was hindered with PAM treatment. These data suggest that long-term BPs, whilst reducing bone turnover, may not interfere with normal endochondral fracture union in healthy individuals. Further work is planned with a longer interval of pre-dosing with Pamidronate as well as experiments in animal models of Osteogenesis Imperfecta.

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Bilateral avascular necrosis of the femoral head and teriparatide: Consequence or coincidence

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Introduction: Avascular necrosis of bone (AVN) is an uncommon focal bone disorder that occurs in both the developing and the adult skeleton. I report a case of spontaneous bilateral AVN of the femoral head in a woman that occurred within three months of the initiating treatment with the Teriparatide (TPTD), recombinant human PTH(1–34). Also, I report my clinical experience of a prospective survey of patients who received an 18 month course of TPTD.

Case report: A 64-year-old woman had a 5-year history of osteoporosis. She presented with a grade 3 wedge deformity at T6. At that time she was taking hormone therapy, Tibolone (2.5 mg/day). Bone mineral density (BMD) measured by dual-energy X-ray absorptiometry (DXA) gave T-scores at L1-4 of -2.4 and at hip of -1.5. Within a year, she was started on Risedronate (35 mg/week), calcium (1000 mg/day) and vitamin D (20 mcg/day). Two years later, T-score at spine was -1.8 and at hip was -1.4. A further 2 years later, following a routine surgical procedure, she developed severe back pain. Bone imaging studies (plain film, radionuclide scan, and magnetic resonance imaging [MRI]) identified vertebral fractures at T9 and L3. Risedronate was stopped; TPTD (20 mcg/day) was initiated with reduced dosage of calcium (500 mg/day) and vitamin D (10 mcg/day). Within 3 months she noted weakness on standing, pelvic pain and difficulty walking. She stopped TPTD. MRI noted bilateral AVN. Orthopaedic consultation recommends bilateral total hip replacement.

Clinical survey: In a prospective clinical survey of patients taking TPTD (20 mcg/day) for 18 months, BMD was measured at lumbar spine and femur, pre- and post-therapy. To date, 40 have completed a course. A change in BMD was deemed significant if it exceeded the least significant change: 0.027 g/cm^2 for lumbar spine; and 0.020 g/cm^2 for total hip. BMD increased substantially more at the spine (13.8±7.4%) than the femur (1.9±6.7%) with a weak correlation between percent change in BMD at spine and femur ($r=0.38$; $p<0.05$). BMD at the spine increased significantly in 38 and was unchanged in 2 patients; BMD at the femur increased in 19, was unchanged in 11, and declined in 10 patients.

Conclusion: In keeping with pivotal studies, BMD increased more at the spine than the femur. BMD declined significantly at the femur in 25% of patients on TPTD. One patient developed bilateral AVN contemporaneous with initiation of TPTD.

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The small molecule N-Methyl pyrrolidone tunes the natriuretic peptide hormone system into a pro osteogenic state

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Introduction: Medical devices derived from biomaterials of the 3rd generation are biocompatible, biodegradable and bioactive. Recently we developed and characterized a 3rd generation guided bone regeneration membrane and showed that the plasticizer N-methyl-pyrrolidone (NMP) is bioactive, since it acts synergistically with bone morphogenetic protein and enhances bone maturation and regeneration in several in vitro and in vivo models. In order to get a broader view on the bioactivity of NMP we performed micro array experiments which revealed that irrespective of BMP, NMP targets the transcription of several genes; two of those belonging to the natriuretic peptide hormone system.

Results: Micro array experiments performed with the multi potent mesenchymal stem cell like C2C12 cells revealed that 4 h exposure of theses cells to 5 mM of NMP halved the expression of natriuretic peptide receptor type 3 (npr3) and increase in the expression of the natriuretic peptide precursor type B (BNP) 1.5 fold. These results were confirmed by low density arrays and RT-pcr.

Discussion: The influence of the natriuretic peptide hormone system on bone growth is manifested in the human disease: Acromesomelic dysplasia Maroteaux type where mutations in the natriuretic peptide receptor 2 induce dwarfism. Over-expression and knock-out experiments in mice showed that also other elements of this system can affect the skeleton. The knock-down of npr-3 in mice, which serves as scavenger receptor, and the over-expression of natriuretic peptide B lead to gigantism. Our results show that the plasticizer NMP decreases npr-3 expression and increases BNP expression, mimicking the knock-out and over-expression of those genes in mice. Therefore, the direct effect of NMP on the transcription of 2 elements of the natriuretic peptide hormone system creates a pro osteogenic status which could at least partially account for the accelerated bone healing seen under the influence of NMP in vivo.

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