The Action of Strontium Ranelate: Myth or Reality

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The present study aimed to show whether the Strontium ranelate was the dual action possessing either antiresorptive or formative properties. This retrograded study included 56 postmenopausal women using the biological bone turnover markers as an evaluation. The antiresorptive property described by the mean value of Beta-crossLap or bCTx before taking 2 grams of Strontium ranelate per day was 0.377 ng/ml compared with the mean of CTx after the 3-month treatment which was 0.409 (p = 0.083) ng/ml. The result indicated that this agent could not suppress the bone resorption, otherwise Strontium ranelate was not able to control the progress of bone resorption. It was found that 67.92 per cent showed the uncontrollable resorption. In addition, the bone formation monitored by PINP was diminished 34.54% and only 60% of the bone formation values was little increased but still below normal (44.5 ng/ml) while 1.8% was no response. The present study displayed that the Strontium ranelate was neither antiresorptive nor formative actions and it was certainly not a dual action via the method of biological bone turnover markers.

Keywords: *Strontium ranelate, bCTx, BetacrossLap, PINP*

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Strontium is located on the periodic table in the alkaline earth metal group. It is in the group that includes calcium, barium, magnesium and beryllium.

Strontium ranelate was widely used in 1950s[1] for the management of osteoporosis. However, the outcomes of the Strontium efficacy are controversial especially its power of increasing bone mass. Ghada[2] pointed that the Strontium having a greater atomic number than calcium would weaken the penetration of x-ray beam. Therefore, this difficulty resulted in an overestimation of measuring the bone mineral density. This comment also mentioned the Strontium had high affinity to hydroxyappatite. As a result, it could replace calcium easily which it is likely to increase bone mass. Moreover, a group of researchers[1,3,6] claimed the Strontium contained the dual action possessing antiresorption and formation. This study using the bone markers as a parameter for proving the double action found that the strontium ranalate had neither antiresorptive nor formative properties.

Material and Method

The retrograde study was done at the Osteoporosis Clinic, Siriraj Hospital. The files of patients' history were randomly selected from Sept 2010-Feb 2011. Fifty-six cases were treated with Strontium ranelate by the following criteria: they were postmenopausal women whose biological bone markers were recorded completely and they took 2 grams of Strontium ranelate per day for three months.

The data were statistically calculated by SPSS version 10.

The antiresorptive marker is Betacrosslap (bCTx). This assay was specific for bone resorption which was achieved by using monoclonal antibody recognized as an octapeptide (beta-8AA) on the C-terminal end of the alpha one chain of type 1 collagen. The serum was automated by the Elecsys analyzer.

The formative markers were detected by the new synthesis of collagen at the N-terminal of collagen type 1 called PINP (Type 1 procollagen N-terminal propeptide).

The analyzed data were compared with the normal standard values[4].

Results

The mean value of antiresorptive power, bCTx of bCTx1 was 0.377 ng/ml and the mean value of antiresorptive power after taking 2 grams of Strontium ranelate named bCTx2 was 0.409 ng/ml. After comparing with both of the mean values, the study found that the bCTx did not decrease significantly (p = 0.083) (Fig. 1 and Table 1).

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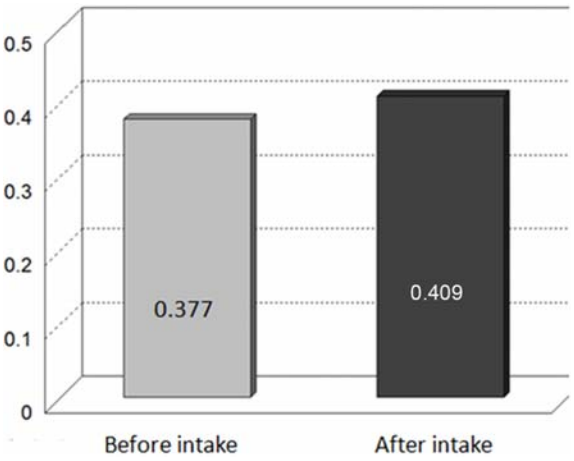

Fig. 1 Unremarkable changes of bone antiresorptive power of Strontium ranelate at the dose of 2 grams per day for 3 months, p = 0.083

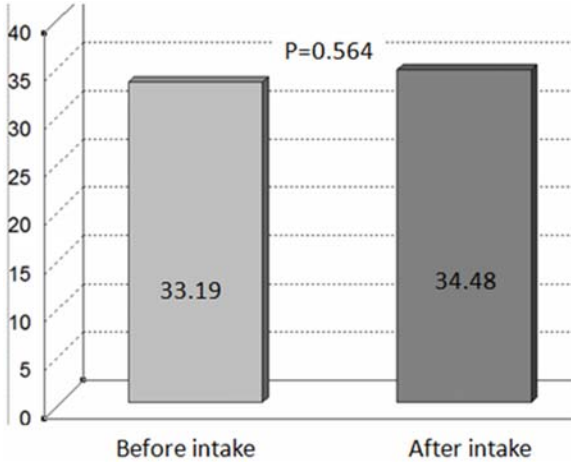

Fig. 2 Comparison of the mean values of both PINP after adjusting PINP to the same base line of bCTx. The bone formative markers were not different statistically (p = 0.564)

The mean value of PINP after being adjusted to the same level of bCTx showed that PINP before and after the intake of Strontium ranelate were not different significantly (p = 0.564) (Fig. 2).

Discussion

The bone turnover markers are used as the parameters for testing the action of Strontium ranelate because the bone markers are recognized as the real time manifestration of bone function and short outcomes. The proper time for evaluation of antiresorption is 3 months[5]. The bone histomorphometry is not preferably used as this method limits the data from paired bone biopsies in patients receiving Strontium ranelate. The appearance of bone cells is hardly confirmed its functions; it displays only the morphology, not the function. In addition, the BMD measurement is not a suitable approach because it takes time for bone mass changes, practically at least from 1 to 2 years.

