Experience of Application: Blood Screening and Bone Turnover Markers for Prevention of Unwanted Effects and Early Outcomes of Teriparatide

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This clinical study aimed to provide awareness of the teriparatide injection and also prevention of unwanted events. The 72 cases aged between 52-69 with the inclusion criteria: back pain proved by the x-ray with one or more collapsed spines, no underlying diseases and no history of bone tumor, hyperparathyroid, hypercalcemia. The blood screening for renal, liver profiles, uric acid, mineral profile and bone turnover markers (bCTx, PINP) are used as 6-month monitor. The results showed that the common unwanted effects were hypercalcemia, hyperuricemia, hypomagnesia: 5.5 %, 54.56% and 43% respectively at the first month of the therapy. At the end of 6th month, these conditions occurred 1.38%, 8.77% and 5.5% respectively. The bone turnover markers, PINP, was a quick response in the first month, the PINP was double increased then triple increased at the end of the 6th month ($p = 0.001$). Teriparatide did not disturb the activity of parathyroid glands because the PTH was within the normal limit during the treatment ($p = 0.001$). The blood screening monitor was useful for preventing the unwanted effects and the bone turnover markers, PINP, was beneficial for evaluation of Teriparatide efficacy in short outcomes leading to physicians and patients' confidence.

***Keywords**: Teriparatide, Bone markers, PTH*

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Teriparatide is a recombinant form of the parathyroid hormone (hPTH1-34), used in the treatment of some forms of osteoporosis in men and women who are at risks of fracture[1]. The Teriparatide should not be prescribed for the cases that are at risks for osteosarcoma including Paget's bone disease and unexplained elevation of alkaline phosphatase. Teriparatide can increase the action of the osteoblasts for creation of bone formation. Teriparatide also enhances the absorption of calcium from the intestine and reabsorbes the calcium at the kidneys to blood. The common side effects comprises of dizziness vertigo, hypotension and pain at the site of injection. Teriparatide is not recommended to people who have a history of renal stone, hypercalcemia, pregnancy and breast feeding.

Material and Method

The 72 menopausal women aged between 50-69 were enrolled for the treatment of Teriparatide within the inclusion criterions: low back pain with one collapsed-vertebra or more, all cases had no history of cancer, diabetes, hypercalcemia, hyperparathyroidism and renal stones. Every case had a subcutaneous injection of 20 micrograms per day. The screening blood consisted of renal, liver functions, fasting blood sugar, uric acid, PTH including the mineral profiles, *e.g.* calcium, phosphorus, magnesium were checked before receiving Teriparatide at 1$^{st.}$, 3$^{rd.}$, and 6$^{th.}$ months. The bone turnover markers: bCTx, PINP were checked simultaneously with the blood screening test.

The results were calculated and analyzed by statistic program named SPSS.

Most reports recognized Teriparatide as 'bone builder' and manifested by late outcomes taking 6-36 months, for example, the increase of BMD Chen P. et al[1] reported there was 30-41% increase of BMD of lumbar spines after the treatment and it decreased the fracture risks. Saag[2] also mentioned Teriparatide prevented the spinal fracture including the property for sustained vertebral fracture risks[3].

Results

The results of blood chemistry and bone turnover markers are shown in Table 1.

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Discussion

The late outcomes of Teriparatide were common reports consisting of increased BMD, decrease of fracture rate and risks which take time for monitoring, *i.e.* months or years[4-7]. As the present study showed the early responses of Teriparatide, it is of great benefit to physicians who can evaluate the result especially at the first month of treatment which Glover[5] recognized as a good response and also prevention of the side effects. The bone turnover markers were widely used[5,6]. In the present study, it was found common unwanted effects: hypercalcemia, hyperuricemia. These effects can be detected by routine blood screening otherwise the bone turnover markers can monitor for changes of bone cells' activities especially the PINP marker that was considered as a marker of early response and reflection of bone formation[5]

Symptoms and signs of hypercalcemia may manifest at any month of treatment. Thus, it is very essential to monthly monitor the blood calcium. The

Table 1. The results of Teriparatide injection in per cent of increase except the magnesium showed per cent of decrease. The parathyroid hormone (PTH) was at the normal limit during the 6-month treatment

