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Changes of the quality-of-life under the treatment of severe senile osteoporosis with teriparatide

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ABSTRACT

Despite being treated with antiresorptive drugs, the severe osteoporosis (SO) is being considered as a condition in which patients are still subject to one or more vertebral or femoral fractures, or non-vertebral or non-femoral fractures, i.e., of other parts of the body such as the wrist, shoulder, tibia, ribs or hip. These patients are defined as non-responders (NRs) to the antiresorptive therapy, and recent research has shown that they represent 10–25% of all SO patients. During the last almost 3 years a new drug has become available in Italy, called teriparatide (rh-PTH-1-34), produced in *Escherichia coli* using the recombinant-DNA technique. It shows remarkable trophic and anabolic actions on the bones, and proved to be very useful for treating the osteoporosis in general. This study describes our experience in using teriparatide for the treatment of SO in a sample of 141 elderly women of mean age 73.4 ± 5.8 years, with a mean number of fractures of 3.0 ± 0.85, with a spine deformity index (SDI) of 5.92 ± 1.27 and a mean vertebral T-Score (L1–L4) of −3.15 ± 0.39, and a mean femoral T-Score of −2.50 ± 0.28. All these patients had been treated with antiresorptive drugs for at least 1 year: specifically 70 of them with Alendronate, 42 of them with Risedronate and 29 of them with Raloxifene. For 18 months, all these patients were injected subcutaneously with 20 μg of teriparatide, with the daily addition of 1 g of calcium and 880 IU of vitamin D. The study was continued for 24 months, at the end of which the patients continued to take only calcium and vitamin D. The patients underwent a CBM-DEXA control of vertebral column and femur every 6 months, and they were also administered a Quality-of-Life Questionnaire of the European Foundation for Osteoporosis (QUALEFFO). The QUALEFFO (41 items) questionnaire to evaluate the changes in the quality-of-life (QoL) and the consumption of non-steroidal anti-inflammatory drugs (NSAIDs) was also recorded. The results showed that teriparatide protected 96.5% against new fractures (only five new fractures occurred), bone mineral density (BMD) increased approximately by 12% in the vertebral column and by 11% in the femur, consumption of NSAIDs was reduced at the early stage approximately 80%, the QoL improved considerably and remained so during the 18 months of teriparatide treatment, with only a slight decrease during the 6 subsequent months.

1. Introduction

The teriparatide (1–34 fraction of PTH, produced by *E. coli* by using the recombinant DNA technique) has become available in Italy since about 3 years, and was used for the treatment of post-menopausal osteoporosis and, more recently, also for male osteoporosis. Teriparatide has a remarkable anabolic action on the bone and improves its microarchitecture, if administered subcutaneously once a day in doses of 20 μg (Dempster et al., 1991; Rubin et al., 2002).

The fraction prevention trial (FPT) carried out on 1637 women with post-menopausal osteoporosis demonstrated the unequivocal effectiveness and safety of this drug when administered for 18 months; bone protection was considerable and there was a marked reduction in vertebral and femoral fractures as well as in non-vertebral and non-femoral fractures (radius, humerus, tibia, etc.) (Neer et al., 2001). Bone-protection was maintained 2–3 years after the suspension of treatment (Jonsson et al., 1999). Moreover, on a smaller sample of patients with male osteoporosis, bone protection was also confirmed, but the BMD began to decrease

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Table 1
Comparison of the main parameters of the study pool during the teriparatide treatment (mean ± S.D.)

Parameter	T_0	T_6	T_{12}	T_{18}	T_{24}
L1–L4					
T-Score	−3.15 ± 0.39	nm	−2.90 ± 0.15	−2.80 ± 0.22	−2.76 ± 0.20
% change			−7.9	−11.1	−12.4
BMD (mg/cm^2)	593 ± 58	nm	647 ± 54	659 ± 52	665 ± 52
% change			+8.4	+11.1	+12.1
Femur in toto					
T-Score	−2.50 ± 0.28	nm	−2.40 ± 0.44	−2.32 ± 0.62	−2.22 ± 0.56
% change			−4.0	−7.2	−11.2
BMD (mg/cm^2)	600 ± 62	nm	625 ± 54	645 ± 62	668 ± 58
% change			+4.2	+7.5	+11.3
QUALEFFO-test	478 ± 60	392 ± 52	285 ± 37	192 ± 37	249 ± 50
% change		−18.0	−40.0	−60.0	−48.0
Use of NSAIDs in 141 patients					
n of patients	131	50	40	30	32
% of them	93.0	35.0	28.0	21.0	23.0

Note: nm, not measured

again when the treatment was suspended (Bilezikian and Kurland, 2001).

