



Original Article

Use of risedronate for consolidation and callus formation in Colles fractures in postmenopausal women: SOLID study



Lindomar Guimarães Oliveira^{a,*}, Sérgio Ragi Eis^{b,†}, Henrique Mota Neto^c, Frederico Barra de Moraes^d, Luiz Antônio Silveira Simões Pires^e, José Wanderley Vasconcelos^f

^a Clínica de Ortopedia e Fraturas, Goiânia, GO, Brazil

^b Clínica de Diagnóstico e Pesquisa da Osteoporose do Espírito Santo, Vitória, ES, Brazil

^c Universidade Estadual do Ceará, Fortaleza, CE, Brazil

^d School of Medicine, Universidade Federal de Goiás, Goiânia, GO, Brazil

^e Orthopedics and Traumatology Service, Hospital São Lucas, Pontifícia Universidade Católica, Porto Alegre, RS, Brazil

^f Centro de Pesquisa SOS Trauma, São Luiz, MA, Brazil

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ABSTRACT

Objective: This open, randomized and blinded parallel-group multicenter study evaluated the efficacy of Actonel® (35 mg) plus calcium/vitamin D versus calcium/vitamin D alone for preserving bone mineral density (BMD) in postmenopausal women with Colles fractures.

Methods: Patients with a Colles fracture for seven days were randomized to receive either Actonel® (35 mg) once a week plus calcium/vitamin D (ACD group) or calcium/vitamin D alone (CD group). The patients were evaluated after 90 and 180 days of treatment.

Results: 59 ACD patients and 56 CD patients completed all the evaluations. At the end of the study, the BMD of the radius at the fracture location showed a negative change in the CD group (32.8%). The loss of BMD in the ACD group (20.8%) was slightly less than that in the CD group. There was a difference in the proportions of patients with BMD losses at the end of the study period in the two treatment groups, in favor of the ACD group, although this was not statistically significant. There was no significant difference in radiological identification of callus formation between the treatment groups. In the majority of the patients, the callus could be radiologically identified after 90 days.

Conclusion: Postmenopausal women with Colles fractures who received risedronate sodium plus calcium/vitamin D did not show any significant difference in BMD loss in forearm

* Corresponding author.

E-mail: Lindomar@terra.com.br (L.G. Oliveira).

† In memoriam.

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fractures, in comparison with those who received calcium/vitamin D alone. Risedronate a protective effect regarding BMD loss due to immobilization. The time taken for fracture consolidation to be achieved was unaffected.

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Uso de risedronato na consolidação e formação do calo na fratura de Colles em mulheres na pós-menopausa – Estudo Solid

R E S U M O

Palavras-chave:

Consolidação da fratura

Fratura de Colles

Difosfonatos

Objetivo: Este estudo multicêntrico, randomizado, aberto, grupo paralelo avaliou a eficácia de Actonel® 35 mg mais cálcio/vitamina D versus cálcio/vitamina D isoladamente na preservação da densidade mineral óssea (DMO) em mulheres pós-menopausadas com fratura de Colles.

Métodos: Pacientes com fratura de Colles em sete dias foram aleatoriamente designadas para receber Actonel® 35 mg semanalmente mais cálcio/vitamina D (Grupo AO [GAO]) ou cálcio/vitamina D (grupo O [GO]) isoladamente. As pacientes foram avaliadas após 90 e 180 dias de tratamento.

Resultados: Completaram as avaliações 59 pacientes no GAO e 56 no OG. No fim do estudo, a DMO do rádio no local da fratura mostrou variação negativa no GO (32,8%) que foi discretamente menor no GAO (20,8%), assim como uma perda menor na DMO no GAO comparado com o OG. Houve diferença na proporção de paciente com perda da DMO no fim do estudo nos dois grupos de tratamento em favor do GAO, apesar de não estatisticamente significativa. Não houve diferença significativa na identificação radiológica da formação do calo entre os grupos de tratamento. Na maioria das pacientes a identificação radiológica do calo ocorreu depois de 90 dias.

Conclusão: Mulheres pós-menopausadas com fratura de Colles que receberam risedronato sódico, além do cálcio/vitamina D, comparado com cálcio/vitamina D não mostraram diferença significativa na perda da DMO na fratura do antebraço, com tendência de efeito protetor do risedronato na perda da DMO devido à imobilização. O tempo até a consolidação da fratura não foi afetado.

