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Preventive treatment with alendronate of loss of bone mineral density in acute traumatic spinal cord injury. Randomized controlled clinical trial

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STUDY DESIGN: Randomized controlled clinical trial of two parallel groups.
OBJECTIVES: Analyse the efficacy of primary prevention with alendronate on the loss of bone mass which occurs during the first year of traumatic SCI, measured by double-energy X-ray bone densitometry (DXA).
SETTING: National Hospital for Paraplegics (HNP), Toledo, Spain.
METHODS: We included 52 people admitted to the HNP with traumatic SCI Grade A and B on the ASIA Impairment Scale and less than 8 weeks of progression, which were randomized to one of the two treatment groups. Both groups received calcifediol and a calcium-enriched diet for 52 weeks. Only one group was administered alendronate 70 mg weekly. The dose of alendronate was adjusted according to changes in serum β-CTX.
RESULTS: 52 Participants were randomized. Of the 26 assigned to each group, 4 patients were lost in the alendronate group and 3 in the control group. The random distribution of women was asymmetrical, so we analysed the effect of treatment on men. In the total left hip, the mean (SD) decrease in bone mass was −22.791% (10.768) in the control group compared to the mean (SD) decrease of −2.693% (6.283) in the same location in the alendronate group ($p < 0.0001$). No patient presented related adverse events.
CONCLUSION: Alendronate administered for one year in the first 8 weeks after traumatic SCI decreases bone loss in the hip in men. This treatment is well tolerated.

Spinal Cord (2022) 60:687–693; https://doi.org/10.1038/s41393-022-00755-4

INTRODUCTION

Complete traumatic motor spinal cord injury (SCI) results in loss of bone mass, which may occur at a rate of 1% per week in certain regions during the first months after injury [1].

A dramatic increase in bone resorption markers begins as early as the first week after injury, reaches its maximum values between the first and fourth month, continues at a slower rate until the sixth month, and then tends to stabilize (though not disappear) around the end of the first year of injury [2–4]. The result is an increase in blood calcium and phosphorus, which are excreted in greater quantities in urine.

SCI induced osteoporosis produces an incidence of fractures between 25% and 34% ten years after the injury, most often located around the knee and ankle (>50%) but also at the hip (7–23%). With regard to the lumbar spine, osteoporosis has characteristically not been found by posterior-anterior DXA [4–7].

Bisphosphonates are potent inhibitors of bone resorption and tissue calcification. When randomized clinical trials of preventive treatment within the first year of SCI are reviewed individually, inclusion criteria are variable, samples are small (between 6 and 31 participants), and results are heterogeneous [8–14].

In a New Zealand study [9] 31 individuals were treated for one year in the first 10 days of an acute SCI with alendronate 70 mg/week versus placebo, without systematic calcium and vitamin D supplementation. Treatment with alendronate decreased the loss of bone mineral density measured in the hips and total body compared to placebo, but with a moderate effect compared to that observed in other populations. The author argues that the daily dose of 10 mg alendronate may be too low in this population and that adequate calcium and vitamin D supplementation may be necessary.

The aim of our work has been to analyse the efficacy of alendronate in primary prevention of the loss of bone mass that occurs during the first year of SCI, by systematically supplementing calcium and vitamin D and adjusting the dose of alendronate based on the variation of β-CTX in serum.

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Received: 29 June 2021 Revised: 14 January 2022 Accepted: 16 January 2022
Published online: 29 January 2022

METHODS

Study design

A blinded evaluator clinical trial of two parallel groups was designed with the main objective being to determine the efficacy of oral alendronate in preventing bone loss in the study population. The main response variable was the difference between groups in the percentage reduction in bone mineral density (BMD) between the start and 52 weeks of treatment. One group was given alendronate plus calcifediol (to maintain serum levels of 25-OH vitamin D ≥ 30 ng/ml) and a calcium-enriched diet (1200 mg/day); the other group was given calcifediol only (to maintain serum levels of 25-OH vitamin D ≥ 30 ng/ml) and a calcium-enriched diet (1200 mg/day).

