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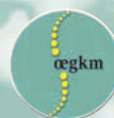
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News-Screen Rheumatologie

R. Lunzer

■ Efficacy and Safety of Strontium Ranelate in the Treatment of Knee Osteoarthritis: Results of a Double-Blind, Randomised Placebo-Controlled Trial

Reginster JY, et al. *Ann Rheum Dis* 2013; 72: 179–86.

Abstract

Background: Strontium ranelate is currently used for osteoporosis. The international, double-blind, randomised, placebo-controlled Strontium ranelate Efficacy in Knee Osteoarthritis trial evaluated its effect on radiological progression of knee osteoarthritis. **Methods:** Patients with knee osteoarthritis (Kellgren and Lawrence grade 2 or 3, and joint space width [JSW] 2.5–5mm) were randomly allocated to strontium ranelate 1 g/day (n = 558), 2 g/day (n = 566) or placebo (n = 559). The primary endpoint was radiographical change in JSW (medial tibiofemoral compartment) over 3 years versus placebo. Secondary endpoints included radiological progression, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score, and knee pain. The trial is registered (ISRCTN41323372). **Results:** The intention-to-treat population included 1371 patients. Treatment with strontium ranelate was associated with smaller degradations in JSW than placebo (1 g/day: -0.23 [SD 0.56] mm; 2 g/day: -0.27 [SD 0.63] mm; placebo: -0.37 [SD 0.59] mm); treatment-placebo differences were 0.14 (SE 0.04), 95 % CI 0.05 to 0.23, $p < 0.001$ for 1 g/day and 0.10 (SE 0.04), 95 % CI 0.02 to 0.19, $p = 0.018$ for 2 g/day. Fewer radiological progressors were observed with strontium ranelate ($p < 0.001$ and $p = 0.012$ for 1 and 2 g/day). There were greater reductions in total WOMAC score ($p = 0.045$), pain subscore ($p = 0.028$), physical function subscore ($p = 0.099$) and knee pain ($p = 0.065$) with strontium ranelate 2g/day. Strontium ranelate was well tolerated. **Conclusions:** Treatment with strontium ranelate 1 and 2 g/day is associated with a significant effect on structure in patients with knee osteoarthritis, and a beneficial effect on symptoms for strontium ranelate 2g/day.

Kommentar

Der Beitrag zeigt die Tendenz, dass dieses Osteoporose-Therapeutikum, das sowohl anabol als auch antiresorptiv wirkt und vor allem bei älteren Patienten gegeben wird, auch einen positiven Einfluss auf die schmerzhafteste Arthrose zeigt, welche in dieser Altersgruppe ja häufig vorliegt.

Nicht unerwähnt sollte aber auch das erhöhte Thromboserisiko unter Protelos® sein.

■ Impact of Age, Sex, Obesity, and Steroid Use on Quinolone-Associated Tendon Disorders

Wise BL, et al. *Am J Med* 2012; 125: 1228.e23–8.

Abstract

Background: Quinolone antibiotics are associated with increased risk of tendinopathy. Identifying at-risk individuals has important clinical implications. We examined whether age, sex, glucocorticoid use, obesity, diabetes, and renal failure/dialysis predispose individuals to the adverse effects of quinolones. **Methods:** Among 6.4 million patients in The Health Improvement Network (THIN) database, 28,907 cases of Achilles tendonitis and 7685 cases of tendon rupture were identified in a case-crossover study. For each participant, we ascertained whether there was a prescription of a quinolone and comparison antibiotic within 30 days before the diagnosis of tendon disorder (case period) and a prescription of the same medications within 30 days 1 year before disease diagnosis (control period). **Results:** Use of quinolones was strongly associated with an increased risk of Achilles tendonitis (odds ratio [OR], 4.3; 95 % confidence interval [CI], 3.2–5.7) and tendon rupture (OR, 2.0; 95 % CI, 1.2–3.3). No association was found between the use of other antibiotics and either outcome. The association with Achilles tendonitis was stronger among participants who were aged more than 60 years (OR, 8.3 vs 1.6), who were nonobese (OR, 7.7 vs 2.4), and who used oral glucocorticoids (OR, 9.1 vs 3.2). The association was nonsignificantly stronger in women (OR, 5.0 vs 3.6), diabetic persons (OR, 7.0 vs 4.1), and those in renal failure or receiving dialysis (OR, 20.0 vs 3.9). The effect for tendon rupture was stronger in women, with borderline significance in glucocorticoid users and nonobese persons. **Conclusion:** Quinolone-associated tendinopathy is more pronounced among elderly persons, nonobese persons, and individuals with concurrent use of glucocorticoids.