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Introduction

The potential for accelerating or improving the formation of a callus and preventing progression of fractures to pseudarthrosis has been correlated with mechanical procedures for stabilizing bone fragments. However, this reality has changes in the light of the proven efficacy of physical methods or medications.¹

Bisphosphonates have been studied regarding their possible positive or negative influence on formation of bone calluses. This gives rise to questions that relate to how bisphosphonates might interfere with bone consolidation; what their influence on the histology, morphology and biomechanics of the callus might be; what the best time after the fracture for starting medication would be; whether bisphosphonates might have any effect on consolidation among patients who used them previously, before the fracture; and whether all types of bisphosphonates act in the same manner with regard to formation of the bone callus.²⁻⁴

At therapeutic doses for osteoporosis, different bisphosphonates have not shown negative effects on bone

consolidation but have shown improvements to the biomechanical aspects of bone.⁵⁻⁹ Experimental studies using risedronate have shown that consolidation occurs, without any change to the time taken, but with bone callus of better histological quality.^{10,11}

The aims of the SOLID study were as follows: 1 – primary aim: to evaluate the efficacy of preservation of bone mineral density (BMD) provided by 35 mg of Actonel® in the proximal forearm, named the region of interest (RI 33%), after 90 days of treatment, based on the difference between treatments (sodium risedronate plus calcium and vitamin D versus calcium and vitamin D alone); 2 – secondary aim: to evaluate the efficacy of preservation of BMD provided by 35 mg of Actonel® in the proximal forearm (RI 33%), after 180 days of treatment; to evaluate the differences in ultradistal BMD between the treatment groups, in the region of callus formation, after 90 and 180 days of treatment; to evaluate the radiological identification of the callus, defined by identifying the bone bridge in three of the four cortical areas identifiable by means of AP and lateral X-ray views during the follow-up; and to evaluate safety.

Materials and methods

Study design

This was a comparative parallel-group open randomized multicenter phase IV study conducted in six study centers in Brazil: Goiânia (one), Fortaleza (one), Niterói (one), São Luís do Maranhão (one) and São Paulo (two). The study was approved by the appropriate ethics committees and the patients gave their free and informed consent in writing, before any procedures relating to the study were started. Furthermore, the study was conducted in accordance with good clinical practices and with the ethical principles that originated from the Declaration of Helsinki.

Each patient was evaluated over a 180-day period, through seven evaluation visits: VO (baseline): visit made seven days after Colles fracture occurred; VR, randomization visit (day 0), made seven days after the baseline; and subsequent visits made 15 (V1), 30 (V2), 45 (V3), 90 (V4) and 180 (V5) days after the randomization date. Among the visits, an interval of three days was allowed.

Patients

Women who had been postmenopausal for at least two years were eligible to participate if they presented a Colles fracture that was confirmed within a period of seven days before entry into the study. The patients were stratified by age in a 1:1 ratio (<65 and ≥65 years) and according to T-score ≤ -2.0 standard deviations in the lumbar spine (L1-L4 and/or L2-L4) and/or femoral neck and/or total femur and/or 33% radius.

The main inclusion and exclusion criteria were as follows:

Inclusion criteria: postmenopausal for at least two years; Colles fracture confirmed with occurrence seven days before entry into the study; T-score ≤ -2.0 standard deviations in the lumbar spine (L1-L4 and/or L2-L4) and/or femoral neck and/or total femur and/or 33% radius.

Exclusion criteria: previous fracture in the same wrist or forearm; fracture that, in the opinion of the orthopedic surgeon or person responsible for the case, should only be treated surgically; distal fracture of the radius or fractures in contralateral bones that occurred previously or concomitantly, which might impede comparisons of the BMD evaluations over the course of the study; use of medications concomitantly that might affect the calcium metabolism; previous treatment with bisphosphonates for more than 12 months over the last 36 months; use of bisphosphonates for any period of time over the last three months; cumulative use of bisphosphonates for more than 36 months on any occasion; rheumatoid arthritis or any other disease with involvement of the wrist; hyper or hypothyroidism that is known to be stable, with or without treatment; hypocalcemia, liver disease, kidney disease or rheumatic diseases.