Table 1. Results of the bone marker turnovers after the 3-month intake of 2 grams of Strontium ranelate

		SD	p
CTx before intake	0.377	0.138	
CTx2 after intake	0.409	0.151	
			0.083
Adjustable PINP1	33.19	16.61	
Adjustable PINP2	34.48	11.75	
			0.564

The Strontium ranelate is generally recognized as the dual action: bone formation and antiresorption[7]. The best approach for investigating its action is bone turnover markers; PINP is the marker of bone formation while the resorption marker is bCTx.

The statistic results of bone resorption marker, bCTx were not reduced significantly (p = 0.083) after the addition of Strontium ranelate.

The present study, additionally, found that 67.92% of the Strontium intakes could not control the levels of bCTx which should be decreased.

The bone formation also failed to increase the bone formation by the pair simple test that showed non-significantly, p = 0.564 (Fig. 2).

In sum, Strontium ranelate has neither an antiresorptive nor formative action. Strontium ranelate is rather expensive; one sachet is 90 Bath. This medication costs 2,700.00 Baht per month or 32,400.00 Baht per year in comparison with other antiresorptive ones such as Risedronate, Alendronate of which the cost is 1,596.00 and 1,460.00 Baht per month respectively. As this medication efficacy is not reliable enough and Thailand is not a rich country to import such a costly medicine for patients to use, physicians must think carefully whether this therapy is worth spending when prescribing it. Although Strontium ranelate is popularly used in many countries, it is not yet approved by FDA in the United States for the treatment and prevention of osteoporosis which still remains under study[8].

Potential conflicts of interest

None.

References

1. Shorr E, Carter AC. The usefulness of strontium as an adjuvant to calcium in the remineralization of the skeleton in man. Bull Hosp Joint Dis 1952; 13: 59-66.
2. Kendler DL, Adachi JD, Josse RG, Slosman DO. Monitoring strontium ranelate therapy in patients with osteoporosis. Osteoporos Int 2009; 20: 1101-6.
3. Marie PJ, Ammann P, Boivin G, Rey C. Mechanisms of action and therapeutic potential of strontium in bone. Calcif Tissue Int 2001; 69: 121-9.
4. Bunyaratavej N, Kitimanon N, Boonthitikul S. Study of the level of biochemical bone markers: NMID osteocalcin and bone resorptive marker (beta CTx) in Thai women. J Med Assoc Thai 2001; 84 (Suppl 2): S560-5.
5. Delmas PD, Eastell R, Garnero P, Seibel MJ, Stepan J. The use of biochemical markers of bone turnover in osteoporosis. Committee of Scientific Advisors of the International Osteoporosis Foundation. Osteoporos Int 2000; 11 (Suppl 6): S2-17.
6. Servier Laboratories Protos(R) Package insert 2005 Sep.
7. Marie PJ, Hott M, Modrowski D, De Pollak C, Guillemain J, Deloffre P, et al. An uncoupling agent containing strontium prevents bone loss by depressing bone resorption and maintaining bone formation in estrogen-deficient rats. J Bone Miner Res 1993; 8: 607-15.
8. Strontium: a better drug for osteoporosis? [database on the Internet]. 2005 [cited 2011 Jun 18]. Available from: http://www.drweil.com/drw/u/id/QAA360803.

ฤทธิ์ยาสตอนเซี่ยมรานิเลตมีคุณสมบัติทั้งตัวที่สร้างกระดูกและห้ามการสลายกระดูกเป็นความจริงหรือฝัน

ณรงค์ บุณยะรัตเวช

การศึกษานี้เป็นการศึกษาใบการรักษาย้อนหลังตั้งแต่ เดือนกันยายน พ.ศ. 2553 ถึง กุมภาพันธ์ พ.ศ. 2554 โดยมีสตรีวัยหมดประจำเดือนจำนวน 56 คนที่ไม่มีโรคแทรกใดๆและไม่ได้รับยาทางกระดูกมาก่อนไม่น้อยกว่า 3 เดือน เป็นกลุ่มตัวอย่าง ผู้ป่วยที่ได้รับยาสตอนเซี่ยมรานิเลต ขนาด 2 กรัมต่อวัน นาน 3 เดือน จุดประสงค์ต้องการดูว่ายามีฤทธิ์สองอย่างอยู่ด้วยกันจริงหรือ คือ มีผลห้ามการสลายกระดูกและ กระตุ้นให้เกิดการสร้างกระดูก โดยใช้โบนมาร์เกอร์ ชนิดเบต้า ซีทีเอ็กซ์ และ พีหนึ่งเอ็นพี วัดดูการสลายกระดูกและการสร้างกระดูกตามลำดับ ผลการศึกษาพบว่า ค่าการวัดการสลายกระดูก หรือ เบต้าซีทีเอ็กซ์ ไม่ลดลงอย่างมีนัยสำคัญ (p = 0.083) และค่าการสร้างกระดูกไม่เพิ่มขึ้น (p = 0.564) กล่าวโดยสรุปยานี้ไม่มีผลลดการสลายกระดูก และช่วยการสร้างกระดูกดังนั้น การใช้ยานี้ควรคำนึงเป็นพิเศษเนื่องจากผู้ป่วยต้องรับภาระรายจ่ายต่อเดือนประมาณ 2,700 บาท ซึ่งแพงกว่ายาที่ลดการสลายกระดูก เช่น ไรซิโดเนต, อเลนโดเนต ที่มีราคาต่อเดือนเพียง 1,596 และ 1,460 บาท ตามลำดับ