Kommentar

Falls bei einer entzündlich rheumatischen Erkrankung unter begleitender Steroidtherapie eine antibiotische Behandlung mit einem Chinolon geplant ist, dann sollte das erhöhte Risiko für Sehnenentzündungen beachtet werden. Warum diese Klasse von Antibiotika (und andere nicht) mit Tendinitis assoziiert ist, bleibt unklar, und der Mechanismus scheint, wie in der Medizin dann oft, „multifaktoriell“ zu sein.

(Anmerkung: Interessant ist hier, dass schlanke Personen eher zur Chinolon-assoziierten Tendinopathie neigen. Dicksein ist nicht immer von Nachteil!)

■ The Risk of Pulmonary Embolism and Deep Vein Thrombosis in Rheumatoid Arthritis: A UK Population-Based Out-patient Cohort Study

Choi HK, et al. *Ann Rheum Dis* 2012 [Epub ahead of print].

Abstract

Background: Recent hospital-based studies have suggested a sixfold increased risk of pulmonary embolism (PE) in rheumatoid arthritis (RA) in the year following admission. We evaluated the risk of PE and deep vein thrombosis (DVT) and associated time trend among RA patients (84.5 % without a history of hospitalisation during the past year) derived from the general population. **Methods:** We conducted a cohort study using an electronic medical records database representative of the UK general population, collected from 1986 to 2010. Primary definitions of the RA cohort (exposure) and PE/DVT outcomes required physician diagnoses followed by corresponding treatments. We estimated relative risks (RRs) of PE and DVT compared with a matched non-RA comparison cohort, adjusting for age, sex, smoking, body mass index, comorbidities and hospitalisations. **Results:** Among 9589 individuals with RA (69 % female, mean age of 58 years), 82 developed PE and 110 developed DVT (incidence rates, 1.5 and 2.1 per 1000 person-years). Compared with non-RA individuals (N = 95776), the age-, sex- and entry-time-matched RRs were 2.23 (95 % CI 1.75 to 2.86) for PE and 2.20 (CI 1.78 to 2.71) for DVT. Adjusting for other covariates, the corresponding RRs were 2.16 (CI 1.68 to 2.79) and 2.16 (CI 1.74 to 2.69). The time-specific RRs for PE were 3.27, 1.88 and 2.35 for follow-up times of < 1 year, 1–4.9 years, and ≥ 5 years, and corresponding RRs for DVT were 3.16, 1.82 and 2.32. **Conclusions:** This population-based study indicates an increased risk of PE and DVT in RA, supporting increased monitoring of venous-thromboembolic complications and risk factors in RA, regardless of hospitalisation.

Kommentar

Das kardiovaskuläre Risiko bei Patienten mit RA ist bekannt, aber auch das mehr als doppelt so hohe (relative) Risiko für Thrombosen und Lungenembolien ist erwähnenswert.

■ A Tight Control Treatment Strategy Aiming for Remission in Early Rheumatoid Arthritis Is More Effective than Usual Care Treatment in Daily Clinical Practice: A Study of Two Cohorts in the Dutch Rheumatoid Arthritis Monitoring Registry

Schipper LG, et al. *Ann Rheum Dis* 2012; 71: 845–50.