The alendronate administered was KERN PHARMA Weekly Alendronic Acid 70 mg tablets, and the calcifediol was Hydroferol ampoules or capsules of 0.266 µg (15960 IU).

Group A participants, who received alendronate 70 mg/week, had their dose adjusted at week 12 of follow-up: if the decrease in β-CTX was less than 30% in serum compared to baseline [15–17], the dose of alendronate was increased to 140 mg/week.

Revocation of informed consent, hypersensitivity reactions to medication, erosions and/or ulcers in the upper gastrointestinal tract, ionic calcium ≥ 5.54 mg/dl, altered renal function (Cl Cr < 35 ml/min), hyperphosphoremia > 6.5 mg/dl, atypical femoral fracture, and mandibular osteonecrosis were established as criteria for withdrawal from the study. Dropouts were not replaced.

Participants

After signing their informed consent, 52 individuals were included in the study who had a traumatic SCI of ASIA Impairment Scale (AIS) grade A and B with less than 8 weeks of progression, from C4 to L1 level, between 18 and 50 years of age, and who had been admitted for rehabilitation in the HNP.

Cases were excluded with causes of osteoporosis other than spinal cord injury, with contraindications for administration of bisphosphonates and/or vitamin D supplements, and people who had received previous therapy with bisphosphonates.

The presence of known risk factors for osteoporosis were collected (Table 1).

Randomization and masking

A statistician performed the randomization. Before the inclusion of participants, a randomization list was drawn up by randomly exchanged blocks and a set of opaque envelopes was prepared, labelled on the outside with the order number of entry into the study, containing a note inside with this order number and the assigned treatment. These were stored at the HNP Pharmacy. The pharmacist opened the envelopes when the formalities for the inclusion in the study were completed. A rehabilitation doctor and an internist recruited and followed up on participants. As it was an open trial, clinicians and participants knew what the assigned treatment was. Only the final evaluator was blind.

Procedures

The measurement of the main variable (bone mass) was carried out by DXA in the anterior lumbar spine, dual hip and total body, in Hologic Explorer / W" equipment, during the baseline and end of study visits.

During baseline and follow-up visits at 4, 8, 12, 16, 20, 24, 36, and 52 weeks, the following were determined in blood: ionic calcium, phosphorus, 25-OH vitamin D (total), β-CTX; and in 24 h urine: calcium, phosphorus and creatinine clearance (Calcium: BAPTA, Roche Cobas 8000, 24 h urine ref: 21.3–29.0 mg/dL, 100–300 mg/24H. Ionic calcium: Total heparinized venous blood. Gem 3000 gasometer. Ref 4.60–5.40 mg/dL. Phosphorus: Phosphomolybdate Method. Roche Cobas 8000, CV 4.10% Ref: 2.7–4.5 mg/dL. 24-hour urine 40.0–140.0 mg/dL, 400–1300 mg/24H. β-CTX (C-Telopeptide): Electrochemiluminescence. Roche Hitachi Modular E170. CV 3.40–12.11%. Ref M: < 0.584 ng/mL F: Premenopausal: 0.114–0.628 ng/mL. 25-OH Vitamin D (Total): Chemiluminescence. Diasorin. Liaison XL, ng/mL. Status 25-OH vitamin D: Deficiency: < 20 ng/mL. Relative insufficiency: 20–30 ng/mL. Sufficiency: > 30 ng/mL. Possible toxicity: > 150 ng/mL).

Plain x-ray of elbows, hips and knees were performed during baseline and final visits to detect heterotopic ossifications; and simple x-rays of the abdomen and urological ultrasound for calcium urinary lithiasis. During these visits, a neurological examination was also carried out according to the standards of the European (ISCOS) and American (ASIA) international SCI associations to determine the level and degree of neurological affectation.

Outcomes

The main objective was to find the difference between groups in the percentage reduction in BMD with respect to the time of injury, after 12 months of treatment.

