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TERIPARATID U LEČENJU OSTEOPOROZE – NAŠA ISKUSTVA

Teriparatid (Forteo amp) je aktivni fragment (1–34) paratireoidnog hormona. Fiziološko delovanje paratireoidnog hormona uključuje stimulaciju stvaranja koštane mase direktnim efektom na ćelije koje stvaraju kost (osteoblaste), indirektno povećanjem intestinalne apsorpcije kalcijuma, povećanje tubularne reapsorpcije kalcijuma i ekskrecije fosfata putem bubrega.

Zbirni pozitivan efekat teriparatida na kosti je povećanje koštane gustine i smanjenje rizika od preloma.

Indikacija za primenu ovog leka je osteoporoza.

Lek se primenjuje u vidu subkutane injekcije (trbuh, nadlaktica ili butina), jednom dnevno u dozi od 20 mcg, kontinuirano 24 meseca. Primenjuje se nezavisno od obroka, a najbolje je svakog dana u približno isto vreme.

Najčešći neželjeni efekti ovog leka su mučnina, vrtoglavice, glavobolje i bolovi u ekstremitetima.

Tokom lečenja teriparatidom može doći do povećanja nivoa kalcijuma i alkalne fosfataze u krvi, pa je potrebno njihovo tromesečno praćenje.

Lek se ne primenjuje kod dece, trudnica, u periodu dojenja, kao i kod povišenog nivoa kalcijuma u krvi (primarni hiperparatireoidizam), povišenog nivoa alkalne fosfataze (Pagetova bolest), teškog oštećenja funkcije bubrega, maligne bolesti kostiju ili neke druge maligne bolesti koja je metastazirala na kosti i posle primene radijacione terapije na kostima.

Na preporuku iz naše ustanove lečeno je sedam pacijentkinja teriparatidom, po ustaljenom terapijskom protokolu.

Svim pacijentkinjama su uzeti anamnestički podaci, urađene biohemijske analize, uključujući kalcijum, fosfor, alkalnu fosfatazu, određen je i nivo PTH i urađen je DEXA pregled na Hologic explorer osteodenzitometru.

Naše pacijentkinje do sada nisu lečene od osteoporoze.

Pacijentkinje lečene teriparatidom SZ, ĐR, SM, JG, ĐM, BS i DG, bile su različitog životnog doba, dve od sedam pacijentkinja nisu imale nijednu pridruženu bolest, ali svaka pacijentkinja je imala jedan ili više preloma kostiju pre početka lečenja. Jedna od njih je duži niz godina primala kortikosteroide, tako da se smatra da je zbog toga

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dobila osteoporozu. Karakteristično za sve pacijentkinje da je njihovo raspoloženje bilo veoma loše pre početka lečenja, ali se znatno popravilo nakon završetka lečenja.

Pacijentkinja SZ, 58 godina, nema tegobe, nije imala pridružene bolesti, imala je prelom desne podlaktice, izgubila menstrualni ciklus u 44. godini života, fizički veoma aktivna, gracilne konstitucije, svetlog tena, male telesne težine.

Analize: kalcijum: 2,25, fosfor: 1,1, PTH: 54,0, ALP: 65,0.

DEXA pregled ukazuje na smanjenu koštanu gustinu na nivou kičme u smislu osteoporozе (T skor – 4,4 na kičmi) i smanjenu koštanu gustinu na nivou kuka u smislu osteopenije (T skor – 2,4).

Nakon završenog lečenja ponovo smo izmerili koštanu gustinu na istom aparatu i utvrdili poboljšanje koštane gustine na kičmi za 7,8%. Koštana gustina na kičmi je i dalje bila na nivou osteoporozе (T skor – 2,7), a koštana gustina se popravila za 4,4% na nivou kuka.

Nije bilo nikakvih neželjenih efekata primenjenog leka i nije bilo nijednog novog preloma, pacijentkinja se dobro osećala, nastavili smo terapiju samo suplementacijom preparatom kalcijuma i i vitamina D.

Druga pacijentkinja JG, 69 godina, žali se na bol u predelu torakalnog dela kičme, koji je nastao naglo, praktično nije mogla da stane na noge. Leči se od visokog krvnog pritiska i šećerne bolesti, na kombinovanoj terapiji OAB i insulinom.

Analize: kalcijum: 2,04, fosfor: 1,13, PTH: 43,9, ALP: 70,0.

Menstrualni ciklus izgubila u 48. godini života.

DEXA pregled ukazuje na smanjenu koštanu gustinu u smislu osteoporozе na nivou kičme i kuka

(T skor – 3,0). Na RTG pregledu TH i L-S kičme vidi se kompresivna fraktura pršljenjskog tela TH-12.