Study treatments

At the randomization visit, the eligible patients were designated to receive one of the two study treatments: Actonel® + Oscal® group (GAO): 35 mg of sodium risedronate

once a week plus 1000 mg of calcium and 400 IU of vitamin D on six days a week (i.e. not on the day on which risedronate would be taken); or Oscal® group (GO): 1000 mg of calcium and 400 IU of vitamin D daily (i.e. seven days a week).

Efficacy assessments

Efficacy was based on the changes seen in the T scores in the proximal region of the forearm (33% of the region of the radius), from the baseline to V4 (90 days) and V5 (180 days) after the treatment and was expressed as percentages for the two arms fractured and non-fractured).

The difference was calculated in the following manner: T score at V4 minus T score at baseline, divided by T score at baseline.

The same calculation was used for the change in T score from the baseline to V5 (180 days); the mean change in T score in the proximal forearm (33% of the region of the radius) from the baseline to V4 and V5 in the two arms (fractured and non-fractured), with radiological identification of callus formation by means of X-rays.

Bone mineral density (BMD): BMD was measured by means of dual-energy X-ray absorptiometry (DXA), using a GE/Lunar densitometer (DPXIQ, DPXNT, MD + Prodigy) or Hologic densitometer (QDR 2000, QDR 200+, QDR 4500, Delphi or Discovery) on the lumbar spine and proximal femur (femoral neck and total hip) and the distal region of the forearm (fractured and non-fractured), at the baseline and then at 90 and 180 days. The BMD measurements were repeated using DXA for the distal region of the forearm (fractured and contralateral).

X-rays: Radiological images of the wrist and arm (fractured and contralateral) were obtained in two views (posteroanterior and lateral), at the baseline and 15, 30, 45 and 180 days after the fracture. The main X-ray parameters for monitoring the consolidation of the fracture were formation and viewing of bone bridges along the fracture lines, identified in the cortex in each view. Fracture consolidation was defined as the presence of bone bridges in three of the four cortical images evaluated in these views.

Quality control procedures were established by means of training and certification of the team involved in using the densitometry and X-ray equipment, with central analysis of the tests performed, performed by the coordinator of the Osteoporosis Research and Diagnosis Center (CEDOES). The examiners were blinded with regard to the study treatment administered in each case.

Safety assessments

Safety was assessed according to the type and severity of the adverse events that were reported by the patients or observed in some other way by the investigator.

Definition of the study population

All the randomized patients who received at least one dose of the study medication were included in the intention-to-treat (ITT) population. The modified intention-to-treat population (ITTm) was formed by treated patients who presented changes in T scores starting from the baseline. The protocol population

(PP) consisted of patients who were treated without significant violations of the protocol who had at least one BMD evaluation in the proximal region of the forearm (33% of the region of the radius) on the side of the fracture, at the baseline and at V4 (90 days).

Statistical plan

All the tests applied were performed using SAS v 9.1 and the statistical significance level was taken to be 5%.

Calculations were based on comparison of the groups regarding the mean change in BMD after 90 days of treatment, expressed as a percentage. Power of 80%, significance level of 5% and discontinuation rate of 10% were used. The standard deviation was assumed to be 0.08, with a difference of interest of 4% between the groups (mean percentage change in BMD after 90 days of treatment). Therefore, the estimated total number to be recruited was 140 patients (70 per group).

The percentage change (%) in BMD after 90 days (V4) and 180 days of treatment was calculated in the following manner:

- % change at V4 = $[(T\text{-score}V4 - T\text{-score}V0)/|T\text{-score}V0|] * 100$
- % change at V5 = $[(T\text{-score}V5 - T\text{-score}V0)/|T\text{-score}V0|] * 100$

The demographic variables of continuous nature were described separately for the two treatment groups using means, standard deviations and ranges. Comparisons between the treatment groups were indicated using Student's t test values. The discrete demographic variables were summarized in frequency tables and comparisons between the treatment groups were based on p values from the chi-square test or Fisher test, depending on the frequency of the events.

The Mann-Whitney U test (independent observations) was applied for comparison between the treatment groups regarding changes in T-scores (%) from the visit V0 to the visit V4 and from the visit V0 to the visit V5.