The secondary objectives were:

- To determine the safety of treatment (hypercalcemia, hypercalciuria, hyperphosphatemia, calcium urinary lithiasis, heterotopic calcifications).
- Describe the evolution of the markers of bone resorption, β-CTX in serum, and calcium in 24 h urine, in the two treatment groups.

Statistical analysis

According to Gilchrist et al. [9], at one year of the SCI the SD of the percentage reduction in total leg bone density in the placebo group was 5.4%. Thirty-three participants per group are required in order to detect, with a statistical power of 80% and a type I error risk of < 5%, a reduction in bone density at the baseline, in the total leg and after 12 months, in the "alendronate" group at least 4% lower and with a SD of 5.4%, as in the cited study, by means of the Mann-Whitney U test and with a loss of participants during follow-up of 10% maximum.

The Mann Whitney U-test was used for inter-group comparison of percentage reduction in bone density and the Bonferroni correction of the P-value was performed for multiple comparisons.

Regarding the analytical variables, for comparison between treatments and throughout the repeated measurements in the follow-up visits, a mixed ANOVA was performed, with a logarithmic transformation of the dependent variable (equivalent to a comparison between geometric means) in order to stabilize the variance when the Levene test detected heterocedasticity. We used the Greenhouse-Geisser correction of the degrees of freedom when the Mauchly test was significant. Finally, a multivariate contrast of the 8 levels of the intra-subject factor based on Pillai's V trace was also made.

When the effect of successive visits is significant, paired "post-hoc" contrasts were made between each visit and the first visit after the start of treatment using the Bonferroni correction.

Analyses were carried out using PASW Statistics, version 18.

RESULTS

Between August 14, 2012 and June 3, 2016, 93 individuals with inclusion criteria were admitted to the HNP. Of these, 52 (56%) were randomized to one of the two treatment groups (Fig. 1). Although the planned sample was 66 participants, it was decided to stop the recruitment four years after the start (twice the time planned for the recruitment period). In all cases compliance was > 80%, verified by tablet counting. Of the 26 assigned to each group, 4 participants in the alendronate group and 3 in the control group dropped out of the study. Final DXA could only be performed on 1 dropout from the control group after 26 weeks of follow-up. The reasons for dropouts were personal and not associated with adverse treatment events.

In both groups, those cases with lumbar spine orthopaedic implants were not included in the lumbar spine bone mass analysis. In the control group, one case that developed heterotopic ossifications around the right hip was excluded from the analysis of the right hip and the total right leg.

The demographic and clinical baseline characteristics of the participants are shown in Table 1. Twelve women were included in the trial, of which 11 were randomized to the control group. The only woman in the alendronate group dropped out of the study at week 12 of follow-up.

As the influence of sex on bone mass is known, we compared the effect of treatment on men. Table 2 presents the description of the main response variables. The differences between the two treatment groups in total hips and their sub-regions, anterior lumbar spine, and both total legs are compared in terms of percentage reduction in BMD. A significant effect of alendronate treatment is observed in both total hips and their sub-regions. This attenuation is very significant in 12 of the 13 locations that

Table 1. Baseline characteristics of the subjects.

Characteristic	Alendronate group ($n = 26$)	Control group ($n = 26$)
[a]Age (years)	32 (±9·37)	31·5 (±10·21)
Gender (male/female)	25/1	15/11
Ethnicity: white	26	26
Level of lesion (cervical/thoracic)	10/16	13/13
ASIA classification (A/B)	20/6	20/6
Orthopaedic surgery	26	25
Spinal implants	26	25
Lumbar spinal implants	4	5
Vertebral fractures (0/1/>1)	0/5/21	1/11/14
Non vertebral fractures	18	16
[a]25-OH D vitamin (pg/ml)	19·53(±6·99)	22·23 (±8·83)
Matching WHO criteria for osteoporosis /osteopenia at any hip	0/4	1/7
Matching WHO criteria for osteoporosis /osteopenia at the lumbar spine	1/3	2/4
[a]Days to enrolment	47·04 (±9·51)	49·35 (±8·65)
[a]BMI (kg/m^2)	20·95 (±3·41)	21·63(±3·83)
Therapeutic walking during study	8	11
Walking regained during study	0	1
Previous fragility fractures	0	0
Family antecedents of hip fracture	0	0
Active cigarette consumption	4	2
Alcohol consumption> 3 units per day	0	1
BMI < 18	5	5
High dose steroids	7	8
Spasticity during study	17	18

