Case Report

The Poor Osteoblastic Functions Can Correct by Teriparatide

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A study of stimulation of poor osteoblastic function by teriparatide and monitored by bone markers. Eighty-one cases were enrolled with poor osteoblastic functions, which were classified with the values of both markers: NMID Osteocalcin was less than 10.81 ng/ml and the PINP was less than 15.88 ng/ml. Most CTx were below 0.1 ng/ml or at any level. Every case took oral bisphosphanates for at least 2 years.

Average age was 68 years old; 79 cases are female the others male .The base line of bone markers: NMID osteocalcin, PINP and CTx are 9.3, 14.3 and 0.08 ng/ml, respectively. The duration of Teriparatide injections was 6 months, dose 20 microgram subcutaneous per day. The blood calcium, uric acid and renal profile were monitored too.

The results of 98 percent of cases showed that dramatic increase of osteoblastic products and at the second month; all markers increased above the normal values that are indicators of osteoblastic resumes and their activities.

The hypercalcemia can occur during treatment (22.2%) and hyperuricemia 12.34%; therefore, blood chemistry and bone markers should be monitored every month as a precaution.

Keywords: *Teriparatide, Parathyroid hormone, Osteoblastic function, Treatment of poor function of osteoblast*

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Failure of osteoblastic functions can be detected with biological bone markers: CTx, PINP and NMID osteocalcin.

We found that when the value of CTx (BetacrossLap) was less than 0.10 ng/ml (0.068 ng/ml), nearly a lack of bone resorption. With this condition, osteoblasts can produce minimal bone markers for bone formation, which was manifested by PINP = 15.88 ng/ml and NMID osteocalcin = 10.81 ng/ml (reference in this issue).

Other manifestations appear if the biological markers of bone resorption are higher than 0.1 ng/ml, but the values of PINP, NMID osteocalcin still below or equal to the values of CTx at 0.10 ng/ml. This phenomenon is also called poor osteoblastic function.

The common causes of poor osteoblastic functions occur post and prolonged use of anti-resorptive agents such as bisphosphonate, senile osteoporosis, post chemotherapy etc. These conditions should not be neglected because bone will become cracked. Prolong application of bisphosphonates may induce stress fracture because bisphosphonates block bone remodeling[6].

Teriparatide is recognized as a bone formative agent and can therefore be applied for the acceleration of fracture healing, as off-label treatment[1]. This study was applied to correct osteoblastic failure. It has been FDA-approved since 2004[2]. Teriparatide is a portion of the human parathyroid hormone, amino acid sequence 1 through 34 of the complete molecule (containing 84 amino acids in humans). It is a recombinant form of the parathyroid hormone. which is an effective anabolic agent[3] and can be used in the treatment of some forms of osteoporosis[4]

Material and Method

The 81 cases of poor osteoblastic function caused by prolonged use of bisphosphonate, averaged 2 years with bone markers of NMID osteocalcin and PINP equal to 8.2-10.4 ng/ml and 12.5-14.8 ng/ml, respectively, with either low CTx value (0.1 ng/ml or below) or high CTx an were included in this study.

Exclusion criteria were Diabetes, Disease of thyroid, a History of allergic conditions.

Each case was checked for bone markers, NMID osteocalcin, PINP and CTx including blood

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calcium, Phosphorus, uric acid, BUN and creatinine every month for 6 months.

The patients were injected with teriparatide (Forteo, Lilly) at 20 microgram/day subcutaneously at buttock or abdomen.

The bone markers CTx, NMID osteocalcin and PINP were detected by monoclonal an antibody method (Roche Diagnostic) which was performed at the central laboratory of Siriraj Hospital.

Discussion

Teriparatide is strong agent for the stimulation of osteoblast with a large outcome result: PINP and NMID osteocalcin, CTx also increased. That is a high bone turnover, which is a sign of bone formation. Long application of teriparatide is not recommended because high bone turnover will make bones crack and it was also reported that osteogenic sarcoma was found in rats. Safe application should not exceed more than 18 months[3]. Our research used only 6 months for stimulation osteoblast. The bone markers are very important for monitoring the change in osteoblastic activities. In most cases (98%), the bone markers increase at the end of the first month, a few case (2%) showed increase in markers at the second month. At the third month, all cases manifested bone markers and increased dramatically above the normal values[5]. In the study group showed no signs of allergic response. They responded well and showed an increase in markers (Fig. 1). In our opinion, the stimulation of osteoblast by teriparatide may be used for 3 months followed by other medication for osteoblast such as vitamin K2, vitamin D and calcium.

