.5 + 7.5 years with osteoporotic fractures were included in the study. We obtained informed consent from all patients and the committee on clinical investigation at La Rabta hospital approved the study protocol. The bone mineral density (BMD) was measured by dual energy X-ray absorptiometry (DEXA) for all women and the mean of T-score was -1.93 + 0.79 in neck of femur and -3.31 + 1.13 in spine. We conducted a randomized, double-blind, active-controlled study. All women received risedronate during 6 months. Group 1 (G1, n=51) received risedronate 5 mg once daily and group 2 (G2, n=51) received 35 mg once a week. Serum alkaline phosphatase (ALP), bone alkaline phosphatase (bone ALP), serum C-termilal telopeptide of type I collagen (CTX) were measured at baseline, 3 months and 6 months after treatment in the two groups.

Statistical significance was defined as $p<0.05$. All statistical analyses were performed using SPSS 10.5. We used t-test of Student for comparison of means.

RESULTS

At baseline, there was no significant difference in ALP, bone ALP and CTX between women of the 2 groups.

All women continued and compelled all 6 months. After 3 months, bone ALP and CTX decreased (respectively -22.1% and -47.6%) in the 2 groups but with no significant difference between them. After 6 months study, bone ALP and CTX decreased respectively by -46.5% and -62.9%; no statistically significant differences between study groups were observed with bone markers (table 1).

Table 1 : Evolution of bone parameters at 3 and 6 months of treatment in the 2 groups of therapeutic protocols

	G1* Risodronate 5mg 51	**G2* Risodronate 35mg**
Number of women at To	91 ± 24	**51**
ALP	0,757 ± 0,334	89 ± 25
CTX	19,78 ± 7,38	0,666 ± 0,284
Bone ALP	51	19 ± 6,82
3 months later	78 ± 18	51
ALP	0,344 ± 0,186	79 ± 25
CTX	14,63 ± 5,97	0,396 ± 0,247
Bone ALP	**51**	14,33 ± 5,81
6 months later	72 ± 18	**51**
ALP	0,242 ± 0,155	70 ± 20
CTX	10,26 ± 3,32	0,250 ± 0,171
Bone ALP		9,05 ± 5,54

*No statistical difference was noted

DISCUSSION

Our results are comparable to those from Brown, Hooper et al and other published studies of risedronate therapy in postmenopausal osteoporotic women [2,3,4]. Primary efficacy assessment of the treatment was performed after 3 months. Our study found that treatment with once weekly risedronate 35 mg is able to decrease CTX and bone ALP compared with risedronate 5 mg once daily, in postmenopausal women with osteoporotic fractures. These various dosing options, including the ability to dose at spaced intervals, are a result of the ability of bisphosphonates to decrease the probability of trabecular perforations, and failure, and increase bone density [5].

Nevertheless, risedronate needs a minimum wait of 30 minutes after dosing before eating or drinking anything other than water. Delmas et al showed that risedronate150 mg once-a-month dose leads to symptoms associated with potential acute phase reaction that occurs more frequently in this group than in the daily dose group [6]. We didn't find those adverse events in the 35 mg once-a-week dose group compared to the once-daily dose group. Based on these results, the effects of risedronate 35 mg once a week are similar in efficacy to daily dosing and may lead less adverse events than once-a-month dose. This therapeutic protocol may provide an alternative for patients who prefer once-a-week oral dosing. Moreover, reducing the dose of risedronate may also reduce the cost of medication.

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