[a]Values are mean ± SD.
BMI Body mass index.

were analysed. In the total left hip, the mean (SD) decrease in bone mass was −22.79% (10.77) in the control group compared to the mean (SD) decrease of −2.69% (6.28) in the same location in the alendronate group ($p < 0.0001$). Even when the effect is analysed with the Bonferroni correction, only the differences in the total left leg and right hip Ward are no longer significant. The results of the analysis for all the participants (males and females, Table 3) maintain the statistically significant difference between the groups. In the control group, one woman with a cervical lesion AIS A at entry recovered ability to walk. In comparison with the other participants in the control group, she lost less BMD (−0.27% in the total left hip and −4.48% in total right hip).

In the anterior lumbar spine, bone mass gain was recorded in the alendronate group versus the control, and the difference was statistically significant (Tables 2 and 3).

When looking at DXA results for each participant, not all of them lost bone mass at study completion. In fact, 38.03% of the measurements performed in the alendronate group showed bone gain versus 7.69% in the control group (Supplementary Information 1).

Markers of bone resorption and safety parameters were analysed in both sexes, considering that laboratory reference values for β-CTX are different for males and females.

β-CTX (C-Telopeptide) was elevated at the baseline visit in all but 1 of the participants. In the group that received alendronate it decreased from week 4 post-treatment to week 52, while in the control group it increased until week 16, after which it decreased progressively until the end. The differences between both groups ($p < 0.0001$) and between visits ($p < 0.0001$) were significant. The estimated difference between the geometric means of β-CTX of the alendronate group and the control group was −0.52 ng/ml (95% CI, −0.68 to −0.40 ng/ml). Alendronate already had a significant effect as of the fourth week, which remained stable throughout the follow-up time (Fig. 2).

The concentration of β-CTX did not decrease below the reference value in any participant throughout the follow-up. At week 52 it was elevated in 5 participants (men) in the group receiving alendronate (≤0.95 ng/ml), while in the control group it remained elevated in 15 participants: 13 men (≤1.55 ng/ml) and 2 women (≤1.19 ng/ml).

The mean concentration of β-CTX at 4 weeks of follow-up with respect to baseline determination in the group receiving alendronate decreased (mean (SD) −40.04% (24.21)) and in the control increased (mean (SD) + 3.59% (24.24)). At 12 weeks it decreased (mean (SD) −46.05% (18.77)) in the alendronate group and it increased in the control group (mean (SD) + 11.33% (40.75)). An average decrease of > 30% was not obtained in the control group until week 52 (mean (SD) −31.51% (19.07)).

The average 24 h urine calcium excretion was elevated at the baseline visit of the study in both groups. The average decrease was significant in the individuals who received alendronate with respect to the control group ($p < 0.0001$) (Fig. 3).

No participant had to be withdrawn according to the withdrawal criteria, or because of other adverse events.

Due to increased bone resorption in these patients there is an outflow of calcium from the bone into the blood. Despite having received dietary calcium supplements we did not find an increase above the reference value of mean ionic calcium in blood in either group; however, in the alendronate group the mean ionic calcium was found to be significantly lower than in the control group throughout the follow-up ($p = 0.001$).

