



DOSE-DEPENDENT EFFECTS OF INTRANASAL SALCATONIN ON BONE HEALTH AND FRACTURE RATES IN ELDERLY WOMEN WITH MODERATE OSTEOPOROSIS

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ABSTRACT

To determine the influence of salmon calcitonin (salcatonin) at the doses that portray dose-response effect using the intranasal route on bone mineral density, bone turnover and as well as determine the impact of salcatonin on the incidence of fracture in the women who have moderate osteoporosis. Randomized group comparison of a placebo value and a technique of a double blind using placebo control. Outpatient clinic used to study osteoporosis. 208 female patients with rather good health, aged 6872 years had average bone mineral content of their distal forearm which was 30 percent less than the average value of young and health non-post menopausal females. The two years of either the amounts (which were 50 IU, 100 IU, 200 IU) of the intranasal salcatonin or placebo were administered to the 208 women who were randomly divided into a four-block group. An Inulin of 500 mgs without a calcium supplementation was administered to all the groups as well. Not every woman participated in the study up to 32 women, 164 women finished the research to the end. Change in the BMD of the lumbar spine and distal forearm and the occurrence of the vertebral and the peripheral fracture after 2 years of the treatment period. Mean alterations shown in bone mineral density of spine revealed that the sites of calcium-treated group exhibited positive values of 1 percent (95 percent confidence interval -0.1 percent to 1.5 percent) or 200 IU of salcatonin treatment at 3 percent (1.8 percent to 4.2 percent). Salcatonin also indicated a very strong dose response effect with the respective effects of 1.0 percent in every 100 IU (0.2 percent to 1.7 percent, $p=0.008$). The relative risk of breakdown rates too was extremely low in the women on salcatonin that was 0.23 (0.07 to 0.77) or approximately two thirds less than the women without salcatonin. Under the results, it is indicated that in event of comparison against calcium alone, it has been discovered that intranasal salcatonin has a relatively low levels of fracture by an average of two thirds in elderly women who showed moderate degree of osteoporosis and had a high amount of spinal bone mass in proportional dose.

Keywords : Salcatonin, Osteoporosis, Bone density, Fracture rates, Dose-dependent

INTRODUCTION

Osteoporosis is a life threatening age small-scale. It is a disease which millions of women have in the world. The experience of the loss of bone density along with the sensitivity to fractures is also observed. After cementing of osteoporosis the sure treatment is non-existent. The use of the fluoride as the bone-promoting drug has been recently covered with the reference to the effects on the fractures

rates. Therapy that aims at slowing the loss of bone that was reconceptualized, and this type is not, per se, directed to augment any substantial benefit on bone mass, and this type of therapy may not, therefore, prevent the occurrence of subsequent fracture. According to the recent studies, it is revealed that estrogen can prevent the bone resorption among osteoporotic women and hence the therapeutic estrogen in the period of osteoporotic women has a significantly higher effect on increasing the density of the bones of the spinal cord as well as lowering the number of vertebral fracture in such patients. It has also been found that bisphosphonate reduces frequency of vertebrae fracture on osteoporotic women. The impact of calcitonin and the consequent impact on bone fracture rates are still an open question but injectable calcitonin is approved to be used to treat advanced osteoporosis. Calcitonin inhibits the process of osteoclastic activity and long-term, it decreases the number of osteoclasts by inhibiting the formation of precursor osteoclast by shortage of development of precursor osteoclasts. The side effects in the systemic body and the pain associated with injections are minimized by this intranasal preparation thus boosting patient compliance. Intranasal calcitonin shown in improvement of bone loss progression within existing osteoporosis and has been proven beneficial clinically, nevertheless, the question of dosage is obscure. The purpose of this paper was to determine the dose-response of the salmon calcitonin (salcatonin) (Sandoz AS) intranasal monotherapy in a prospective-randomised-double-blind-placebo-controlled trial during two years on the bone mass and turnover as well as its effect to the fracture rate [1-3].

METHODS

Source subjects the information will be sourced through the sampling of the questionnaires that will be distributed to the whole population of women aged between 68-72 years, 1522 were received and 788 women passed the major selection points which is that they were not immobile, never experienced any coronary infarction, stroke or cancer or were taking sex hormones or other drugs capable of altering the calcium metabolism. Through this, these women received a chance of performing medical screening and one of the tests included calcium metabolism. The 512 subjects in attendance comprised of 270 women with at least 2 standard deviations lesser bone mineral density of a normative premenopausal woman in the distal forearm region and without the diseases that had at a certain point or the other been recognised to exert influence in the process of calcium metabolism. A total of 7% of these women consented to participate in a two year placebo-controlled, randomized and a double-blinded study of dose-response intranasal development of salcatonin. The ethics committee of the area approved of the research program and a written consent of all the involved persons was in place. The various groups of four subjects were chosen through random methods to obtain an intranasal treatment and the strength of the salcatonin measured in IU used per day was 50, 100/IU, 200, or a placebo. Each of them was provided with calcium supplement of 500 mg each day. During the research time line of two years, the examination was carried out after every three months [4-8].

