Zoledronic acid plus Prednisolone versus

Anglin RE, Samaan Z, Walter SD, et al. Vitamin D deficiency and depression in patients with knee OA. We specially thank the participants who made this study possible, and we gratefully acknowledge the role of Vitamin D Effect on Osteoarthritis Study staff and volunteers in collecting the data. Acknowledgements: These findings suggest that vitamin D supplementation and maintaining sufficient vitamin D levels over 24 months may have beneficial effects on depression in patients with knee OA.

REFERENCES:

Acknowledgements: We specially thank the participants who made this study possible, and we gratefully acknowledge the role of Vitamin D Effect on Osteoarthritis Study staff and volunteers in collecting the data.

Disclosure of Interest: None declared

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Zoledronic acid Plus Prednisolone versus Zoledronic acid Alone or Placebo in the Treatment of Knee Osteoarthritis: A Randomised Trial

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Background: Disease-modifying therapeutic options are needed for patients with osteoarthritis (OA). Zoledronic acid (ZA) is a potent option as it reduced both knee pain and knee bone marrow lesion (BML) size over 6 months in patients with knee OA. However, ZA infusions are often accompanied by a suite of side effects within 3 days of infusion (acute phase reactions (APRs)), which include flu-like symptoms. These may be caused by upregulation of pro-inflammatory cytokines. A preliminary study (n=20) suggested that a combination of ZA and prednisolone (VOLT01) was superior to ZA alone in reducing APR and knee pain in knee OA patients. A larger study was needed to confirm these findings and examine the new combination’s effect on OA outcomes.

Objectives: To compare the effect of one-off infusion of ZA, VOLT01 and placebo on APRs, knee BML size and knee pain symptoms over 6 months in patients with knee OA patients with significant knee pain and BMLs.

Methods: Knee OA patients ≥50 years with significant knee pain (defined as a 100 mm Visual Analogue Scale (VAS) >40 mm) and knee BMLs visualised on proton density weighted MRI were randomised to receive one infusion of ZA (5 mg in 100 ml saline), VOLT01 (5 mg ZA in 100 ml saline plus a 10 mg prednisolone bolus) or placebo (100 ml saline). Co-primary hypotheses were that VOLT01 would significantly reduce APRs compared to ZA, and that VOLT01 would be non-inferior to ZA in reducing BML size over 6 months. Secondary hypothesis was that VOLT01 would be non-inferior to ZA in improving knee pain and dysfunction (assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and VAS) over 6 months. Mixed effect models were performed for data analyses. Analyses for change in knee pain and function scores were adjusted for baseline imbalanced values (baseline pain and utility scores, and pain medications). Non-inferiority margins were defined as 140 mm² for change in knee BML size and 8 mm for change in knee pain and function scores (WOMAC pain and function scores were averaged to a 100 mm VAS).

Results: 117 knee OA patients (63 females, mean ±standard deviation (SD) age 62.2±6.1 years) were enrolled. At baseline, mean ±SD knee pain VAS score was 50.1±18.9 mm and median BML size 370 mm². APRs were more frequent in the two active treatment groups (ZA: 87%; VOLT01: 90%) than the placebo group (55%) (both p<0.01). Compared to placebo, neither ZA nor VOLT01 significantly reduced BML size (ZA mean difference [95% CI] –21.6 [-103.0 to +59.9], VOLT01 –62.0 [-142.5 to +18.4]) or knee pain scores (WOMAC pain: ZA 2.6 [8.5 to +13.8], VOLT01 –8.1 [18.8 to +2.6]; VAS pain: ZA 5.4 [6.4 to +17.1], VOLT01 –7.7 [-19.0 to +8.6]) over 6 months, but WOMAC knee function improved significantly (–9.9 [-18.2 to –1.6]; p=0.02) in VOLT01-treated group. VOLT01 was non-inferior to ZA in reducing knee BML size and superior to ZA in reducing knee pain and function scores (figure 1).

Conclusions: Combining prednisolone with ZA does not appear useful for reducing APRs, though there may be a small benefit over ZA alone for knee symptoms. Neither showed evidence of disease modification by changing BML size.