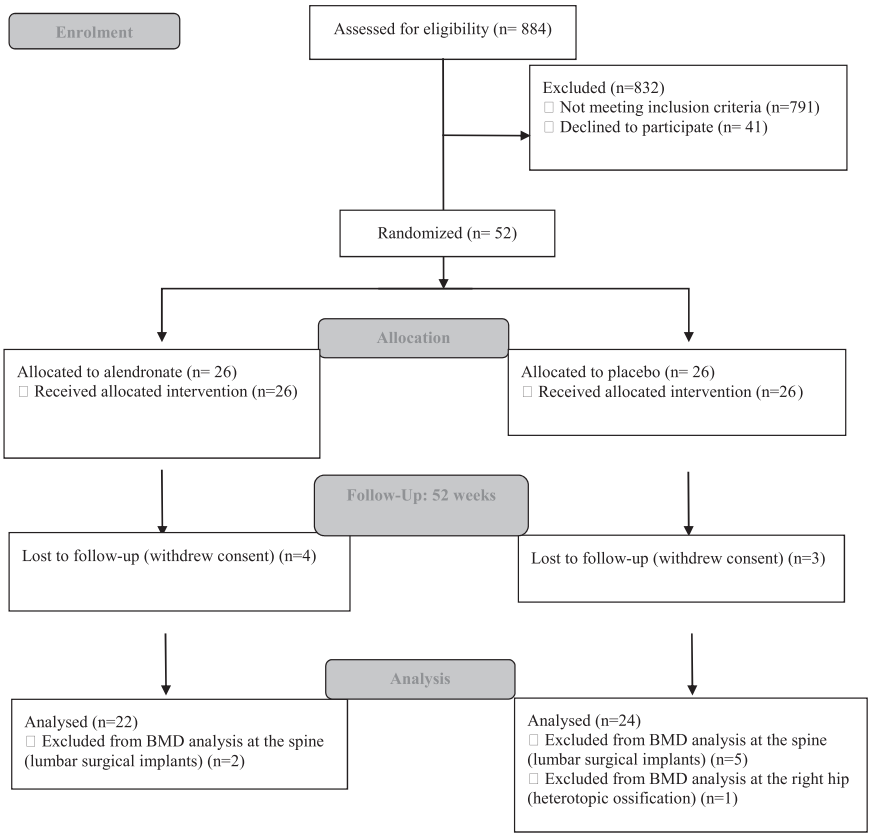

Fig. 1 CONSORT 2010 Flow Diagram.

One man in the alendronate group was given an overdose of vitamin D. He was administered, by mistake, the dose of 15,960 IU of calcifediol, prescribed every two weeks, on a daily basis for several days in a row (since this administration occurred in another centre, we do not have exact data on the number of days in which this course was followed), in spite of which the patient did not develop hypercalcemia.

Eight years after the first participant was included in the trial, a telephone follow-up visit was made to all the participants. Only 1 woman of the control group has presented so far a supracondylar femur fracture after a minor trauma, which occurred 7 years since her enrolment. We plan to continue this follow-up annually.

The mean serum phosphorus concentration was high (>4.5 mg/dl) at the baseline visit in participants from both groups: 30.8% of group A and 32% of group B (≤5.4 mg/dl). Starting with week 4 it decreased and from week 12 onward it normalized in both groups. There was no difference in the number of individuals with high serum phosphorus between the groups during follow-up (Fisher's exact test).

One patient in the control group was diagnosed with heterotopic ossification around the right hip at the final visit of the trial.

Two patients in the control group had multiple bladder lithiasis in the follow-up. Analysis of the stones was, in one case, struvite (magnesium ammonium phosphate), carbonic apatite (crystalline calcium phosphate), and bruxite (hydrated calcium phosphate); and in the other case, struvite and carbonic apatite. In the first case, the calciurias were ≤ 516.8 mg/24 h and the phosphaturias ≤ 906.3 mg/24 h. In the second case, the calciurias were ≤ 580 mg/24 h and the phosphaturias were ≤ 144 mg/24 h.

Mean urinary calcium excretion in 24 h urine remained above the reference value (>300 mg/24 h) in some participants in the two groups during the 52-week follow-up. There were more persons in the control group than in the alendronate group with elevated mean 24 h urine calcium excretion (>300 mg/24 h) significantly up to week 12 of follow-up (Fisher's exact test).

The average 24 h urine phosphorus excretion was normal, with isolated exceptions. The differences in the number of individuals with average high phosphorus excretion in 24 h urine were not significant (Fisher's exact test).