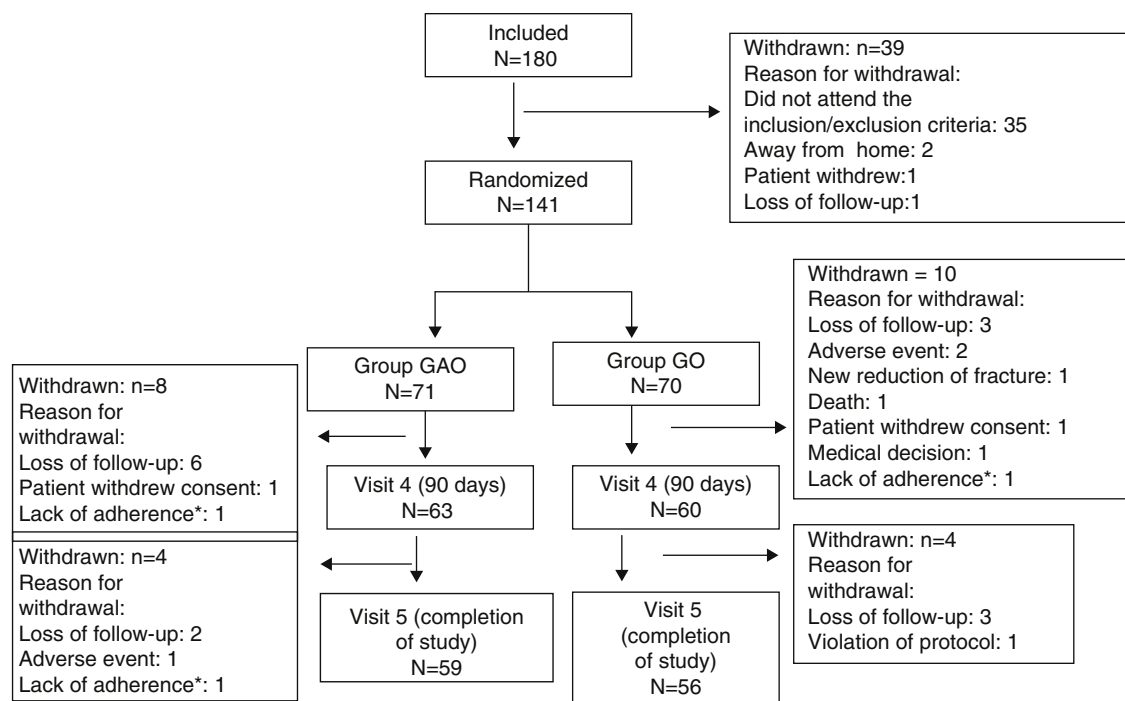
The Wilcoxon signed rank test (dependent observations) was applied to compare the visits (V4 and V5) regarding changes in T-score (%), in each treatment group. To compare the treatment groups between the visits regarding mean T-scores, a model of analysis of variance (ANOVA) was applied, with the factors from the treatment groups (Actonel+Oscal and Oscal), visits (V0, V4 and V5) and the respective interactions between them. To compare the treatment groups with regard to radiological identification of the callus, the chi-square test or Fisher F test was applied, according to the frequency of the events.

Results

Patients

The patients' distribution is presented in Fig. 1. At the end of the study, 59 patients in GAO and 56 in GO had completed all the evaluations as planned. A total of 137 patients (70 in GAO and 67 in GO) received at least one dose of study medication and were evaluated regarding efficacy and safety. The groups were shown to be homogenous at the baseline regarding demographic and clinical characteristics (Table 1).

There were no statistically significant differences between the groups in relation to the side on which the fracture occurred: 36/71 patients (50.7%) had a Colles fracture in the left forearm in GAO and 38/70 (54.3%) in GO ($p=0.670$). For the majority of the patients, the universal classification of



*Use of less than 80% of the study medication

Fig. 1 – Distribution of the patients.

Table 1 – Demographic characteristics and baseline clinical characteristics.