Disclosure of Interest: None declared


Central Sensitisation in Hand Osteoarthritis and Associations with Radiographic Severity, Synovitis on Ultrasound and Symptom Duration

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Background: Patients with painful hand osteoarthritis (HOA) have enhanced central pain sensitisation (CS). Structural and inflammatory joint tissue damage over time might lead to CS. However, increased pain sensitisation can also represent an ‘a priori trait’ of a subgroup of patients.

Objectives: This study explored whether structural pathology, inflammation and symptom duration of HOA are associated with enhanced CS.

Methods: Through a cross-sectional study we included 300 subjects (89% women, median age 61 years (IQR 57, 67), mean body mass index (BMI) 26.5 (SD 4.9) kg/m²) with clinical and/or ultrasound verified HOA. All were examined with ultrasound (grey scale (GS) synovitis and power Doppler activity (PD)) and conventional radiographs of both hands. GS-synovitis was scored on a semi-quantitative 0–3 scale and PD to be present or not. The bilateral interphalangeal, metacarpophalangeal, first carpometacarpal and scaphotrapeziotrapezoidal joints were scored for global HOA (using Kellgren and Lawrence score (KL) 0–4). Erosive HOA in the interphalangeal joints was defined with the Verbruggen-Veys anatomical phase score (VV). In addition, participants answered a question about the year of onset of their hand symptoms.

CS was measured with temporal summation (TS), the increase in perceived pain to repetitive noxious stimuli, using a mechanical probe. First, probes with increasing weight (32, 64, 128, 256 or 512mN) were applied at the wrist until the patients reported pain of at least 4/10. The selected probe was applied to the wrist times at
1 Hz. Subjects reported pain on first, fifth and tenth touch. Enhanced TS is a marker of central sensitisation and we defined the magnitude of TS as TSΔ, highest pain value of fifth or tenth touch minus the first pain value.

We analysed whether sum scores of KL (0–128), GS (0–90), PD (0–30), number of erosive interphalangeal joints (0–20) and symptom duration were associated with TSΔ using separate models of linear regression with adjustments for age, sex and BMI.

**Results:** Median radiographic KL sum score was 28 (IQR 15, 44) and ultrasound sum scores (GS, PD) were 3 (IQR 1, 7) and 0 (IQR 0, 1), respectively. Median number of erosive joints was 0 (IQR 0, 1) and symptom duration was 6 (IQR 3, 13) years. Median TSΔ among the participants was 1 (IQR 0, 2).

Neither KL sum score (p=0.18), GS-synovitis sum score (p=0.18), PD sum score (p=0.86), number of joints with erosive HOA (p=0.078) nor symptom duration (p=0.21) were associated with TSΔ (table 1).

Table 1 Associations between OA features and temporal summation *

<table>
<thead>
<tr>
<th>Feature</th>
<th>Unstandardized beta (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom duration in years</td>
<td>0.015 (-0.01, 0.04)</td>
<td>0.21</td>
</tr>
<tr>
<td>Kellgren-Lawrence sum score</td>
<td>0.007 (-0.00, 0.02)</td>
<td>0.18</td>
</tr>
<tr>
<td>Grey scale synovitis sum score</td>
<td>-0.001 (-0.03, 0.00)</td>
<td>0.96</td>
</tr>
<tr>
<td>Power Doppler sum score</td>
<td>0.001 (-0.05, 0.06)</td>
<td>0.86</td>
</tr>
<tr>
<td>Number of erosive joints</td>
<td>0.070 (-0.01, 0.15)</td>
<td>0.08</td>
</tr>
</tbody>
</table>

*Adjusted for sex, age and BMI.

**Conclusions:** We found no relationship between the severity of HOA pathology and TSΔ. This is in line with the hypothesis that factors other than OA disease severity itself contribute to CS associated pain, and that CS may be a trait in some individuals. However, it does not exclude other aspects of HOA as an initiator of CS in a subgroup of patients.

**Disclosure of Interest:** None declared

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