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Research Article

Beneficial effect of Strontium Ranelate on vertebral fracture in Osteoporotic mature women

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Abstract

Background:osteoporosis is consider one of the most common causes of vertebral fracture especially in postmenopausal women . **Objectives**:to evaluate the role of strontium ranelate in reduction of incidence of osteoporosis. **Patients and methods**:this study was conducted in the department of obstetric and gynecology of Al-Azhar university hospital(assuit)Egypt, as comparative study that compare the reduction of incidence of vertebral fracture in premature, mature and post mature osteoporotic women by strontium ranelate ,go osteoporotic women were divided into 3 groups according to their age Group I (30 participants) premature women age < 40 years-Group II (30 participants) mature women age 40-50 years –Group III (30 participants) post mature women age 50-60 years,then each Group were subdivided into 2 subgroup. Subgroup(A)…….received vita D+calcium+2g strontium ranelate.Subgroup (B)…….received vita D+ calcium only. **Results: in group (I)**the incidence of vertebral fracture was about 3.7% ,this present in subgroup B (7.7%) and no fracture in subgroup A,So strontium ranelate reduce the incidence of fracture by about 100% . **in group (II)**the incidence of vertebral fracture was about 12% ,this present in subgroup A (7.7%) and in subgroup B(16.7%),So strontium ranelate reduce the incidence of fracture by about 50% . **in group (III)**the incidence of vertebral fracture was about 12% this present in subgroup A (7.7%) and in subgroup B(16.7%),So strontium ranelate reduce the incidence of fracture by about 50% . **conclusion:** Although strontiumranelate decreased the incidence of vertebral fracture in group I by about 100% and in group II and group III by about 50% ,but Unfortunately statistical difference were non significant.

Keywords: mature women ,strontiumranelate ,vertebral fracture.

Introduction

Vertebral fractures a serious consequence of osteoporosis, lead to acute and chronic back pain, spinal deformity, and a reduction in survival equivalent to that caused by hip fractures***(Nevitt et al, 1998).*** The health care burden in financial terms is substantial. Vertebral deformities predict further vertebral fracture even within one year.

The bone fragility that characterizes osteoporosis after menopause results both from an imbalance in bone remodeling at the cellular level, which causes bone resorption to exceed bone formation, and from an increase in the rate of remodeling at the tissue level ***(Ray et al, 1997).***

Antiresorptive therapies reduce the rate of bone remodeling and lower the fracture rate by 30 to 50 percent. Antiresorptive agents however do not increase bone tissue mass. Instead the increase in bone mineral density observed in clinical trials of antiresorptive drugs is the result of a more complete secondary mineralization of the existing (but reduced) bone tissue mass. Restoration of bone tissue mass and bone structure is not achieved with antiresorptive drugs and requires the use of anabolic agents ***(Lindsay et al, 2001).***

Strontium ranelate is a new orally active agent consisting of two atoms of stable strontium and an

organic moiety (ranelic acid). It stimulates the formation of new bone tissue and decreases bone resorption.

Strontium ranelate prevents bone loss in ovariectomized rats, increases bone mass in osteopenic animals and increases bone strength in normal animals. To date no deleterious effects on the primary or secondary mineralization of bone in laboratory animals or humans have been reported. Results from a one-year placebo-controlled, phase 2, dose–response study involving 90 premature,mature, post mature women with osteoporosis suggested that ingestion of 2 g a day of oral strontium ranelate reduced the incidence of vertebral fractures during the first year of treatment and simultaneously increased bone mineral density.***(Seeman et al,2000).***

In order to confirm these results (Black *et al*,1993)designed the Spinal Osteoporosis Therapeutic Intervention study to test the safety of strontium ranelate and its efficacy against vertebral fracture when given orally at a dose of 2 g per day for one year in women with osteoporosis and no history of vertebral fracture.***(Black et al, 1993).***

Aim of The Study: To evaluate the role of (proteolos) strontium ranelate on the reduction of incidence of vertebral fracture in pre mature , mature and post mature osteoporotic women .