Abstract

There is strong evidence from clinical trials that a “treat to target” strategy is effective in reaching remission in rheu-

matoid arthritis (RA). However, the question is whether these results can be translated into daily clinical practice and clinical remission is a reachable target indeed. **Objective:** The study aims to investigate whether in early RA a treatment strategy aiming at Disease Activity Score (DAS) 28 < 2.6 is more effective than “usual care” treatment for reaching clinical remission after 1 year. **Methods:** Two early RA inception cohorts from two different regions including patients who fulfilled the American College of Rheumatology criteria for RA were compared. Patients in the tight-control cohort (n = 126) were treated according to a DAS28-driven step-up treatment strategy starting with methotrexate, addition of sulphasalazine (SSZ) and exchange of SSZ by anti-tumour necrosis factor in case of failure. Patients in the usual-care cohort (n = 126) were treated with methotrexate or SSZ, without DAS28-guided treatment decisions. The primary outcome was the percentage remission (DAS28 < 2.6) at 1 year. Time to first remission and change in DAS28 were secondary outcomes. **Results:** After 1 year, 55 % of tight-control patients had a DAS28 < 2.6 versus 30 % of usual care patients (OR 3.1, 95 % CI 1.8 to 5.2). The median time to first remission was 25 weeks for tight control and more than 52 weeks for usual care (p < 0.0001). The DAS28 decreased with –2.5 in tight control and –1.5 in usual care (p < 0.0001). **Conclusion:** In early RA, a tight control treatment strategy aiming for remission leads to more rapid DAS28 remission and higher percentages of remission after 1 year than does a usual care treatment.

Kommentar

Dass in der Medizin engmaschige Kontrollen und eine entsprechend rasche Therapieanpassung von Vorteil sind, steht außer Frage. Aber beeindruckend ist schon, dass in der engmaschigeren Gruppe knapp $\frac{2}{3}$ der Patienten eine Remission erreicht hatten und „nur“ $\frac{1}{3}$ der routinemäßig kontrollierten Patienten. Bemerkenswert ist auch, dass bereits 50 % der „Tight-control“-Gruppe nach 25 Wochen in Remission waren. Da beide Gruppe mit der gleichen Therapiestrategie behandelt wurden, kann also der Rheumatologe auch einen entscheidenden Beitrag zur Reduktion der entzündlichen Aktivität leisten.

■ A Systematic Review and Meta-Analysis Comparing Complications Following Total Joint Arthroplasty for Rheumatoid Arthritis Versus for Osteoarthritis

Ravi B, et al. *Arthritis Rheum* 2012; 64: 3839–49.

Abstract

Objective: Most of the evidence regarding complications following total hip arthroplasty (THA) and total knee arthroplasty (TKA) is based on studies of patients with osteoarthritis (OA), with little being known about outcomes in patients with rheumatoid arthritis (RA). The objective of the present study was to review the current evidence regarding rates of THA/TKA complications in RA versus OA. **Methods:** Data sources used were Medline, EMBase, Cinahl, Web of Science,

and reference lists of articles. We included reports published between 1990 and 2011 that described studies of primary total joint arthroplasty of the hip or knee and contained information on outcomes in ≥ 200 RA and OA joints. Outcomes of interest included revision, hip dislocation, infection, 90-day mortality, and venous thromboembolic events. Two reviewers independently assessed each study for quality and extracted data. Where appropriate, meta-analysis was performed; if this was not possible, the level of evidence was assessed qualitatively. **Results:** Forty studies were included in this review. The results indicated that patients with RA are at increased risk of dislocation following THA (adjusted odds ratio 2.16 [95 % confidence interval 1.52–3.07]). There was fair evidence to support the notion that risk of infection and risk of early revision following TKA are increased in RA versus OA. There was no evidence of any differences in rates of revision at later time points, 90-day mortality, or rates of venous thromboembolic events following THA or TKA in patients with RA versus OA. RA was explicitly defined in only 3 studies (7.5 %), and only 11 studies (27.5 %) included adjustment for covariates (e.g., age, sex, and comorbidity). **Conclusion:** The findings of this literature review and meta-analysis indicate that, compared to patients with OA, patients with RA are at higher risk of dislocation following THA and higher risk of infection following TKA.