	M1	M3	M6
Uric acid	24.56	8.77	8.77
Calcium	5.5	5.5	1.38
Magnesium*	43	12.5	5.5
PTH	39.55	25.03	27.23
PINP	288	292	307.5

* Percent of decrease

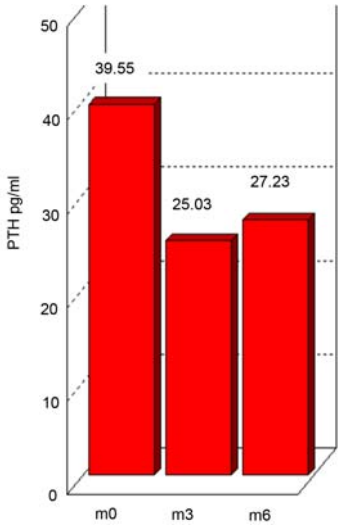

Fig. 1 Teriparatide injection does not disturb the intact parathyroid gland which showed the PTH secretion is normal limit. (15-65 pg/ml)

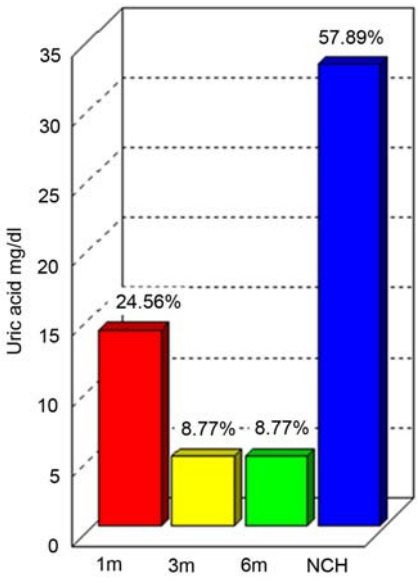

Fig. 2 In some cases manifested hyperuricemia, so monthly monitoring is necessary. (NCH= not change)

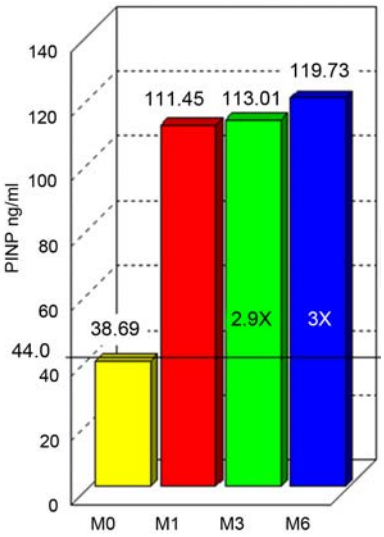

Fig. 3 Change of type1 procollgen N-terminal propeptide (PINP), the bone formation marker after Teriparatide injection which was monitored month by month increased dramatically, the value was triple from the base line at the 6th month

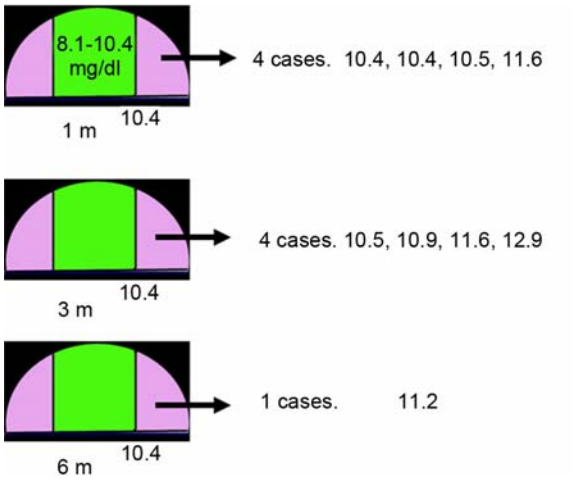

Fig. 4 Some cases presented hypercalcemia which showed through the blood screening for calcium