Patients and methods

Go women (pre mature, mature and post mature)were recruited from those patients attending our gynecology clinic in Al-azhar university hospital (assiut) for this prospective study. women were eligible for the study if they were at premature or mature or postmatureage and had a lumbar-spine bone mineral density of 0.840 g per square centimeter or less (measured with Hologic instruments). Women were ineligible if they had severe diseases or conditions that could interfere with bone metabolism or if they used antiosteoporotic treatments (fluoride salts and bisphosphonates taken for more than 14 days within the previous 12 months, or estrogen, calcitonin, or calcitriol taken for more than 1 month in the previous 6 months). All participants provided written informed consent before enrollment in the study.

Women were classified according to their age into:
Group I….(30pateints) pre mature women age<40 years.
Group II….(30pateints) mature women age 40-50 years.
Group III…(30pateints) post mature women 50-60 years.
Then each group were subdivided into 2 groups;
Subgroup (A) received vita D+ calcium + 2g strontium ranelate.

Subgroup (B) received vita D+ calcium only.

The primary efficacy parameter was the percent variation in the incidence of the vertebral fracture during one year in each age group and the reduction of vertebral fracture in subgroup A compared to subgroup B .

Treatment Protocol and Follow-up:

Throughout the study subjects received daily calcium supplements at lunchtime (up to 1000 mg of elemental calcium) to maintain a daily calcium intake above 1500 mg and vitamin D (800 IU). After a run-in period of 2 weeks the subjects were randomly assigned to receive 2 g a day of strontium ranelate (two packets a day of a powder that they mixed with water) or calcium and vita D only one years. Subjects were instructed to take the study drug once daily, at bedtime, (one packet 30 at bedtime).

Two methods of assessing vertebral fracture were used. First a semi quantitative visual assessment of each vertebra, from T4 to L4, was performed by the same reader throughout the study. The semi quantitative grading scale was as follows: grade 0, normal; grade 1, a decrease in the height of any vertebra of 20 to 25 percent; grade 2, a decrease of 25 to 40 percent; and grade 3, a decrease of 40 percent or more***.(Genant et al, 1993).***

For primary analysis, a new fracture was defined by a change in the score of a vertebra from grade 0 at base line to a subsequent grade of 1 or more. Second, quantitative assessment was also performed: anterior, middle, and posterior vertebral heights were measured for each vertebra from T4 to L4. A new fracture was defined by a decrease in height of at least 15 percent (or 3 mm) on a vertebra graded 0 at base line and with

a grade on the semi quantitative scale of 1, 2, or 3. ***(Wu CY et al, 1997)***

(The study did not have sufficient power for adequate statistical comparison of the two groups).

Bone mineral density at the lumbar spine was measured by dual-energy x-ray absorptiometry at base line and at six-month intervals (Hologic). All the scans were analyzed centrally. A quality-control program was conducted throughout the study.(***Slosman et al, 1999).***

Results

*This study was conducted on 90 osteoporotic women (30 participants) for each group:
In group I: there were 3 cases dropped out and failed to be followed up for one year and were excluded from the study.
In group II: there were 5 cases dropped out and failed to be followed up for one year and were excluded from the study.
In group III: there were 5 cases dropped out and failed to be followed up for one year and were excluded from the study.

Discussion

Prevention of fractures is the primary aim of antiosteoporotic treatment. In this present study strontium ranelate ingested daily reduced the risk of new vertebral fractures by 100% in age group (1)and by 50% in age group (2) and by 50% in age group (3) percent at one year . Although data from direct comparisons with other antiosteoporotic treatments are lacking the reduction in the risk of vertebral fracture seems similar to the reduction reported with alendronate (47 percent) ***(Black et al, 1996).***

5 mg of risedronate (49 percent) (Reginster,et al 2000). 60 mg of raloxifene (30 percent***) (Ettinger et al, 1999).*** and parathyroid hormone (65 percent after 21 months of treatment***).(Neer et al, 2001).***