Demographic characteristics	GAO N = 71	GO N = 70	p value (GAO vs. GO ^a)
<i>Age, years</i>			
Mean ± SD	67.1 ± 10.9	64.9 ± 10.4	0.224 ^a
Limits	44–90	44–92	
<i>Age stratum, N (%)</i>			
<65 years	33 (46.5)	34 (48.6)	
≥65 years	38 (53.5)	36 (51.4)	
<i>Ethnicity</i>			
White	50 (70.4)	57 (81.4)	0.389 ^b
Black	6 (8.5)	4 (5.7)	
Mixed	15 (21.1)	9 (12.9)	
<i>Weight (kg)</i>			
Mean ± SD	58.5 ± 11.5	61.3 ± 12.0	0.1502 ^a
Limits	36–88	34–89	
<i>Height (cm)</i>			
Mean ± SD	150 ± 6	152 ± 6	0.0482 ^a
Limits	137–165	140–174	
<i>Length of time since menopause (years)</i>			
Mean ± SD	19.8 ± 12.1	18.3 ± 9.8	0.4392 ^a
Limits	3–55	2–43	
<i>Length of time from Colles fracture occurrence to baseline, days</i>			
Mean ± SD	3.5 ± 1.7	3.4 ± 1.8	0.580 ^a

^a t test for independent variables.
^b Chi-square test.

Table 2 – Change in T score in proximal forearm (33%) on fractured side, expressed as percentage, in modified ITT population.

	V4	V5	p value ^a
GAO			
No. of patients	N = 59	N = 59	
Mean ± SD	–25.7 ± 40.7	–20.8 ± 39.5	
Min/Median/Max	–200/–15.2/27.8	–200/–9.1/15.4	0.727
GO			
No. of patients	N = 57	N = 56	
Mean ± SD	–31.9 ± 62.5	–32.8 ± 68.0	
Min/Median/Max	–400/–21.4/75	–366.7/–18.9/90	0.769
p value ^b (groups)	0.352	0.069	

^a Wilcoxon signed rank test.
^b Mann-Whitney U test.

the Colles fracture was I or II/IIa: 15/71 patients (21.1%) and 46/71 (64.8%), respectively, in GAO; and 16/70 (22.9%) and 43/70 (61.4%), respectively, in GO ($p = 0.917$).

The BMD measurement (evaluated by means of the T score) did not show any statistically significant difference between the treatment groups at the baseline, in forearms diagnosed with fractures, in forearms without fractures and in the lumbar spine, femoral neck and total femur. The majority of the patients in the two treatment groups used at least 80% of the total number of pills planned per visit.

Findings on the side of the fractured forearm

On the side of the fractured forearm, a decrease in BMD was observed (evaluated using the % of the T score) from V0 to

V4 (90 days) and V5 (180 days) in the two treatment groups, ranging from 20.8% to 32.8% (Table 2).

There was a tendency toward greater reduction in BMD (evaluated using the T score) among the patients in GO. At V4, this reduction was approximately 15% in GAO and 21% in GO. At V5, this loss of BMD was approximately 9% in GAO and 19% in GO. No statistically significant difference between the groups was reached at either visit: $p = 0.352$ and 0.069 for V4 and V5, respectively (Table 2). Likewise, no statistically significant difference in T score variation was found in comparing V4 and V5 in the two groups ($p = 0.727$ and 0.769 for GAO and GO, respectively).

The same tendency toward greater reduction in BMD was observed in the protocol population (PP) for GO, in comparison with GAO, and there was no statistically significant difference between the groups ($p = 0.110$) (Table 3).

Table 3 – Change in T score in proximal forearm (33%) on fractured side, expressed as percentage, in PP population.

Groups	V4	p value (groups) ^a
GAO		
No. of patients	N = 45	
Mean ± SD	-24.6 ± 41.9	
Min/Median/Max	-200/-15.2/27.8	
GO		
No. of patients	N = 46	
Mean ± SD	-27.4 ± 30.8	
Min/Median/Max	-166.7/-23.0/20%	0.110

^a Mann-Whitney U test.

From V0 to V4 (day 90), most of the patients in the two treatment groups presented loss of BMD: 46/63 (73.0%) in GAO and 46/60 (76.7%) in GO. The mean ± SD for the loss of BMD was -0.5 (0.4) in GAO and -0.7 (0.4) in GO. Comparing V0 with V5 (day 180), a loss of BMD could be seen in 39/59 patients (66.1%) in GAO and in 43/56 (76.8%) patients in GO. The mean ± DP of the difference in BMD between V0 and V5 was -0.5 (0.4) for GAO and -0.7 (0.4) for GO.

Findings on the non-fractured side

In the non-fractured forearm, the BMD evaluated according to the change in T score (%) from V0 until the visits V4 and V5 ranged from 4.2% upwards (an increase from V0 to V4, i.e. day 90) to -6.0% downwards (a reduction from V0 to V5, i.e. day 180) (Table 4).