Konsultovan i ortoped koji je indikovao nošenje rasteretnog midera.

Nakon 10 dana od početka upotrebe teriparatida i rasteretnog midera naša pacijentkinja se vratila redovnim kućnim poslovima.

Kontrolni DEXA pregled nakon završene terapije teriparatid ampulama pokazao je poboljšanje koštane gustine za 10% i na kičmi i na kuku, tako da je koštana gustina sada na nivou osteopenije (T skor na kičmi – 2,3), nastavili smo dalju terapiju vitaminom D. Što je najvažnije, pacijentkinja se normalno kreće i nije bilo novih preloma kostiju.

Pacijentkinja ĐR, 64 godine, ima bolove u lumbalnom delu kičme, koji traju godinama. Duži niz godina bila na terapiji kortikosteroidima, koje je primala intramuskularno. Imala četiri preloma, dva na malu traumu, čak i prelom palca desne noge prilikom udarca u nogaru fotelje.

Menstrualni ciklus izgubila u 44. godini života.

Analize: kalcijum: 2,35, fosfor: 1,15, PTH: 60,0, ALP: 75,0.

DEXA pregled je ukazao na značajan nivo osteoporoze na kičmi (T skor – 4,4) i normalnu koštanu gustinu na kuku.

Nakon uvođenja terapije teriparatidom pacijentkinja nije više primila kortikosteroide, jer su bolovi u lumbalnom delu kičme prestali. Pacijentkinja je u dva navrata u zimskom periodu imala pad, koji nisu bili praćeni prelomima kostiju. Oseća se odlično, nema bolove i trenutno je samo na terapiji preparatom vitamina D i kalcijuma.

Kontrolni DEXA pregled nakon dvogodišnje terapije teriparatidom ukazuje na poboljšanje koštane gustine za 10,0% na nivou kičme, ali je i dalje nalaz koštane gustine na nivou osteoporoze (T skor na kičmi – 2,8). Zakazan kontrolni DEXA pregled za godinu dana, a terapija do kontrole vitamin D i preparat kalcijuma.

Naredna pacijentkinja koja je bila na tretmanu teriparatid ampulama je DG, 54 godine, žali se na bolove u predelu grudnog koša, loše raspoloženje, zna za smanjenu funkciju štitaste žlezde, na supstituciji je, imala dva preloma kostiju u prethodnom periodu.

Menstrualni ciklus izgubila sa 47 godina.

Analize: kalcijum: 2,33, fosfor: 1,19, PTH: 35,2, ALP: 60,0.

DEXA pregled ukazuje na smanjenu koštanu gustinu u smislu osteoporoze (T skor – 4,8) i smanjenu koštanu gustinu na nivou kuka u smislu osteoporoze (T skor – 2,6).

Nakon dvogodišnjeg tretmana teriparatid ampulama imamo poboljšanje koštane gustine na nivou kičme za 22,5% (T skor – 2,7) i poboljšanje koštane gustine na nivou kuka za 13,4% (T skor – 2,0).

Pacijentkinja se odlično oseća, mnogo je bolje raspoložena, nije bilo preloma kostiju i ponovo nosi visoke potpetice. Sada je na suplementaciji preparatom vitamina D i kalcijuma, redovno se kontroliše.

Gospođa ĐM, 60 godina, nema tegoba, leči se kod psihijatra i od smanjene funkcije štitaste žlezde, imala prelom levog maleolusa. Menstrualni ciklus prestao u 53. godini života.

Analize: kalcijum: 2,36, fosfor: 1,1, PTH 38,0, ALP: 63,0.

Donosi izveštaj ortopeda: Fractura malleolii l. Sin.

DEXA pregled ukazuje na smanjenu koštanu gustinu na nivou kičme u smislu osteoporoze

(T skor – 3,0).

Godinu dana nakon primene teriparatida izmerili smo koštanu gustinu koja je pokazivala poboljšanje koštane gustine na nivou kičme za 10%, kvalitet života naše pacijentkinje se znatno poboljšao i do tada nije bilo nijednog preloma kostiju.

Nakon dvogodišnjeg tretmana teriparatidom vidi se poboljšanje koštane gustine na nivou kičme

(T skor – 2,6), ali je i dalje u blagoj osteoporozi.

Pacijentkinja SM, 56 godina, gracilne građe, nije bilo preloma kostiju, leči se od smanjene funkcije štitaste žlezde. Majka pacijentkinje je imala više preloma kostiju i sestra ima dijagnostikovanu osteoporozu.