MEASUREMENT OF BONE MASS

The bone mineral content of a distal forearm was measured using single photon absorptiometry using an iodine-125 (3-7Gbpq), photopeak of 27 keV. To calculate the bone mineral density is performed statistically with an average measure of 6 measurements, 4 millimeters apart, of a specific area that is slightly above where the ending of the ulna and the radius is 8 millimeters. The percentage of in vivo error in our department is 1 percent after months of long trial. Bone mineral content was measured by the use of the dual energy x-ray absorptiometry technique on the lumbar spine [9]. Very collimated dual energy x-ray source (70 kVp and 140 kVp) is used in the system. All the patients have their bone mineral density measured at L2-L4 and in intervertebral discs, and this measurement is expressed in grams, after calibration internally. Our department has done long term study and the long term precision of this method is 1.5 in vivo [10].

MEASUREMENT OF BONE TURNOVER

The sample of blood, which was taken, was on fasting condition and with no tobacco smoking time in the morning. Serum alkaline phosphatase, plasma bone Gla protein (a mark of bone formation) and fasting urinary hydroxyproline urinary hydroxyproline (a mark of bone formation) were measured by appropriate standard methods with due allowance against creatinine excretion [11-13].

ASSESSMENT OF VERTEBRAL AND PERIPHERAL FRACTURES

The radiographs of the thoracic and lumbar spine were repeated once a year and radiothoracic and lumbar spine optical radiographs after standardisation were radiographed at the same standardised conditions which was the same film-focus distance as when the participant was being radiographed in a fixed lateral position. By the end of the research, the radiographs of all the individuals that took part in the research were placed in chronological format and were presented using blinded method so that the radiograph was compared to a position of vertebrae T4 to L5. Two different forms of the radiographs were employed and in either of the ways, a clear ruler has measured the heights of the anterior, midvertebral and posterior clearances of all the vertebral bodies to the nearest millimeter. The variance of the readings in an observer was 2.5 percent (1.5 to 3.8 percent) [14-16].

RESULTS

Table.1 Gross Morphological and Baseline Values of Bone Mass Measurements and Vertebral Fractures in Four Treatment Groups

Treatment Group	No of Patients	Age (years)	Menopausal Age (years)
Salcatonin 50 IU	40	70(1)	21(5)
Salcatonin 100 IU	43	70(1)	24(7)
Salcatonin 200 IU	41	70(1)	21(4)
Placebo	40	70(1)	23(5)
Salcatonin 50 IU	52	70(1)	22(5)
Salcatonin 100 IU	52	70(1)	23(7)

Table.2 Baseline Biochemical Parameter Values in Four Treatment Groups

Treatment Group	No of Patients	Plasma Bone Gla Protein (ng/l)	Serum Alkaline Phosphatase (U/l)
Salcatonin 50 IU	40	11.9(7.7-18.5)	192(150-243)
Salcatonin 100 IU	43	10.9(7.6-15.7)	178(142-224)
Salcatonin 200 IU	41	9.9(6.3-15.5)	177(148-212)
Placebo	40	10.5(6.6-16.9)	167(135-205)
Salcatonin 50 IU	52	11.4(7.2-18.0)	188(148-240)
Salcatonin 100 IU	52	10.8(7.5-15.6)	175(138-223)

The baseline values of the measurement of bone mass and biochemical parameter of the four study groups viz. Salcatonin 50 IU, Salcatonin 100 IU, Salcatonin 200 IU and Placebo will be assumed as the baseline with its results reflected in Table 1 and 2. The data are of different types of physical and biochemical data of the 150 patients who participated in the survey of the effect of the salcatonin on the condition of the bones. Table 1 gave the gross morphological values and base line values of bone mass measurement i.e. age, age of menopause, weight, height and bone mineral content. The average in all the groups was level at 70 years with a small deviation in as far as menopausal age is regarded with the margin indicating 21 years to 24 years. The bone mineral content of distal forearm and lumbar spine was ambivalently as far as variations in the treatment group is concerned; the mean bone mineral content of Salcatonin 200 IU treatment group was more impressive compared to that placebo. The results in this table indicate that the Bone mineral present was varying in the group of treatments but

the treatment indicated the encouraging results of the bone present in 200 IU of Salcatonin. Biochemical characteristics of the base that is contained in it in plasma bone Gla protein (a form of a bone) and serum alkaline phosphatase (a bone turnover enzyme) are explained in Table 2. The combination that was injected with 50 IU of Salcatonin produced the highest serum concentration of the bone Gla protein in plasma with 11.9 ng/l which demonstrates the level of bone formation process is better in the combination as compared to the rest. There was also the result that serum alkaline phosphatase levels were relatively higher in the groups treated with Salcatonin compared placebo and they were highest at Salcatonin 50 IU of 192U/l. In fact, such observations point to the possible application of Salcatonin in bone formation and turnover and this is why it finds application in the therapy of osteoporosis. When put along with each another they would provide a generalized illustration of the baseline data on the characteristics, as well as, the biochemical measures that will subsequently be utilized in forming the centre of the interpretation of the effect of Salcatonin regarding the bone health at the termination of the study [17].