In 2006, Boonen et al. (2006), on a group of 244 patients over the age of 75 years confirmed the effectiveness of teriparatide: vertebral and femoral BMD increased by 9.2% and 1.9%, respectively, after a 12-month treatment. These changes of bone mass were similar to those of a group of 841 control patients under the age of 75 (+9.1% and 2.9%, respectively): Boonen et al. (2006) concluded, therefore, that the effectiveness of teriparatide was not age-related and applied to all age groups.

The same can be said regarding the safety of teriparatide, in so far as similar results were achieved in patients over and under 75 years of age, showing the same side effects, such as nausea, leg cramps and dizziness. However, apart from its greater effectiveness in terms of reducing the number of new fractures, by giving over 65% total protection, what brings teriparatide in pole position among the drugs used to treat osteoporosis is its considerable ability to improve patients' QoL, which is the first objective to be pursued from a geriatric perspective.

In many previous studies (Lips and Van Schoor, 2005; Brenneman et al., 2006; Marcinkowska et al., 2006; Gold and Silverman, 2007; Marquis et al., 2007; Salaffi et al., 2007; Silverman et al., 2007) having used various drugs available for the treatment of osteoporosis, such as Alendronate, Risedronate, Oestrogen, Raloxifene and Strontium Ranelate, aspects concerning the reduction of back pain and overall pain, the consequent consumption of NSAID, and the patients' QoL, were also examined and, even though different evaluation systems were used, the results always showed a certain improvement in the patient's QoL.

In one of our previous studies (Manuele et al., 2007) we have already verified that teriparatide immediately and unequivocally improves the QoL of patients, while protecting the fragile osteoporotic skeleton. In addition to assessing the anti-osteoporotic efficacy of teriparatide in the traditional sense (reduction of new fractures, increase in BMD), our research also aimed at evaluating the effect on the QoL of elderly patients suffering from SO, during the permitted 18-month cycle of treatment and during the subsequent 6 months after the treatment was suspended.

2. Patients and methods

Our study pool consisted of 141 elderly female patients with SO, treated at our centers in Catania, Canosa and Patti. Their mean age was 73.4 ± 5.8 years and they had been treated for at least 1 year with antiresorptive drugs (70 of them with Alendronate, 70 mg/week, 42 with Risedronate, 35 mg/week, and 29 with Raloxifene, 60 mg/day), however, all of them were NR to this therapy. According to recent data, such as the ICARO and OSSO studies (Adami et al., 2006; Cooper et al., 2007) NR patients represent 10–25% of all SO patients. The mean SDI of our patients was 5.92 ± 1.27, their mean vertebral T-Score was −3.15 ± 0.39, their main femoral T-Score was −2.50 ± 0.38.

All these patients received for 18 months 20 μg/day of teriparatide in form of subcutaneous injections, and were taking also a supplementation of 1 g/day calcium and 800 IU of vitamin D_3; then for other 6 months they received only the same amounts of calcium and vitamin D_3.

The patients included in this study underwent a BMD analysis (DEXA-Lunar-DPX-P) on their lumbar vertebral column, and on their femur at start of the treatment (T_0), as well as after 12, 18 and 24 months, respectively (T_{12}, T_{18}, and T_{24}). In addition, we monitored the changes in use of NSAIDs during treatment and the QoL by using the QUALEFFO-test (Lips et al., 1999) (41 items) at times T_0, T_6, T_{12}, T_{18}, and T_{24}.

Table 2
Detailed results of the QUALEFFO-test during the teriparatide treatment (mean ± S.D.)

Parameter	T_0	T_6	T_{12}	T_{18}	T_{24}
Daily activities	420 ± 62	340 ± 54	280 ± 48	200 ± 44	240 ± 52
% change		−19.0	−33.0	−52.0	−42.0
Domestic jobs	442 ± 48	380 ± 45	276 ± 42	200 ± 40	240 ± 52
% change		−14.0	−37.0	−54.0	−45.0
Locomotor functions	522 ± 60	440 ± 56	280 ± 42	170 ± 28	270 ± 38
% change		−16.0	−46.0	−67.0	−48.0
Social activities	420 ± 52	340 ± 44	240 ± 38	164 ± 32	200 ± 52
% change		−19.0	−48.0	−61.0	−52.0
Self-perception of own health	484 ± 62	444 ± 62	318 ± 40	206 ± 38	240 ± 46
% change		−8.0	−32.0	−57.0	−50.0
Pain	500 ± 56	420 ± 48	280 ± 32	165 ± 30	240 ± 48
% change		−17.0	−56.0	−65.0	−52.0
Humor	560 ± 82	386 ± 66	318 ± 60	240 ± 44	318 ± 62
% change		−31.0	−43.0	−57.0	−43.0

3. Results

Our main findings are summarized in Tables 1 and 2. By the end of the study period, the BMD values expressed in terms of T-Score in our total pool displayed important changes. Namely the mean value of this parameter decreased about 12% indicating an improvement in the BMD: this increased in both the measured regions about 11–12% (Table 1).