DISCUSSION

Treatment with alendronate is well tolerated and effective in mitigating bone loss at 52 weeks of follow-up in hips after traumatic SCI with AIS grades A and B in men. In the anterior lumbar spine, where bone mass gain was recorded in the alendronate group versus the control, the difference, even though it was statistically significant, is less clinically relevant. Though it has been published that individuals with chronic SCI may have bone loss of the lumbar spine that is more evident on lateral DXA, this site has not been reported as a fracture-prone area [18].

Previous trials to evaluate the effects of bisphosphonates in the prevention of bone loss in the acute phase of SCI have been conducted with small samples and heterogeneous patients (complete and incomplete motor lesions, lack of systematic collection of risk factors and calcium and vitamin D supplementation) [19], so it is doubtful whether they are actually effective when the spinal cord injury is complete [20, 21].

Four studies with zoledronate have been published since the start of our trial [22–25]. The four of them have also small samples and one trial includes participants with complete and incomplete motor injuries [24]. Three of them have looked at the knee with different results, showing that the benefit of bisphosphonates for preserving bone loss at the knee is still unclear [22, 23, 25].

Our trial was conducted with the largest homogeneous sample of participants to date and with systematic calcium and vitamin D supplementation in both groups, and the dose of alendronate was

Table 2. DXA in men.

DXA IN MEN. Variation of bone mass in % of the final measurement with respect to the baseline.											
											Mann-Whitney U
		Valid	Losses	Mean	SD		Valid	Losses	Mean	SD	Exact significance (bilateral)
Total LEFT Hip	Alendronate	22	4	−2.693	6.283	Control	14	1	−22.791	10.768	$p < 0.0001$
LEFT Femoral Neck		22	4	−0.833	5.838		14	1	−20.768	8.744	$p < 0.0001$
LEFT Hip Trochanter		22	4	−3.112	8.836		14	1	−24.696	11.327	$p < 0.0001$
LEFT Hip Inter-trochanteric		22	4	−2.445	7.619		14	1	−22.386	11.127	$p < 0.0001$
LEFT Hip Ward		22	4	4.225	10.218		14	1	−18.16	14.956	$p < 0.0001$
Total RIGHT Hip		22	4	−3.709	5.737		13	2	−21	13.54	$p < 0.0001$
RIGHT Femoral Neck		22	4	−2.958	8.701		13	2	−18.307	9.38	$p < 0.0001$
RIGHT Hip Trochanter		22	4	−3.663	8.483		13	2	−23.087	13.317	$p < 0.0001$
RIGHT Hip Inter-trochanteric		22	4	−4.473	5.679		13	2	−21.001	13.78	$p < 0.0001$
RIGHT Hip Ward		22	4	−1.189	12.256		13	2	−14.158	18.592	$p = 0.008$
Anterior LUMBAR Spine		20	6	5.997	3.543		12	3	−1.2574	8.6	$p < 0.0001$
LEFT Leg		22	4	−8.228	5.460		14	1	−13.614	5.354	$p = 0.011$
RIGHT Leg		22	4	−9.966	4.987		13	2	−12.539	6.799	$p = 0.203$

After Bonferroni correction, only the differences in the LEFT leg and RIGHT hip Ward are no longer significant

Table 3. Variation of bone mass (both sexes).

