Improvement in health-related quality of life in osteoporosis patients treated with teriparatide

Arthur Lau,1* Sammy H. Ali,1* Anna M. Sawka, MD, PhD, FRCPC,2 Lehana Thabane, PhD,3,4 Alexandra Papaioannou, MD, MSc, FRCPC,5 Amiram Gafni, PhD,3,6 Jonathan D. Adachi, MD, FRCPC7

*These authors contributed equally to this manuscript

1Medical Student, McMaster University, Hamilton, Ontario, Canada
2Division of Endocrinology and Department of Medicine, University Health Network and University of Toronto, Toronto, Ontario, Canada
3Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario, Canada
4Centre for Evaluation of Medicines, St. Joseph’s Healthcare, Hamilton, Ontario, Canada
5Division of Geriatrics and Department of Medicine, Hamilton Health Sciences and McMaster University, Hamilton, Ontario, Canada
6Centre for Health Economics and Policy Analysis, McMaster University, Hamilton, Ontario
7Division of Rheumatology and Department of Medicine, St. Joseph’s Healthcare and McMaster University, Hamilton, Ontario, Canada
Correspondence

Jonathan D. Adachi MD, FRCPC
501-25 Charlton Ave E
Hamilton, ON
L8N 1Y2
e-mail: jd.adachi@sympatico.ca
fax: (905) 521-1297

Sources of support: This study was an unfunded and was a project undertaken by Arthur Lau and Sammy Ali, both medical students at McMaster University. Dr. Adachi has received consulting fees from Amgen, Astra Zeneca, Eli Lilly, Glaxo Smith Kline, Merck, Novartis, Pfizer, Procter & Gamble, Roche, Sanofi Aventis, Servier
ABSTRACT
Background: Individuals with osteoporosis and recent vertebral fractures suffer from pain and impaired health-related quality of life (HRQL).
Objective: To determine whether patients with osteoporosis treated with teriperatide experienced improvement in HRQL and pain symptoms after several months of therapy.
Methods: We retrospectively studied a sample of osteoporosis patients treated with teriperatide in a Canadian rheumatology practice. We included patients that received teriperatide therapy with baseline and follow-up Mini-Osteoporosis Quality of Life Questionnaire (OQLQ) data. Follow-up data was measured at three or six months (last available measurement used). We used a paired Student’s t-test to compare baseline and follow-up measurements for each of the questionnaire’s ten questions (five domains).
Results: 57 patients were included in the study, including 47 women. The mean age was 63.8 years (standard deviation 12.1 years). About sixty five percent (37/57) had previously sustained one or more osteoporotic fractures and almost half (28/57) had experienced multiple osteoporotic fractures. About a quarter (15/57) of individuals were taking one or more types of pain medications regularly prior to starting therapy. At follow-up, significant improvements were observed in the OQLQ domains of pain symptoms and emotional functioning (p≤0.035). Respondents also reported improvement in physical functioning relating to lifting (p=0.004). However, there was no significant improvement observed in the domains of activities of daily living and leisure.
Conclusions: Teriperatide use may be associated with improvements in HRQL in osteoporosis patients, in particular alleviation of pain symptoms. These findings should be confirmed in larger prospective studies with a suitable control group.

Key words: Osteoporosis, Parathyroid hormone-related peptide Teriperatide, Back pain, Quality of life
Introduction

Osteoporosis is a disease leading to progressive decreases in bone mineral density, decreased bone strength and increased risk of skeletal fractures (1). Approximately 30% of women will have sustained at least one vertebral fracture by the age of 75 (2). There are over 700,000 incident vertebral fractures related to osteoporosis each year in the United States (2). Both clinical and radiographical fractures are associated with an increase mortality rate. One study identified a 16% reduction in expected 5 year survivability. Approximately 75% of patients who present with a clinical vertebral fracture will experience chronic pain (3). Back pain due to vertebral fractures has a significant impact on osteoporotic patients (4). The number and severity of vertebral fractures also increases the risk of developing chronic back pain (5). This has a significant impact on quality of life and functional impairment on the affected patients (6).