At V4, the increase in BMD (evaluated according to the T score) was seen to be greater in GO (4.2%) than in GAO (1.9%); and at V5, there was a reduction in BMD (evaluated according to the T score) in the two groups. It was greater in GO (-5.7%) than in GAO (-2.2%). No statistically significant differences were observed between the treatment groups at the two visits or between the visits for the two treatment groups (Table 4).

Furthermore, approximately 30% and 42% of the patients in the two treatment groups showed losses of BMD from the baseline to V4 (day 90) and to V5 (day 180), respectively.

In relation to the proportion of patients with losses of BMD at V4, there was a statistically significant difference

Table 5 – Loss of BMD in the proximal forearm (33% of radius) between visits V0 and V5 (day 180), in modified ITT population.

	GAO	GO
Fractured		
N	59	56
Loss of BMD	39 (66.1%)	43 (76.8%)
Mean ± SD	-0.5 (0.4)	-0.7 (0.4)
Non-fractured		
N	59	56
Loss of BMD	25 (42.4%)	24 (42.9%)
Mean ± SD	-0.3 (0.3)	-0.3 (0.2)
p value ^a	0.010	0.0003

^a Chi-square test.

between the fractured and non-fractured sides in the two treatment groups (GAO and GO; $p < 0.0001$ for both). This difference in pattern observed in the forearms between the sides was probably related to the immobilization of the fractured side (Table 5).

The ANOVA model compared the mean T scores in the two treatment groups between the visits, using the treatment group (GAO or GO) and the visits (V0, V4 and V5) as factors, along with their respective interactions. There was no evidence of significant interaction between the factors, either for the side with the fracture ($p = 0.134$) or for the non-fractured side ($p = 0.982$). This suggests that the two treatment groups had similar patterns over the course of time (Figs. 2 and 3).

On the side with the fracture, there was a statistically significant difference between the visits, such that the mean T scores were significantly lower at V4 and V5, in relation to V0 ($p < 0.001$), although no differences were found between the treatment groups ($p = 0.825$) (Fig. 2). On the side with the fracture, there was no evidence of any statistically significant variation between the groups ($p = 0.554$) or visits ($p = 0.081$) (Fig. 3).

Radiological evaluation

The results from radiological identification of the callus over the course of the visits did not show any evidence of any significant difference between the treatment groups at the visits

Table 4 – Change in T score in proximal forearm (33%) on non-fractured side, expressed as percentage, in modified ITT population.

	V4	V5	p value ^a (visits)
GAO			
No. of patients	N = 59	N = 59	
Mean ± SD	1.9 ± 17.4	-2.2 ± 28.2	
Min/Median/Max	-36.4/0/79.2	-133.3/0/75.5	0.223
GO			
No. of patients	N = 57	N = 56	
Mean ± SD	4.2 ± 37.4	-5.7 ± 29.8	
Min/Median/Max	-142.9/3.8/150	-142.9/0/34.6	0.128
p value ^b (groups)	0.438	0.861	

^a Wilcoxon signed rank test.

^b Mann-Whitney U test.

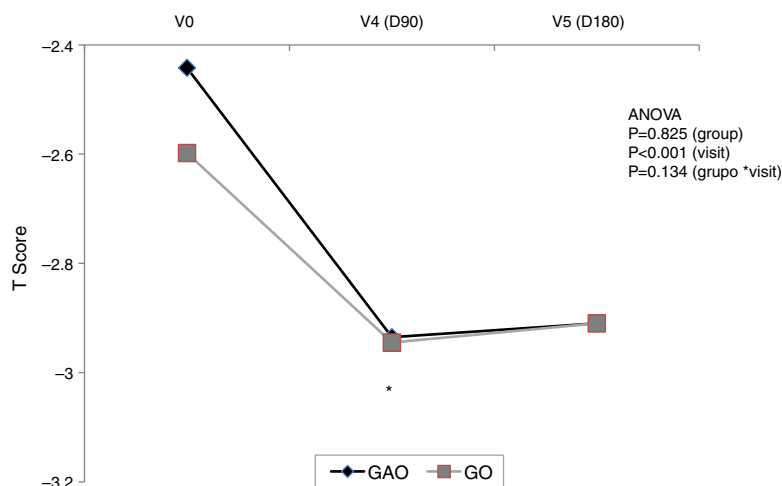


Fig. 2 – Results from the ANOVA model for the fractured side.