DXA IN BOTH SEXES. Variation of bone mass in % of the final measurement with respect to the baseline.											
											Mann-Whitney U
		Valid	Losses	Mean	SD		Valid	Losses	Mean	SD	Exact significance (bilateral)
Total LEFT Hip	Alendronate	22	4	−2.693	6.283	Control	24	2	−18.798	10.823	$p < 0.0001$
LEFT Femoral Neck		22	4	−0.833	5.838		24	2	−15.420	10.050	$p < 0.0001$
LEFT Hip Trochanter		22	4	−3.112	8.836		24	2	−20.287	12.159	$p < 0.0001$
LEFT Hip Inter-trochanteric		22	4	−2.445	7.619		24	2	−18.578	11.245	$p < 0.0001$
LEFT Hip Ward		22	4	4.225	10.218		24	2	−13.146	14.083	$p < 0.0001$
Total RIGHT Hip		22	4	−3.709	5.737		23	3	−18.535	12.076	$p < 0.0001$
RIGHT Femoral Neck		22	4	−2.958	8.701		23	3	−15.490	8.711	$p < 0.0001$
RIGHT Hip Trochanter		22	4	−3.663	8.483		23	3	−19.984	12.730	$p < 0.0001$
RIGHT Hip Inter-trochanteric		22	4	−4.473	5.679		23	3	−18.535	12.004	$p < 0.0001$
RIGHT Hip Ward		22	4	−1.189	12.256		23	3	−14.008	15.113	$p = 0.001$
Anterior LUMBAR Spine		20	6	5.997	3.543		17	9	−0.351	7.596	$p < 0.0001$
LEFT Leg		22	4	−8.228	5.460		24	2	−13.391	7.852	$p = 0.018$
RIGHT Leg		22	4	−9.966	4.987		23	3	−12.196	6.022	$p = 0.210$

After Bonferroni correction, only the differences in the LEFT leg are no longer significant.

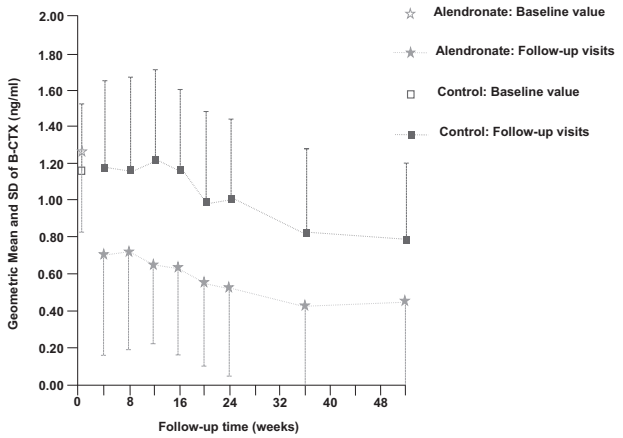

Fig. 2 β-CTX (ng/ml), both sexes. Changes in β-CTX from baseline over 52 weeks for alendronate or control.

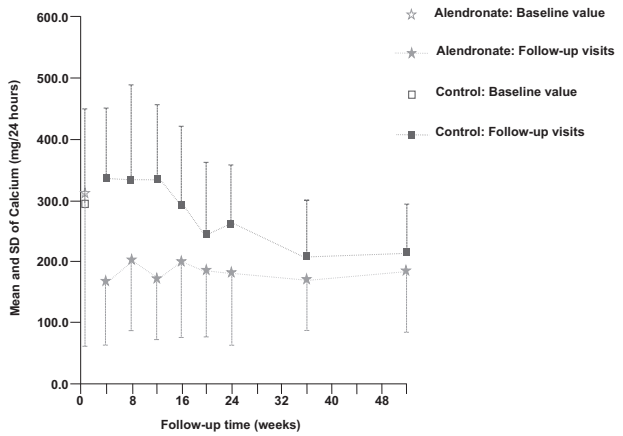

Fig. 3 Urinary calcium excretion (mg/24h). Changes in 24 h urine calcium excretion from baseline over 52 weeks for alendronate or control.

adjusted by variation from β-CTX, to avoid the confounders of other articles. Nevertheless, our study has several disadvantages. First, no densitometry has been performed on the knee and ankle, which are the preferred locations for fractures in this population, as we do not have a standardized, commercially available method for this. Lazo et al. reported that measurement of femoral neck BMD can be used to quantify fracture risk in SCI patients and nearly 20% of their fractures occur at the proximal femur [6]. So we believe that, though not optimal, DXA in dual hip could be a valid method to asses bone mass after SCI, specially when it is the only one available.

Second, the random distribution of women was asymmetrical, so we cannot establish the effect of alendronate in their BMD. Therefore, stratification of women is essential in future trials.