Conventional treatments for osteoporosis, including bisphosphonates, selective estrogen receptor modulators (SERMs), calcitonin and estrogen, have been shown to reduce the rate of bone resorption and preserve bone mass (7). However, none of these have been shown to stimulate new bone formation (7). Teriparatide [recombinant human PTH-(1-34)] is an agent shown to increase both bone mass and bone strength (8). In the Fracture Prevention Trial (FPT), teriparatide was shown to increase lumbar spine and femoral neck BMD and decreased fracture risk of both vertebral and non-vertebral fractures in post-menopausal women with osteoporosis (2). Aside from its effect on BMD, teriparatide also had a positive effect on the non-BMD determinants of bone strength (9).

In the FPT trial comparing the effect of Teraparatide 20µg/day to placebo in post-menopausal women, the incidence of back pain was 17% in the treatment group, and 23% in the placebo group (8). Teriparatide’s role in preventing back pain in osteoporotic patients was assessed through a meta-analysis of four completed, randomized, double-blinded trials of teriparatide versus a comparator (2). Nevitt and colleagues reported the teriparatide-treated group had a significant reduction in new or worsening back pain versus comparators (RR 0.73, 95% CI 0.61 to 0.87), over a time period encompassing the clinical trial plus 30 months of post-treatment follow-up assessment (2).

The goal of this study is to determine whether patients in every day clinical practice with osteoporosis, treated with teriparatide, experienced improvement in HRQL and pain symptoms after several months of therapy in a clinic setting. Measuring only pain scores for these patients would be insufficient, because aside from acute and chronic back pain, patients with vertebral fractures also suffer from impaired activities of daily living, anxiety and constant fear about falling and suffering another fracture (10). A follow-up Mini-Osteoporosis Quality
of Life Questionnaire (OQLQ) was used to quantify the patient’s pain and impact on quality of life (11). This is primarily an exploratory study whose sample size is determined by the available data. In addition, this is the first study to compare patient’s HRQL data in pre and post-teriparatide therapy.

Methods

Study Group and Inclusion Criteria
We conducted a review of osteoporosis patients who had been placed on teriparatide therapy in a Canadian rheumatology practice. Two reviewers abstracted data on demographic information, pain medications, previous fracture history, bone mineral density and health related quality of life (HRQL). In order to be eligible for the study, participants must have completed a baseline and follow-up mini-OQLQ questionnaire prior and subsequent to commencement of teriparatide therapy (at 3 or 6 months) (Figure 2).

Measurement of Health-Related Quality of Life
HRQL was assessed using the mini-OQLQ (11), which was developed for clinical practice as an abbreviated form of the original 30-item OQLQ (11). As with the original questionnaire, the mini-OQLQ is comprised of five domains: symptoms, physical functioning, emotional functioning, activities of daily living and leisure. The mini-OQLQ has ten items, constructed from the two items with the highest impact in each of the five domains on the original OQLQ. It is a self-administered questionnaire that takes approximately 3 minutes to complete and was designed to be administered in a clinic setting (11). The OQLQ uses a 7-point scale with a score of 1 representing the worst possible function, and a score of 7 representing the best possible function. A change of approximately 0.5 within each domain is considered to be a clinical relevant difference in quality of life (13, 14). The mini-OQLQ has been validated as a sensitive measure of HRQL in osteoporosis patients with vertebral fracture pain. The application of this tool by Adachi et al. (14) found patients with vertebral fracture had higher scores on all five domains than patients without fracture (Appendix).

The Mini-Osteopososis Quality of Life Questionnaire (OQLQ) (11) was completed by the patient at each visit and reviewed with the specialist or nurse clinician. Patients were given the mini-OQLQ prior to initiation of teriparatide and at 3 and/or 6 months follow-up. The last available HRQL data (from 3 or 6 months) was used in the analysis.