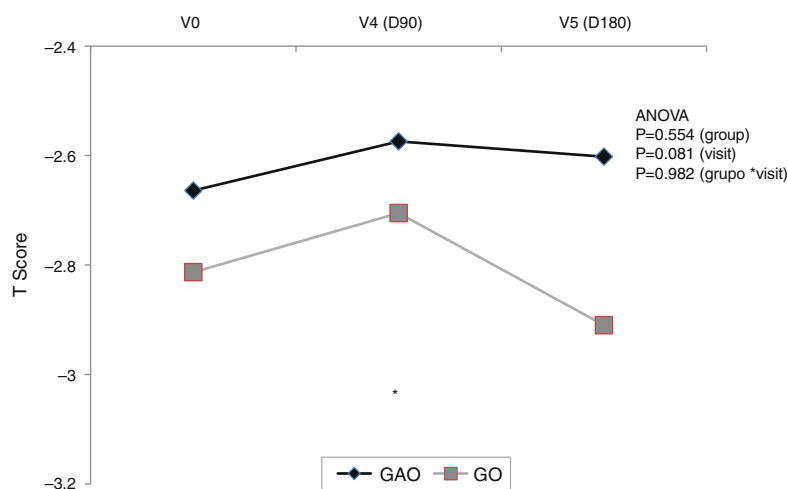


Fig. 3 – Results from the ANOVA model for the non-fractured side.

V1 ($p = 0.674$), V2 ($p = 0.755$) and V3 ($p = 0.749$), with regard to the proportion of the patients in whom the callus was identified on X-rays. At the other visits (V4 and V5), the callus was seen by means of X-rays in almost all the patients, in both groups, and no statistical comparison was made.

Safety

In GAO, 23/71 randomized patients (32.4%) reported that at least one adverse event occurred during the study period, totaling 34 such events. In GO, 23/70 randomized patients (32.9%) reported that adverse events occurred during the study period, totaling 41 such events. Three adverse events were considered by the investigator to be serious. In GAO, one case of renewed fracturing of the wrist was reported. This was considered to be of moderate intensity and needed hospitalization and surgery for external fixation to be implemented. It was reported that the patient had recovered. In GO, two cases of adverse events occurred. One of these consisted of a hypochoic accumulation in the right calf, which was considered to be of moderate intensity. This case required hospitalization

and the patient was still recovering at the time of this report. The other adverse event comprised cardiorespiratory arrest, which occurred at the patient's home, was of severe intensity and resulted in death.

None of these three adverse events was considered by the investigator to be related to the study medication. In GO, both of the adverse events led to interruption of the treatment. For the patient in GAO, administration of the study medication was not immediately stopped because of the adverse event, but the event led to withdrawal from the study.

Overall, the treatments were withdrawn in the cases of three patients because of adverse events relating to the treatment: 1/71 patients (1.4%) in GAO presented acute gastritis and one patient (1.4%) in GO presented epigastric burning and discomfort and another patient (1.4%) presented gastric pain. In addition, another two patients were withdrawn from the study, but without any relationship with the study treatment. In GO, one case of cardiorespiratory arrest was reported; another patient was reported to have had a psychotic episode and a further patient presented a hypochoic accumulation in the right calf.

Discussion

In the present study, after 90 days of risedronate use, no significant variation in the loss of BMD was seen in the fractured arm, or in the non-fractured arm. The same pattern was observed after 180 days of treatment, which suggests that risedronate has a protective effect due to the immobilization.

Several medications have been used to improve bone consolidation, both for accelerating the process and also for improving the quality of the bone callus, i.e. through improving the microarchitecture, volume and biomechanical strength of the callus. These medications include strontium ranelate and drugs that act on the Wnt signaling system, such as teriparatide and the antibodies anti-sclerostin and DKK-1.¹²⁻¹⁵ Some medications have been recognized as harmful to callus formation and these include corticoids, chemotherapeutic agents, antibiotics, anti-inflammatory agents, anticoagulants and anticonvulsants.¹⁶