Menstrualni ciklus prestao u 48. godini života.

DEXA pregledom je utvrđena smanjena koštana gustina na nivou osteoporozе (T skor – 3,6) i smanjenu koštanu gustinu na nivou kuka u smislu osteopenije (T skor – 2,6).

Pacijentkinja je odmah prihvatila terapiju teriparatid ampulama. Primala je preporučenu terapiju, nakon dve godine smo napravili novi DEXA pregled koji je pokazao poboljšanje koštane gustine na nivou kičme, za 6 %, tako da je T skor na kičmi – 3,1, a na kuku poboljšanje koštane gustine za 4 %, tako da je sada koštana gustina na nivou kuka na nivou osteopenije (T skor -2,1).

Pacijentkinja BS, 64 godine, izgubila 5 cm u telesnoj visini, za godinu dana imala četiri preloma kostiju.

Menstrualni ciklus prestao u 46. godini života.

Do sada nije merila koštanu gustinu, negira druga oboljenja.

DEXA pregledom je utvrđena osteoporozа na nivou kičme (T skor – 3,2%) i smanjena koštana gustina na nivou kuka u smislu osteopenije (T skor – 1,5).

Pacijentkinji je predložena terapija teriparatidom, koju je primala dve godine i nije imala nikakvih nusfekata leka, prestala je da gubi u telesnoj visini i više nije bilo nijednog preloma kostiju.

Na kontrolnom DEXA pregledu utvrđeno je poboljšanje koštane gustine na nivou kičme za 5,7%, tako da je nalaz na nivou kičme i dalje smanjen na nivou osteoporozе (T skor – 2,7) i poboljšanje koštane gustinu na nivou kuka za 10,7%, i sada je T skor na kuku – 0,2.

Što je najvažnije, pacijentkinja se mnogo lakše kretala i njeno raspoloženje se popravilo.

Najbolji uspeh teriparatid je postigao kod pacijentkinje DG!

Sve pacijentkinje kojima je predložena terapija teriparatidom u našoj ustanovi su u potpunosti ispoštovale terapijsku proceduru. Po završenoj proceduri uzimanja leka urađen je kontrolni DEXA pregled.

Sve pacijentkinje su odlično podnosile lek i nisu imale nijedan neželjeni efekat.

Kvalitet života svih pacijentkinja koje su bile na tretmanu teriparatidom je poboljšan, lakše su obavljale sve poslove, bile su mnogo bolje raspoložene i, što je najvažnije, nijedna više nije imala nijedan prelom kostiju.

Do sada se pacijentkinje osećaju dobro, nemaju nikakve tegobe i nisu prijavile nijedan novi prelom kostiju.

Rezultati opservacione studije Efekti Teriparatida kod pacijenata sa osteoporozom u kliničkoj praksi: 42-mesečni rezultati tokom i posle lečenja iz Evropske proširene opservacione studije Forsteo (EkFos), koja je sprovedena na 1.400 pacijenata, prosečne starosti 70 godina, od kojih su 90% bile pacijentkinje ženskog pola. Studija je pokazala smanjenje fraktura za 47%, poboljšanje kvaliteta života, kao i značajno smanjenje intenziteta bola u leđima.

Zaključak: Terapija teriparatidom kod svih naših pacijentkinja je dala odličan efekat prvenstveno, jer do sada nije zabeležen nijedan novi prelom kostiju i značajno je poboljšana kvaliteta njihovog života.

Literatura

1. Nicola Napoli et al. Effects of Teriparatide in Patients with Osteoporosis in Clinical Practice: 42-Month Results During and After Discontinuation of Treatment From the European Extended Forsteo Observational Study (ExFOS). *Calcif Tissue int*, 103(4), 359–371, oct, 2018.
2. Kendler LD et al. Publishing online, november 9, 2017. Effects of teriparatide and riserodronate on new fractures in post- menopausal Women with severe osteoporosis (VERO) a multicentre, double-blind, double-dummy, randomised controlled trial.

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TERIPARATID IN THE TREATMENT OF OSTEOPOROSIS – OUR EXPERIENCES

Teriparatide (Forteo amp) is an active fragment (1-34) of parathyroid hormone. The physiological action of parathyroid hormone includes stimulation of bone mass production by a direct effect on bone-forming cells (osteoblasts), indirectly by increasing intestinal calcium absorption, increased tubular calcium reabsorption and renal phosphate excretion.

The cumulative positive effect of teriparatide on bone is an increase in bone density and a reduction in the risk of fractures.

The indication for the use of this medicine is osteoporosis.