Statistical analyses
As mentioned earlier, this is an exploratory study whose sample size is primarily determined by the available data. The results of this study will provide us with some further insight about the potential effect of teriparatide on health-related quality of life in primary care of patients with osteoporosis which can be explored further in major study.
Descriptive data were reported as means (standard deviations [SD]) or median [minimum [min] – maximum [max]) for continuous or discrete variables and count (percentage) for categorical variables. We used the paired Student’s T-tests to compare scores on questions of the mini OQLQ prior to and during teriperatide treatment. We used normal probability plots to assess the Normality assumption. The criterion for statistical significance was set apriori at alpha = 0.05. We used SPSS 12.0 for all statistical analyses.

**Results**

**Participant characteristics**
The study sample included 57 participants, with 82.5% (n=47) being female. The mean age was 63.9 (SD=12.1). From the 57 total participants, 37 received their QOL assessment at the 6 month follow up period. The remaining 20 participants were evaluated at the 3-month follow up period. A majority of patients (64.9%) reported that they had previously suffered at least one vertebral or non-vertebral fracture. At baseline, 26.3 % of participants (n=15) reported taking a pain medication for pre-existing back pain. There were 9 participants taking Acetaminophen, Aspirin, NSAIDS or COX-2 inhibitors. One participant was taking narcotics alone for relief of back pain, while five participants were taking a combination of narcotics plus Acetaminophen, Aspirin, NSAIDS or COX-2 inhibitors for pain relief (Table 1).

**HRQL Domains and Teraperatide**
The mini-ORQL can be divided into five distinct domains relating to HRQ: symptoms (Q1, Q2), emotional function (Q3, Q4), physical function (Q5, Q6), activities of daily living (Q7, Q8), and leisure (Q9, Q10). Each question was analyzed individually and grouped according to the domains that they represent (Figure 2).

**Symptoms**
The HRQL domain of symptoms showed significant decreases post-teraperatide therapy for both questions that addressed it. Data are expressed as (mean; standard deviation). Baseline data for Q1 (4.30; 1.935) was reduced in follow-up data (3.05; 1.62) (p<0.0001). Similarly baseline data for Q2 (4.00; 2.20) was lower in the follow-up data (3.02; 1.716) (p=0.001).

**Emotional Functioning**
The questions addressing emotional functioning also demonstrated significant improvements in each question. Baselines for both Q3 (3.26; 2.13) and Q4 (3.28; 2.00) were lower in post-therapy results (2.51; 1.75, p=0.007) and (2.70; 1.99, p=0.035) respectively.
Physical Functioning
Data for the physical functioning domain was divided, with only one question showing significant improvement. The improvement in physical function was found in Q5 (3.90; 1.99 to 3.20; 1.87, p=0.004). No significant change was found in Q6, however the trend was towards improvement with teriparatide..

Activities of Daily Living and Leisure
Neither the ADL or leisure domains resulted in significant improvements post teriperatide therapy. Both domains did demonstrate trends towards improvement but failed to be statistically distinct from baseline values.

Discussion
Vertebral fractures are an important and common cause of morbidity in osteoporotic patients (16). Vertebral fractures are among the top health conditions accounting for length of hospital stay, and added significantly to the length of stay to patients admitted for other medical problems (17). Aside from the physical limitations suffered by these patients, chronic back pain has a significant impact on the patient’s quality of life (18). Patients suffering from vertebral fractures often have impaired physical functioning, limited activities of daily living, limited leisure and recreational activities, and significant emotional distress (11). The use of teriparatide in the treatment of postmenopausal osteoporosis revealed a decrease in the risk of both vertebral and non-vertebral fractures, along with a significant increase in vertebral, femoral neck, and total body-bone mineral density (8). The goal of our study is to evaluate the effect of teriparatide treatment on the risk of back pain and health related quality of life in osteoporotic patients in a clinical practice setting. Studies in the past have investigated the effect of teriparatide on back pain risk in a randomized control trial setting (2). Nevitt and associates’ systematic review identified five randomized clinical trials (RCTs) that evaluated prevention of back pain in teriparatide treated osteoporotic patients. In contrast, our study investigates patients with pre-existing back pain, and we measured the improvement in pain severity and effect on quality of life after initiating teriparatide therapy. Also, the incidence of back pain was not the primary outcome in any of these studies, with new vertebral fractures (n=1) or changes in bone mineral density (n=4) as the primary outcomes (2). Back pain data were collected through spontaneous reporting by patients as adverse events. The conclusion of the meta-analysis was that patients randomized to teriparatide had a reduced risk of new or worsening back pain compared to patients randomized to placebo or anti-resorptive therapies (2). RCTs have several disadvantages. Although RCTs are able to demonstrate the efficacy of a therapy, it has certain limitations in demonstrating the therapy’s effectiveness in a real world patient population. Firstly, patients in RCTs represent a very homogeneous patient population that may not reflect the target patient population. These patients are also self
selected, therefore they have higher likelihood of having a high compliance rate to treatment (19).