However, bisphosphonates are the drugs that have been studied most. These favor formation of a more voluminous callus with mineralization and make the callus mechanically more competent, but with a slower remodeling rate.¹⁷⁻²² Another factor discussed in the literature has been the time at which bisphosphonate use should start, after a fracture has occurred. Some evidence favors starting to use bisphosphonates 15 days after the event, while other evidence suggests that, independent of the time at which they are administered, they do not interfere with bone consolidation or with postoperative healing following occurrences of osteoporotic fractures.^{23,24} The time taken to reach consolidation is unrelated to the severity of the osteoporosis or the type of fracture.²⁵ Therapy using bisphosphonates can be continued after occurrences of fractures of the distal radius, without deleterious clinical effects on consolidation.²⁶

When used for long periods, bisphosphonates may increase the occurrences of micro and macrofractures in animals and humans. They also give rise to preferential fracture sites. However, biomechanical gains regarding the bone callus are observed (size and external diameter). It seems that the organism compensates for the negative effect of the medication and modulates the morphology of the callus so as to obtain better biomechanical function (mechanostat).²⁷

The effects of risedronate have been studied both in relation to improvement of bone mineral density and fracture prevention in patients with osteoporosis and in relation to use during bone consolidation. It has been observed that risedronate does not interfere negatively with bone callus formation and can be used without deleterious effects on consolidation. On the contrary, it increases the volume of the callus and its biomechanical resistance.^{28,29}

The BMD of 33% of the radius on the fractured side at the end of six months (V5) presented a negative change of 32.8% in the Oscal group and only 20.8% in the Actonel + Oscal group, which showed that risedronate had a tendency toward having a protective effect against loss of BMD caused by post-fracture immobilization ($p=0.069$). Even though there was no statistically significant difference between the two groups, it was seen that there was lower loss of BMD (evaluated using T scores) in the group treated with Actonel+Oscal (mean

decrease of -0.5), in relation to the group that used Oscal alone (mean decrease of -0.7), as shown in Table 5. This was possibly due to the great variability of the data.

The BMD of 33% of the radius on the non-fractured side at the end of six months (V5) presented a negative change of 5.7% in GO and only 2.2% in GAO, with a difference of 3% in favor of risedronate. However, there was no statistically significant difference ($p=0.861$) (Table 4).

As shown in Fig. 2, the initial BMD of 33% of the radius on the fractured side (measured using the T score) decreased significantly ($p<0.001$) during the treatment (from V0 to V5), while this difference was not observed on the non-fractured side. This shows the significant influence of immobilization of a fracture on bone loss. Regarding the proportion of patients with loss of BMD at V5, there was a statistically significant difference between the fractured and non-fractured sides, for both treatment groups (GAO, $p=0.010$; GO, $p=0.0003$) (Table 5). This pattern of difference observed between the groups was probably related to immobilization of the fractured side (Table 5). These data show that risedronate provided protection in relation to loss of BMD during the immobilization of a limb (osteoporosis of disuse), which is discussed in other studies.³⁰

There was no significant difference in radiological identification of the bone callus at the times of the visits (V1 to V5), or between the treatment groups. Thus, use of risedronate in our study did not present any negative clinical effect on bone consolidation. In most of the patients, radiological identification of the callus occurred at V3, with a similar pattern in the two groups. Furthermore, the safety profile of risedronate was shown to be similar to that of the control group.

Limitations of the study: Given that this study was designed without comparison with placebo, we believe that there may have been an important effect on BMD, since the tests were evaluated centrally, as described in the methodology. However, based on the well-established side effects that have been described previously for this class of medications, an effect in interpreting the safety data cannot be totally ruled out.

Conclusions

Postmenopausal women with Colles fractures who received sodium risedronate plus calcium and vitamin D, in comparison with calcium and vitamin D only, did not show any significant difference regarding loss of BMD in the fractured and non-fractured forearm after 90 days (primary objective) and 180 days (secondary objective). Risedronate was shown to have a tendency toward a protective effect regarding loss of BMD due to immobilization. The time taken to reach fracture consolidation was unaffected and the two groups showed similar safety patterns.

Conflicts of interest

Dr. Lindomar G. Oliveira, Dr. Frederico Barra de Moraes, Dr. Luiz Antônio Silveira Simões Pires and Dr. José Wanderley Vasconcelos declare that they did not have any conflicts of interest. Dr. Henrique Mota Neto Júnior received fees from Novartis, Servier and GlaxoSmithKline and participated in studies

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