The drug is administered as a subcutaneous injection (abdomen, upper arm or thigh), once a day in a dose of 20 mcg, continuously for 24 months. It is applied regardless of the meal, and it is best every day at approximately the same time.

The most common side effects of this medicine are nausea, dizziness, headaches and pain in the extremities.

During treatment with teriparatide, there may be an increase in calcium and alkaline phosphatase levels in the blood, so they need to be monitored quarterly.

The drug is not used in children, pregnant women, during breastfeeding, as well as with elevated levels of calcium in the blood (primary hyperparathyroidism), elevated levels of alkaline phosphatase (Paget's disease), severe impairment of kidney function, malignant bone disease or some other malignant disease that has metastasized to the bone and after the application of radiation therapy to the bones.

On the recommendation from our institution, seven patients were treated with teriparatide, according to the established therapeutic protocol.

All patients had anamnestic data, biochemical analyzes were performed, including calcium, phosphorus, alkaline phosphatase, PTH levels were determined and DEXA examination was performed on a Hologic explorer osteodensitometer.

Our patients have not been treated for osteoporosis so far.

Patients treated with teriparatide SZ, ĐR, SM, JG, ĐM, BS and DG were of different ages, two of the seven patients did not have any associated disease, but each patient had one or more bone fractures before treatment. One of them has been receiving corticosteroids for many years, so it is believed that she got osteoporosis

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because of that. It is characteristic of all patients that their mood was very bad before the start of treatment, but significantly improved after the end of treatment.

Patient SZ, 58 years old, has no problems, had no associated diseases, had a fracture of the right forearm, lost her menstrual cycle at the age of 44, is physically very active, has a graceful constitution, light complexion, and low body weight.

Analyzes: calcium: 2.25, phosphorus, 1.1, PTH: 54.0. ALP: 65.0.

DEXA examination indicates reduced bone density at the level of the spine in terms of osteoporosis (T score -4.4 on the spine) and reduced bone density at the level of the hip in terms of osteopenia (T score - 2.4).

After the end of the treatment, we measured the bone density again on the same device, and determined the improvement of the bone density on the spine by 7.8%. Bone density on the spine was still at the level of osteoporosis (T score - 2.7), and bone density improved by 4.4% at the level of the hip.

There were no side effects of the drug and there were no new fractures, the patient felt well, we started the therapy only with supplementation with calcium and vitamin D.

Another patient, JG, 69, complains of pain in the area of the thoracic spine, which arose suddenly, she could practically not stand on her feet. It is treated for high blood pressure and diabetes, in combination therapy with OAB and insulin.

Analyzes: calcium: 2.04, phosphorus: 1.13, PTH: 43.9, ALP: 70.0.

She lost her menstrual cycle at the age of 48.

DEXA examination indicates reduced bone density in terms of osteoporosis at the level of the spine and hips

(T score - 3.0). An X-ray examination of the TH and L-S spine shows a compressive fracture of the vertebral body TH-12.

An orthopedist who indicated wearing a relief midsole was also consulted.

After 10 days from the beginning of the use of teriparatide and relief midsole, our patient returned to regular household chores.

The control DEXA examination after the end of the therapy with teriparatide ampoules showed an improvement of bone density by 10% on both the spine and the hip, so that the bone density is now at the level of osteopenia (T-score on the spine -2.3), we continued further vitamin D therapy. Most importantly, the patient was moving normally and there were no new bone fractures.

Patient DR, 64 years old, has pain in the lumbar spine, which lasts for years. For many years, she was on corticosteroid therapy, which she received intramuscularly. She had four fractures, two with minor trauma, and even a fracture of the big toe of her right foot when hitting the leg of the armchair.

She lost her menstrual cycle at the age of 44.

Analyzes: calcium: 2.35, phosphorus: 1.15, PTH: 60.0, ALP: 75.0.

DEXA examination indicated a significant level of osteoporosis in the spine (T score - 4.4) and normal bone density in the hip.

After the introduction of teriparatide therapy, the patient no longer received corticosteroids, because the pain in the lumbar spine stopped. The patient had a fall on two occasions during the winter period, which was not accompanied by bone fractures. She feels great, has no pain and is currently only on therapy with vitamin D and calcium.

Control DEXA examination after two years of therapy with teriparatide indicates an improvement in bone density by 10.0% at the level of the spine, but the finding of bone density at the level of osteoporosis is still (T-score on the spine -2.8). Scheduled control DEXA examination for a year, and therapy to control vitamin D and calcium preparation.

The next patient who was treated with teriparatide ampoules is DG, 54 years old, complains of chest pain, bad mood, knows about reduced thyroid function, she had two bone fractures in the previous period on the substitution.