DISCUSSION

On the one hand, this studies state that the frequency of holor fractures amongst women decreased two third parts during the duration that these women received salcatonin relative to those patients who were not administered with salcatonin. There was also a dose -related increase of the spinal bones mass in a noteworthy way. The experiment has been carried out on the large homogeneous and representative sample of old osteoporotic women and its characteristic was an average bone mineral content of distal forearm being 30 lower than the average of healthy premenopausal women. The samples used in the study were recruited through low bone mass but not on pre-existing fracture like in the other literature works done on fractures. Under such a procedure we were capable of assessing incidence of diversionary fractures alongside with the new fracture rate. In other tests, we use women with preexisting fractures in the fact that they find it really easy to build new ones [18]. The fact that we were able to select women based on low bone mass reinforces the fact that the incidence level of new fracture is low in women who have undergone administration of salcatonin as opposed to the others. No secret to the truth that radiologic diagnostic procedures can distinguish on quantitative and qualitative procedures. We used quantitative approach and integrated measurement of height of the participants with accuracy and 25 Unadjusted cut off of height change and 20% Adjusted cut off of height change. This is the requirement that makes sure that the deformation is pronounced. There are certain criteria which are meant to define a vertebral fracture but they do not have a universal application but it has been proved that gross decreases in height should also be large enough to enable the vertebral deformities to be regarded as being osteoporotic. The lower back and thoracic vertebrae possess a comparatively low ratio of the fore-to-aft height (a ratio of anterior height to posterior) to the mid-thoracic vertebrae and is, therefore, likely to cause the appearance of a wedge-type fracture [19]. Adjusted method of Melton et al. takes these common variations to consideration and therefore we have used lower adjusting method threshold instead of non-adjusted one which was used. We found the rate of new vertebral fracture that we have observed similar with the rates contained in a study which regarded vertebral fracture that was treated using bisphosphonates. In this trial, the variation has been found in the incidence rate of new vertebral fractures within two years of acquisition in the bisphosphonate arms 29.5/1000 patient year and 62.9 in the individual who got the placebo. To a great part salcatonin activity affected bone mass especially of the spine which increased one percent per 100 IU dose dependently in 2 years time. The inconsistency in the spine and forearm to bone responses was also present in other studies. Even in a study of women aged 70 years only, we were able to show that the bone response which indicates past bone loss was associated with corresponding net effect in the forearms as well as in the spine [20]. The speed of demolishing of the forearm bones exceeds that of demolishing the spine bones at the age of 70 years leading to rise of the spinal bone mass and avoidance of bone loss reduction in the forearm through the use of salcatonin as the treatment of the diseases. The difference that was found between the active treatment group and the placebo group of 2 percent compared to 3.5 percent difference in the spinal bone mass was a little

bit less [21]. When we carried out the same experiment, we considered that calcium would be our co-therapy, whereas, in the experiment conducted by Watts et al., they applied phosphate. In another research undertaken in our group, calcium was found to exert moderate effects on both bone mass and turnover between salcatonin treatment and non-salcatonin treatment. As most of us are aware, response window could be encouraged through co-therapy and the placebo effects. The influence of co-therapy and the placebo effects would accentuate on the fact that real differences which were supposed to have transpired did in fact occur destined to have occurred than those that had occurred in our study between salcatonin and placebo group. Not so in the drugs of longer response window because it is easier to prove that they are good. In a relatively not so great number of women who have had the experience of recently knowing osteoporosis, we found that the difference in the vertebral cracks greatly put a gap between the estro-treated and non-estro-treated group after one year. That was all we have discovered in the study, and the impact of salcatonin was the best in the first year of treatment, when the volume of the spine bone was increasing already, and the turnover to the bone was close to steady-state. This holds in comparison to the other work done by our crew to state that the treatment using salcatonin has to be done in intermittencies e.g. a year of treatment and a year of withdrawal period [22]. A summary was made to indicate the intranasal salcatonin has been used in elderly women with moderate osteoporosis incidence which decreased the new fractures to the two-thirds lesser than the one occurring on calcium treatment. It also promotes dose dependently the spinal bone mass [23].

CONCLUSION

The findings obtained through the use of intranasal formulation of salcatonin reduced the incidence rate of fracture among elderly women having moderately osteoporotic features by 2/3 rds of the calcium alone group demonstrated by evidence in a final note of this research paper. Its findings also show that, dose dependent measures were taken in that the more the salcatonin was applied the lower the quantitative increase in the bone mass. The results show that salcatonin has a potential as a drug that will assure safety and non-toxicity in the treatment against osteoporosis since salcatonin serves as an alternative to the standard method of treatment. Further, it is also supported by the fact that the sample used by the study was low-bone mass women who did not suffer any pre-existing fractures yet since this aspect alone makes the study unique because salcatonin in question prevented new fractures. These findings suggest the insight that salcatonin will be a prospective drug that can boost the health of the bones of older women with osteoporosis as well as protect them against bone fractures.

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