The consumption of NSAIDs also decreased considerably for the entire pool: from 93% of the patients who consumed NSAIDs at T_0, it dropped to 23% by the T_{24} (Table 1).

As regards the total results with the QUALEFFO-test, the values decreased continuously during the treatment, showing the largest decrease (−60.0%) at the T_{18} and somewhat smaller one (−48.0%) at T_{24} (Table 1).

Details of the QUALEFFO-test are described in Table 2. All parameters improved considerably during the treatment of 24 months. It is of particular importance that the pain levels decreased to a large extent (Table 2), but also all other domains of this test (the daily activities, the domestic tasks, the locomotor functions, the leisure and social activities, the self-perception of personal health state, including the humor of the patients (Table 2).

4. Discussion

Nowadays, the increasing age of the population seems to be a general phenomenon in the Western countries, and from a demographic point of view, this so-called "Elderly boom" has changed considerably the age pyramid and has practically almost inverted it. The medium life span for the women is now about 84 (rounded), while for men it is closer to 79 years. However, the last years of the elderly people in Italy are more surviving than living years.

The elderly people suffer of many diseases, and among them the SSO is becoming more and more common. It frequently involves vertebral, femoral, non-vertebral and non-femoral fractures, which lead rapidly not only to a more or less serious disability, the loss of self-sufficiency, and institutionalization, but also to death. This is now the case for approximately 25–30% of the elderly within the first year subsequent to a hip-fracture.

The goal to be achieved in geriatric ages with pharmaceutical treatment is not to cure the diseases, because at this stage in the life of the elderly, it is frequently possible only to slow it down, as is the case with Alzheimer's disease, where slight or moderate conditions are treated with acetylcholine-esterase inhibitors, or to delay the stages of relapse with a combined beta-2-agonist and topical cortisone therapy for chronic obstructive pulmonary disease (COPD). The goal is also to improve the QoL so that it can be lived in the best possible way. As Martial said, "Non est vivere sed valere vita est". The QoL of the elderly with SSO is considerably compromised and the correct treatment must quickly reduce the possibility of new fractures and improve the QoL.

During the past 10 years, all the anti-osteoporotic drugs that were used both in registration studies and by public health services (bisphosphonates; selective estrogen receptor modulators, SERMs) achieved the aim of an approximately 50% reduction of new fractures over 3 years, but they had little effect on the QoL of the patients, who often continued to have pains and were forced to take NSAIDs. During the last 2–3 years, the strontium ranelate, part of a new category of dual action bone activity (DABA) drugs, which associated a certain antiresorptive action with the primary trophic action, has also been used for SSO and the reduction of new fractures was about 40%, of pain was about 30%, and there was also some improvement in the QoL of the elderly patients treated.

The recent appearance of teriparatide made a significant change to the course of osteoporosis in general, and to SSO in particular. In terms of the reduction of new fractures, the 50% threshold has been increased to almost 70%, but what is very important, especially in geriatric medicine, is that during treatment, the pain disappeared almost totally and the QoL significantly improved.

In Italy, treatment with teriparatide is permitted for 18 months only, and although the metabolic disease of the bones continued to slow down and there was continual protection from fractures in general, at 6 months after its suspension both the pain and the QoL appeared to worsen, practically demonstrating the drug's direct action on pain (at central level) and on the overall state of health.

5. Conclusions

In the light of our results, the conclusions are that the use of teriparatide to treat SSO and SO in NRs at all the previous stages of their life, should be the first choice of drug, because it gives more protection from new fractures than the other drugs used today, and unequivocally improves also the QoL of patients suffering from osteoporosis. Since in our study pool most of the parameters having been improved during the first 18 months of treatment displayed some tendencies of worsening during the last 6 months after the cessation of the teriparatide treatment, we are of the opinion that it is worth to maintain the treatment even for longer times than the actually tested 18 months.

Conflicts of Interest Statement

None declared.

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