During injection of teriparatide, the level of total calcium, uric acid should be monitored every month of treatment to prevent hypercalcemia. Calcium should be omitted. Our study found 18 cases (22.2%) of hypercalcemia and 10 cases of hyperuricemia (12.34%). Every case can resume osteoblastic function normally after the cessation of teriparatide injections. This study will help physicians to be aware of low bone turnover, especially in cases of prolonged use of bisphosphonate, which now is believed to be the main cause of bone fatigue leading to low energy fracture[6-8].

Summary

Osteoblasts are bone-forming cells of the bone. These cells have high correlation with osteoclast, a bone resorbing cell. They perform activities together by a process of bone remodeling.

Table 1. The base line characteristics of cases

Gender	79F	2M
Age	68**	
NMID	9.3*	
PINP	14.3*	
CTx	0.08*	

* Average bone marker, ng/ml; ** Average age

Table 2. The means of the levels of bone markers after injection of Teriparatide monthly

Month	CTx	NMID	PINP
M0	0.08	9.3	14.13
M1	0.51	20.5	32.5
M2	0.9	35.0	82.04
M3	0.728	55.6	112.56
M4	0.615	28.73	91.65
M5	1.8	98.3	112.5
M6	1.95	46.83	224.0

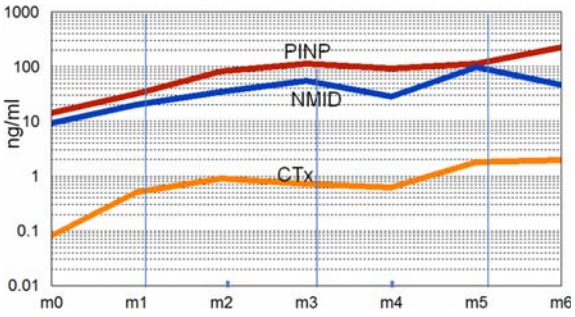

Fig. 1 Graphs of bone makers: CTx, NMID osteocalcin, PINP which increased monthly. At sixth month: CTx = 1.95 ng/ml, NMID osteocalcin = 46.83 ng/ml and PINP = 224.1 ng/ml. Comparing to the base line: CTx = 0.08 ng/ml, NMID osteocalcin = 9.3 ng/ml and PINP = 14.13 ng/ml (p = 0.001).

Some conditions such as prolonged bisphosphonate intake will stop the normal activities of bone cells so new bone formation does not synthesize which is harmful to bone texture.

We used the following bone markers: CTx, NMID osteocalcin and PINP for detection of abnormal activities or poor osteoblastic function that NMID osteocalcin, PINP equal to or below 10.81, 15.88 nanograms per milliliter, respectively, of which the value of CTx is at any level.

A poor osteoblastic function can be corrected by the injection of Teriparatide at the proper time after which the bone cells will resume their activities.

The purpose of this study will help physicians adjust the duration or doses of bisphosphonate and chemotoxic agent-intake and make them aware of any excessive treatment with these medicines.

Potential conflicts of interest

None.

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การแก้ไขภาวะหน้าที่บกพร่องของเซลล์ออสติโอบาสติกด้วยเทอริพาราไทด์

ณรงค์ บุณยะรัตเวช

การแก้ไขภาวะบกพร่องในเซลล์ออสติโอบาสติกที่วินิจฉัยด้วยการดูค่าของโบนมาร์เกอร์ต่ำคือค่า เอ็นมิท ออสติโอคาลซินและพีวันเอ็นพีต่ำกว่า 10.81, 15.88 นาโนกรัมต่อมิลลิลิตรตามลำดับไม่ว่าค่าซีทีเอกซ์จะมีค่าเท่าใดที่พบบ่อยเป็นภาวะเกิดจากการได้รับยาบิสฟอสฟอเนตนาน ๆ เช่นนี้ถ้าไม่แก้ไขกระดูกจะร้าวหักง่ายถ้าไม่ใช้โบนมาร์เกอร์ตรวจหา

ได้ศึกษาในกลุ่มคนเช่นนี้ 81 ราย เป็นหญิง 79 ราย อายุเฉลี่ย 68 ปีได้รับยาบิสฟอสฟอเนตไม่ต่ำ 2 ปี มีค่าซีทีเอกซ์ เอ็นมิทออสติโอคัลซินและพีวันเอ็นพี 0.08, 9.3 และ 14.13 นาโนกรัมต่อมิลลิลิตรตามลำดับ ผู้ป่วยได้รับฉีดยาเทอริพาราไทด์ขนาด 20 ไมโครกรัม ฉีดที่หน้าท้องทุกวันติดต่อกัน 6 เดือน และต้องได้รับการตรวจเลือดหาโบนมาร์เกอร์และแคลเซียม ฟอสฟอรัส ยูริก ระหว่างรักษาห้ามกินแคลเซียม

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