Analysis of our HRQL data in our patients’ pre and post-teriparatide therapy revealed statistically significant improvements in the domains of symptoms and emotional functioning. Improvements in physical functioning, ADL and leisure were seen, but were not significantly different from baseline measurements. The symptoms domain inquired about discomfort/distress related to pain, while the emotional functioning domain addressed the patients’ fears of two major complications, fractures and falling. A reduction in the symptoms domain indicates that patients who received teriparatide therapy went on to experience less pain than prior to therapy. An improvement in emotional functioning scores suggests that patients treated with teriparatide had less fear of falls or fractures than they experienced before receiving the medication. Therefore patients had less pain discomfort and less fear of complications three to six months after being started on teriparatide. There are several limitations to our study, including missing data resulting in exclusion of some participants, pooling of 3 and 6 month data, and lack of a control group.

In conclusion, previous studies have demonstrated that teriparatide therapy results in decreased fractures and pain symptoms in patients with osteoporosis. In this study, we have confirmed that patients with osteoporosis treated with teriparatide experience improvements in pain symptoms. Furthermore, emotional functioning appears to improve with therapy. Our findings need to be validated in a larger prospective study with a suitable control group.
Reference:

1) NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis and Therapy. Osteoporosis prevention, diagnosis and therapy. *JAMA*. 2001; 285:785-795


Figure Legends:

Figure 1: Enrollment- 105 patients on teriparatide therapy were screened for eligibility. 48 patients were excluded: 2 had not completed baseline questionnaires, 2 withdrew prior to follow up due to adverse effects and 44 had no follow up data at 3 or 6 months for the most part because they did not have a follow-up appointment at these time points.

Figure 2: Box plot comparing mini-OQLQ patient scores at baseline and follow-up for each for the 5 domains.
Appendix: Shortened Osteoporosis Quality of Life Questionnaire

1) How much distress or discomfort have you had because of pain in the last two weeks?
2) How much distress or discomfort you had in last two weeks because it had been painful to stand for a long time
3) How often in the last two weeks have you felt afraid of fractures?
4) How often in the last two weeks have you felt afraid of falling?
5) How difficult has it been for you to lift things in the last two weeks?
6) How difficult has it been for you to carry things in the last two weeks, because of back problems due to osteoporosis?
7) How difficult has it been for you to vaccum in the last two weeks?
8) How difficult has it been for you to housework in the last two weeks?
9) How difficult has it been for you to travel in the last two weeks?
10) How difficult has it been for you to take the type of vacation or holiday you enjoy because of your back problems due to osteoporosis?
105 teriparatide patients screened

- 2 patients had no baseline data
- 2 patients withdrew prior to 3 to 6 month follow up due to adverse effects
- 57 patients with baseline and 3 or 6 month follow up data

44 patients had no follow up data at 3 or 6 months

37 patients had follow up at 6 months
20 patients had follow up at 3 months
Additional files provided with this submission:

Additional file 1: bmc tables 1 and 2.doc, 59K
http://www.biomedcentral.com/imedia/8057171911857200/supp1.doc