The methods of assessing vertebral fractures involving both semiquantitative and morphometric evaluations were similar to the methods used in these other reports. Strontium ranelate also reduced the risk of multiple vertebral fractures and the risk of symptomatic fractures. ***(Ettinger et al, 1999).***
Most antiresorptive agents prevent bone destruction by reducing the rate of bone remodeling as reflected by a decrease in both markers of bone resorption (more than 50 percent with bisphosphonates and about 30 percent with raloxifene) and markers of bone formation (about 50 percent with bisphosphonates and 20 percent with raloxifene). ***(Delmas et al ,2000).***
Treatment with parathyroid hormone increases both bone formation and bone resorption***.(Lindsay et al, 1997).***

When parathyroid hormone and alendronate are combined, there is unexpectedly no potentiation of their effects on biochemical bone markers***.(Black et al, 2003).***

The mechanism of action of strontium ranelate is probably different from those of these drugs. Each time the patients were evaluated during our study, bone formation had increased in the group assigned to strontium ranelate . The mechanisms for the apparent dissociation between reduced bone resorption and increased bone formation are not yet understood, but they probably differ from the mechanisms of current treatments***. (Lufkin et al, 1992).***

Any metal with an atomic number higher than that of calcium can be expected to influence bone mineral density***.(Nielsen et al, 1999).***

In experiments, strontium in bone correlated with strontium in plasma.(***Dahl et al, 2001).***

In summary, in spite of strontium ranelate given orally at a dose of 2 g daily appears to reduce the risk of vertebral fractures rapidly, effectively, among pre mature ,mature and post mature osteoporotic women ,but statistical difference were non significant .

Conclusion and Recommendations:

The quality of life depends upon multiple factors. However one of the most important factors is bone healthy, as osteoporosis is more common in women. Screening of osteoporosis is recommended for menopausal women management.
Upon this study recommend the followings:
1-screening of osteoporosis is recommended in highly risk women as:

Table 1: vertebral fracture and results of DEXA in group I (pre mature women) subgroups:

Results,of DEXA"Tscore" after 1year	FRACTURE OF VERTEBRAL				No FRACTURE			
	(Subgroup A) N=14		(Subgroup B) N=13		(Subgroup A) N=14		(Subgroup B) N=13	
	No.	%	No.	%	No.	%	No.	%
Osteopenic	0	0.0	0	0.0	11	78.6	1	7.7
Osteoporosis	0	0.0	1	7.7	3	21.4	11	84.6
Total	0	0.0	1	7.7	14	100.0	12	92.3
P. value	0.291				0.001**			

(p.value very significant in no fracture cases =0.001)

Table 2: vertebral fracture and results of DEXA in group II (mature women) subgroups:

Results,of DEXA"Tscore" after 1year	FRACTURE OF VERTEBRAL				No FRACTURE			
	(Subgroup A) N=13		(Subgroup B) N=12		(Subgroup A) N=13		(Subgroup B) N=12	
	No.	%	No.	%	No.	%	No.	%
Osteopenic	0	0.0	0	0.0	5	38.5	1	8.3
Osteoporosis	1	7.7	2	16.7	7	53.8	9	75.0
Total	1	7.7	2	16.7	12	92.3	10	83.3
P. value	0.489				0.097			

(p.value = 0.097 non significant)

Table 3: vertebral fracture and results of DEXA in group III (post mature women) subgroups:\

Results,of DEXA"Tscore" after 1year	FRACTURE OF VERTEBRAL				No FRACTURE			
	(Subgroup A) N=13		(Subgroup B) N=12		(Subgroup A) N=13		(Subgroup B) N=12	
	No.	%	No.	%	No.	%	No.	%
Osteopenic	0	0.0	0	0.0	5	38.5	1	8.3
Osteoporosis	1	7.7	2	16.7	7	53.8	9	75.0
Total	1	7.7	2	16.7	12	92.3	10	83.3
P. value	0.489				0.097			

(p.value = 0.097 non significant)

A-postmenopausal women.
B-women with past history of fracture.
C-women with family history of osteoporosis.

2-in case of osteoporotic women treatment should be started to avoided vertebral fracture.

3- In case of osteoporotic women treatment with strontium ranelate+ ca+ vita D is better than treatment with calcium and vita D only as S.R improving T score of DEXA and decreased risk of vertebral fracture by about 50%.

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