Finally, a comparison of incidence of fragility fractures between the groups was not possible because of the limited duration of the study. All trials with bisphosphonates in acute SCI have been carried out with a small number of subjects because of the difficulty and slowness of their recruitment, as the incidence of the SCI is low and the physical and emotional state of the patients in this phase of trauma makes them reluctant to participate. In fact, we had to double the recruitment time initially planned. Anyway, their publication is still useful as future meta-analysis may cast light on bisphosphonates role in osteoporosis secondary to SCI.

Currently some investigators have not found research with bisphosphonates to prevent bone loss after SCI encouraging [26]. We believe that it is necessary to optimize the time (as soon as possible after the SCI) and the dose (probably adjusted by bone biomarkers of resorption) of bisphosphonates after SCI, as well as to study sequential therapies with other antiresorptive medications.

Gifre et al. conducted a study in individuals with SCI of less than 6 months of progression and found that RANKL levels are increased after injury and are related to bone mass loss at the proximal femur level while becoming undetectable during treatment with denosumab [27]. In another open study by the same group, 14 persons already with osteoporosis secondary to SCI were treated with denosumab, and a discrete increase in bone mass was observed by densitometry in the lumbar spine and hip [28]. Recently, Cirnigliaro et al. tested the efficacy of denosumab in a randomized, double-blinded, placebo-controlled clinical trial which included 26 participants with subacute (≤90 days) motor complete SCI. Denosumab generally maintained BMD at the knee at 18 months [26]. However, the authors highlight that discontinuing denosumab has been demonstrated to result in rapid bone loss. To our group, this suggests that a strategy for preventing bone mass loss in SCI that includes denosumab and bisphosphonates could be studied.

Regarding bone remodelling markers, in the serum resorption bone marker β-CTX we have found statistically significant differences between the two groups. A significant drop occurs as a result of alendronate treatment after 4 weeks of treatment in most individuals. This has resulted in less bone mass reduction in the group treated with alendronate.

The excretion of calcium in 24 h urine has also proved to be useful in the follow-up of treatment, since it decreases significantly in patients who received alendronate.

In conclusion, our study shows that alendronate administered for one year in the first 8 weeks after traumatic SCI decreases bone loss in the hip in men. This treatment is well tolerated. Calcium and calcifediol supplementation is also safe. β-CTX may be useful for monitoring and adjusting treatment in these people. It remains to be determined in future follow-up whether the results actually translate into fewer fragile fractures in the treated persons.

DATA AVAILABILITY

The datasets generated and/or analyzed during the current study can be found in Supplementary Information 1 and are also available from the corresponding author on reasonable request.

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ACKNOWLEDGEMENTS

The Foundation and the Management of the National Hospital for Paraplegics. All the staff of the Rehabilitation[a], Internal Medicine[a], Clinical Analysis[a,b], Pharmacy[a], Nuclear Medicine[c] and Radiology[a] services of the National Hospital for Paraplegics[a], University Hospital of Toledo[b] and Quirónsalud Hospital[c], Toledo (Spain).

AUTHOR CONTRIBUTIONS

BBS, RCB, MSDM, MTFD, DGM, CLB, and LMD contributed to study design. MSDM, MTFD, DGM, CLB, and LMD contributed to data collection. RCB, MSDM, MTFD, and DGM contributed to data analysis. All authors contributed to data interpretation and writing of the report and are responsible for the report. The study funded by Independent Investigation Grants 2011, granted by the Spanish Ministry of Health and Consumer Affairs (reference EC11–498), the beneficiary of which was the National Hospital for Paraplegics Foundation G-45568441, Carmen Labarta Bertol being the principal investigator.

COMPETING INTERESTS

The authors declare no competing interests.

ETHICAL APPROVAL

The trial was approved by the Ethics Committee of Clinical Research of the Health Area of Toledo and the Clinical Research Committee of the National Hospital for Paraplegics (Hospital Nacional de Parapléjicos—HNP) of Toledo (Spain).

ADDITIONAL INFORMATION

Supplementary information The online version contains supplementary material available at https://doi.org/10.1038/s41393-022-00755-4.

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