Kommentar

Die derzeitige Evidenz zu Komplikationen einer Totalendoprothese des Hüft- oder Kniegelenks (Hüft-TEP oder Knie-TEP) beruht vor allem auf Patienten mit Arthrose. Zur Prognose bei Patienten mit rheumatoider Arthritis ist relativ wenig publiziert. Dieser Abstract (systematischer Review/Metaanalyse, Toronto) verglich die Komplikationen nach TEP bei RA- oder Arthrosepatienten (40 Studien zwischen 1990 und 2011, mindestens 200 Gelenke mit Hüft- oder Knie-TEP wegen RA oder Arthrose). Endpunkte: Häufigkeit von Dislokationen, Infektionen, Revisionen und thromboembolischen Ereignissen sowie die 90-Tage-Mortalität.

Ergebnis:

- Erhöhtes Dislokationsrisiko nach Hüft-TEP wegen RA; die adjustierte Odds Ratio gegenüber Patienten mit Arthrose betrug 2,2 (95-%-Konfidenzintervall: 1,5–3,1).
- Infektions- und frühes Revisionsrisiko nach Knie-TEP wegen RA ist höher als nach Knie-TEP wegen Arthrose.
- Kein sicherer Anhaltspunkt für unterschiedliche Revisionsraten zu späteren Zeitpunkten, unterschiedliche Thromboembolieraten und eine unterschiedliche 90-Tage-Mortalität nach Hüft- oder Knie-TEP wegen RA oder Arthrose.

Zusammenfassend: Patienten mit RA zeigen ein höheres Dislokationsrisiko nach Hüft-TEP und ein höheres Infektionsrisiko nach Knie-TEP.

■ Changes in Bone Mineral Density During Long-Term Treatment with Adalimumab in Patients with Rheumatoid Arthritis: A Cohort Study

Krieckaert CL, et al. *Rheumatology (Oxford)* 2013; 52: 547–53.

Abstract

Objective: To investigate the effect of long-term adalimumab treatment on BMD of the lumbar spine, total hip and hands in patients with RA. **Methods:** In 184 established RA patients treated with adalimumab for at least 1 year, BMD measurements of the total hip and lumbar spine were performed using dual-energy X-ray absorptiometry. Metacarpal cortex BMD was measured using digital X-ray radiogrammetry. **Results:** After 1 year of treatment, BMD of the hip and lumbar spine remained stable, while BMD of the hands decreased significantly by -1.41% ($P < 0.0001$). After a mean follow-up of 4.0 (S.D. 1.0) years, mean BMD change per year was -0.58% and 0.07% for the hip and lumbar spine, respectively (overall P-value of hip was < 0.0001 and spine was 0.67). Predictors for BMD loss of the hip were anti-CCP positivity, non-use of bisphosphonates at baseline and BMI. In European League Against Rheumatism (EULAR) non-responders at 52 weeks, BMD change of the hip and spine was -1.25% and 1.08% , respectively, for moderate responders -0.61% and -1.87% , respectively, and in EULAR good responders, BMD remained stable: -0.02% and 0.06% , respectively. BMD of the hands decreased in non-, moderate and good responders (-2.85% , -1.47% and -1.26% , respectively). **Conclusion:** In patients with severe, established RA, loss of BMD in the spine was arrested over 4 years of adalimumab treatment, whereas BMD of the hands and hip continued to decrease after 1 and 4 years, respectively. The changes in BMD are related to disease activity, underlining the importance of monitoring disease activity.

Kommentar

Wenn die entzündliche Aktivität der RA unter Kontrolle ist, wirkt sich dies auch deutlich positiv auf die nicht weiter fortschreitende Osteoporose aus. Insbesondere bei diesen Patienten, bei denen ein sehr gutes Ansprechen der Biologikatherapie gegeben ist, bleibt die BMD der Hüfte und LWS nahezu ident – im Verlauf von 4 Jahren.

Korrespondenzadresse:

OA Dr. Raimund Lunzer

Interne Abteilung

Krankenhaus der Barmherzigen Brüder Graz-Eggenberg

A-8020 Graz, Bergstraße 27

E-Mail: raimund.lunzer@begg.at

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