She lost her menstrual cycle at the age of 47.

Analyzes: calcium: 2.33, phosphorus: 1.19, PTH: 35.2, ALP: 60.0.

DEXA examination indicates reduced bone density in terms of osteoporosis (T score -4.8), and decreased bone density at the hip level in terms of osteoporosis (T score -2.6).

After two years of treatment with teriparatide ampoules, we have an improvement in bone density at the spine level by 22.5% (T score - 2.7) and an improvement in bone density at the hip level by 13.4% (T score - 2.0).

The patient feels great, she is in a much better mood, there were no broken bones and she is wearing high heels again. He is now on a supplement with vitamin D and calcium, and he is checked regularly.

Ms. DM, 60 years old, has no problems, is being treated by a psychiatrist and has a fracture of the left malleolus due to reduced thyroid function. The menstrual cycle stopped at the age of 53.

Analyzes: calcium: 2.36, Phosphorus: 1.1, PTH 38.0, ALP: 63.0.

Reports orthopedist: Fractura malleolii l. Son.

DEXA examination indicates reduced bone density at the level of the spine in terms of osteoporosis (T score - 3.0).

One year after the application of teriparatide, we measured bone density, which showed an improvement in bone density at the level of the spine by 10%, the quality of life of our patient significantly improved and until then there were no more bone fractures.

After two years of treatment with teriparatide, there is an improvement in bone density at the level of the spine.

(T score - 2.6), but is still mildly osteoporous.

Patient SM, 56 years old, graceful, had no bone fractures, is being treated for reduced thyroid function. The patient's mother had several bone fractures and her sister was diagnosed with osteoporosis.

The menstrual cycle ceased 48 years of age.

DEXA examination revealed reduced bone density at the level of osteoporosis (T score - 3.6) and reduced bone at the level of the hip in terms of osteoporosis (T score - 2.6).

The patient immediately accepted therapy with teriparatide ampoules. She was receiving the recommended therapy, after two years we did a new DEXA examination which showed an improvement in bone density at the level of the spine, by 6%, so that the T score on the spine - 3.1, and on the hip improvement in bone density by 4%, so that now the bone density at the hip level is at the osteopenia level (T score -2.1).

The BS patient, 64 years old, lost 5 cm in body height and had four bone fractures in one year.

The menstrual cycle stopped at 46 years of age.

So far, she has not measured bone density, she denies other diseases.

DEXA examination revealed osteoporosis at the level of the spine (T score - 3.2%) and reduced bone density at the level of the hip in terms of osteopenia (T score - 1.5).

The patient was offered teriparatide therapy, which she received for two years and did not have any side effects of the drug, she stopped losing body height and there were no more bone fractures.

The control of DEXA examination showed an improvement in bone density at the level of the spine by 5.7%, so that the finding is still at the level of the spine and further reduced to the level of osteoporosis (T score - 2.7) and an improvement in bone density at the level of the hip for 10.7%, and now the T score on the hip is 0.2.

Most importantly, the patient moved much easier and her mood improved.

Teriparatide achieved the best success in patient DG!

All patients who were offered teriparatide therapy in our institution fully complied with the therapeutic procedure. After the procedure of taking the medicine, a control DEXA examination was performed.

All patients tolerated the drug very well and did not have any side effects.

The quality of life of all patients who were treated with teriparatide was improved, they performed all tasks more easily, they were in a much better mood and, most importantly, none of them had any more bone fractures.

So far, the patients are feeling well, have no problems and have not reported any new bone fractures.

Results of an observational study Effects of Teriparatide in patients with osteoporosis in clinical practice: 42 monthly results during and after treatment from the European Extended Observation Study Forsteo (EkFos) conducted on 1400 patients, mean age 70 years, 90% of whom were female . The study showed a 47% reduction in fractures, an improvement in quality of life, as well as a significantly reduced intensity of back pain.

Conclusion: Teriparatide therapy in all our patients gave an excellent effect primarily, because so far no new bone fractures have been recorded and their quality of life has significantly improved.

Literature:

1. Nicola Napoli et al, Effects of Teriparatide in Patients with Osteoporosis in Clinical Practice: 42 –Month Results During and After Discontinuation of Treatment From the European Extended Forsteo Observational Study (ExFOS), *Calcif Tissue int*, 103 (4), 359- 371, Oct, 2018.
2. Kendler L D, et al, Publishing online, November 9, 2017, Effects of teriparatide and risedronate on new fractures in post- menopausal Women with severe osteoporosis (VERO) a multicenter, double-blind, double-dummy, randomized controlled trial.