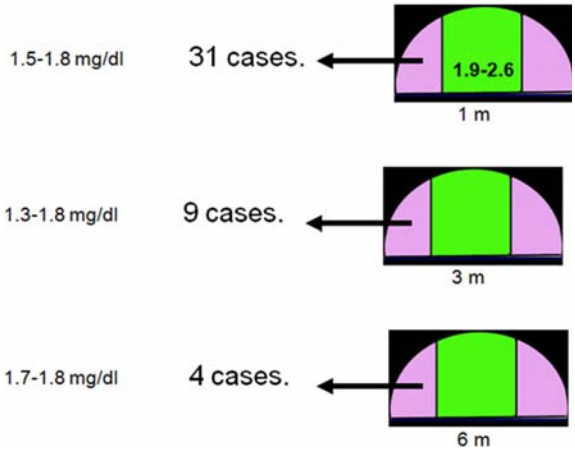

Fig. 5 The hypomagnesia can develop especially in the first month of treatment; however, the blood screening for magnesium should be monitored every month

symptoms and signs of hypercalcemia can be traced by dyspepsia, loss of appetite, constipation and high blood pressure which sometimes will lead to misdiagnosis if there is neglect of blood calcium monitoring. The hypercalcemia can develop at any time of the treatment especially in the first month of the three-month therapy and the level will decrease at the 6th month (Table 1, Fig. 4).

Forty-three percent showing the hypomagnesia occurred commonly at the first month in this study, and then it slowly decreased at the 3rd and 6th months. However, the administration of magnesium is necessary for correction the status of calcium and heart condition (Fig. 5).

The present study found 42.11% of the hyperuricemia which was a high amount (Fig. 2). This condition possibly causes harm to kidneys such as renal stone and interstitial nephritis.

Sukree's study[8] showed the intact PTH in postmenopausal women aged 50-69 were within normal limit. This report showed the Teriparatide did not disturb the PTH ($p = 0.001$) during the therapy (Fig. 1).

Potential conflicts of interest

None.

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ประสบการณ์ในการใช้การตรวจเลือดทั่วไปและการใช้โบนมาร์เกอร์ เพื่อป้องกันภาวะแทรกซ้อน และการดูผลในระยะแรกของการใช้ยา เทอริพาราไทด์

ณรงค์ บุณยะรัตเวช

จากการศึกษาผลของยา เทอริพาราไทด์ ในผู้ป่วยสตรีวัยหมดประจำเดือน 72 ราย ที่มาด้วยอาการปวดหลัง และมีกระดูกยุบตั้งแต่ หนึ่งปล้อง โดยที่ผู้ป่วยไม่มีประวัติโรคมะเร็งกระดูก, ภาวะแคลเซียมสูง, ภาวะโรคต่อพาราไทรอยด์ ในการศึกษานี้ใช้การตรวจเลือดทั่วไปที่ประกอบด้วย หน้าที่ตับและไต, ตรวจแร่ธาตุ เช่น แคลเซียม แมกนิเซียม, การตรวจยูริก สำหรับกระดูกจะใช้โบนมาร์เกอร์ ได้แก่ PINP และ bCTx ทั้งหมดนี้ ใช้เป็นตัวเฝ้าระวัง ตั้งแต่ก่อนได้ยาและทุกเดือนที่ 1, 3 และ 6 ตามลำดับ พบว่า เกิดภาวะแคลเซียมในเลือดสูง, ภาวะกรดยูริกสูง และ ภาวะแมกนิเซียมต่ำ ในช่วงเดือนแรก พบ 5.5%, 8.77% และ 43.0% ตามลำดับ ส่วนระดับพาราไทรอยด์ในเลือดไม่เปลี่ยนแปลง แต่ ค่า PINP เพิ่มขึ้นอย่างมีนัยสำคัญ กล่าวคือเพิ่มเป็น 2 เท่า ในเดือนแรกและเป็น 3 เท่าในเดือนที่ หก แสดงว่าเทอริพาราไทด์มีผลช่วยเกิดการสร้างกระดูก การใช้ปัจจัยดังกล่าว ช่วยในการเฝ้าติดตามช่วยให้การรักษามีประสิทธิภาพ สามารถแก้การเกิดภาวะแทรกซ้อนได้ทันและโบนมาร์เกอร์ PINP ยังช่วยบอกประสิทธิภายของยาว่าได้ผลเพียงใด ทำให้ทั้งผู้รักษาและผู้ป่วยมีความมั่นใจและ เป็นการป้องกันไม่ให้ใช้ยาเกินจำเป็น