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Research

X-ref ***For other Roundups in this issue that cross-reference with Research see: Hip & Pelvis Roundup 1; Spine Roundup 6; Trauma Roundups 3, 7 & 8.***

Vancomycin toxic to chondrocytes

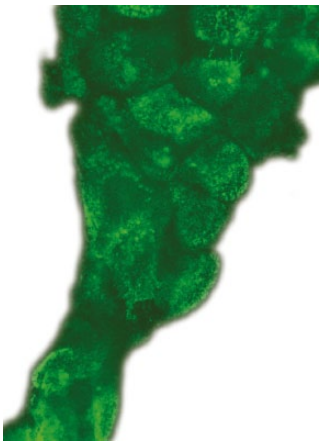
There is a current trend of local delivery of topical vancomycin into at-risk wounds, or for treatment of localized musculoskeletal infection. Although there is emerging evidence surrounding the benefits of topical vancomycin from a wound infection perspective, here at *360*, we have been somewhat concerned about the possibility of chondral toxicity when topical vancomycin is applied directly to the joint surface. The authors of this study from **Charleston, South Carolina (USA)** attempted to pinpoint the safe concentrations of vancomycin in a porcine model.[1] The authors harvested osteochondral samples from juvenile porcine knees, exposed them to vancomycin concentrations of 2 mg/ml, 5 mg/ml, and 10 mg/ml, and compared the viability of the harvest chondrocytes with those of saline. The authors undertook a predominantly histological study and graded the chondrocyte viability using the Mankin criteria and a live/dead stain to establish the viability of the chondrocytes with each of the solutions. This was then supplemented using calcein acetoxymethyl ester stain and confocal laser scanning microscopy. There were no differences between the control and the 2 mg/ml group in terms of chondrocyte viability. However, there was a significantly higher rate of non-viable chondrocytes in the 5 mg/ml and 10 mg/ml groups. There is some evidence here that vancomycin should be treated with a certain amount of caution and there is clearly the potential, at least, for chondrocyte death. It is far from clear yet if the benefits outweigh the risks or vice versa. Infection is also chondrotoxic, and post-septic arthritis degenerative arthrosis can be challenging to treat. Although the arguments are currently being weighed up, a longitudinal study – or better still, a properly powered trial – is what is really needed here.

Aspirin as good as rivaroxaban **X-ref**

In what can perhaps be considered a landmark paper, the *New England Journal of Medicine* yet again publishes game-changing research in orthopaedic surgery. This large clinical randomized controlled trial of 3424 patients (1804 undergoing total hip arthroplasty (THA) and 1620 undergoing total knee arthroplasty (TKA)) originates from across **Canada** and tests the efficacy of rivaroxaban and aspirin with the primary endpoint of symptomatic venous thromboembolism (SVTE).[2] All patients received oral rivaroxaban (10 mg) once daily until postoperative day 5, and were then randomly assigned to either continue rivaroxaban or switch to aspirin (81 mg daily) for an additional nine days after TKA or for 30 days after THA. Follow-up was to 90 days and the trial was constructed as a double-blinded randomized controlled trial. Overall, there was a 0.64% event rate in the aspirin group and 0.70% in the rivaroxaban group. The trial was significant for non-inferiority but not significant for superiority. In terms of secondary outcomes, there was no difference in the major bleeding events (0.47% for aspirin *vs* 0.29% for rivaroxaban). Similarly, there were no significant differences in the clinically important bleeding events in the aspirin and rivaroxaban groups (1.29% for aspirin *vs* 0.99% for rivaroxaban). This trial does not give any insight into inpatient thromboprophylaxis; nevertheless, it is fairly compelling with regard to outpatient extended thromboprophylaxis. With no differences in the primary endpoint or subsequent secondary outcome measures in this large, well-conducted, randomized controlled trial, we can surmise that aspirin is equally as effective as rivaroxaban.

Evidence synthesis: a better way?

As trials are becoming more and more commonplace, so is evidence synthesis, offering the opportunity to combine trials and increase the power of the studies such that more reliable conclusions can be reached. The major drawback of this approach is that the trials have to be published, and pairwise meta-analysis has to be undertaken. This is a lengthy process and only allows consideration of simple questions. There are other approaches, with the network or Bayesian meta-analysis gaining popularity, that allow for more refined analysis using a network method to test several interventions against the 'central node'. Although this offers a more discriminating approach and multiple questions can be answered, these methods still lag behind the current trial data. A collaborative led by methodologists in **Bern (Switzerland)** have proposed a 'living' network meta-analysis approach, where the continuous updating of networks of prospectively planned randomized controlled trials (RCTs) is used.[3] The authors provide strong evidence against the null hypothesis in comparative effectiveness of medical interventions earlier than the updating of conventional, pairwise meta-analysis. The authors set out to establish the time period that meta-analyses reporting outcomes of medical interventions took to become positive – both as a network approach and a pairwise approach. They included all meta-analysis reporting the outcomes of at least 20 RCTs. The authors identified 49 comparisons reported in 44 networks. The comparisons were informed by both direct and indirect evidence (n=29), indirect evidence alone (n=13), or direct evidence alone (n=7). For seven comparisons, network and pairwise meta-analysis provided strong evidence; however,



for an additional ten comparisons, only network meta-analysis provided strong evidence against the null hypothesis. The authors also established some timelines, with a median time to strong evidence against the null hypothesis of 19 years with living network meta-analysis *versus* 23 years with living pairwise meta-analysis. It seems that the best approach here is that of a living network, where studies are added as they are reported, allowing both direct and indirect comparisons, and potentially reducing the time to answer by four years.

What gives a positive Waddell sign? X-ref

■ The Waddell signs are a widely popularized series of physical signs that relate specifically to inorganic pathology. The signs themselves have taken on a near mystical quality, such is the widespread acceptance that this group of tests gives a high likelihood, if positive, that the patient's lumbar spine pain is inorganic in nature. The authors of this paper from **Portland, Oregon (USA)** ask whether there is any predisposition to positive Waddell's signs associated with patient demographics, or with perception of their quality of life.[4] The authors report a prospective cross-sectional study of 479 adult patients, all with a diagnosis of back pain. The participants completed a 12-Item Short-Form Health Survey (SF-12) score, Oswestry Disability Index (ODI), and spinal examination to elicit Waddell signs. Functional outcome scores were significantly worse in those with a single Waddell sign; however, the perception of disability (not the disability itself) increased in patients with three or more Waddell signs. The authors conclude that positive Waddell signs are a potential indicator of central sensitization, and also indicate a likelihood of having functional limitations and an impaired quality of life, particularly in young women.

Rainfall and joint or back pain: retrospective claims analysis X-ref

■ Patients often relate symptoms to the weather, complaining of greater pain in the cold and of stiffness in the winter. These comments are so frequent that the majority of musculoskeletal physicians accept this as fact. The difficulty is that there is little support in the literature for such associations. It is known that the threshold value of pain in the peripheral nerve changes with atmospheric pressure and temperature, and this is the suggested mechanism for this 'bad-weather pain'. When it rains, in general, pressure and temperature will be lower. The authors of this study from **Champaign, Illinois (USA)** used the Medicare insurance claims data and linked these to rainfall data from weather stations in the United States, allowing them to establish what the weather was like when 1 552 842 adults aged ⩾ 65 years attended a total of 11 673 392 outpatient consultations with their doctor.[5] They then went on to determine what proportion of the outpatient visits were for joint- or back pain-related conditions (which they defined for coding purposes as rheumatoid arthritis, OA, spondylosis, intervertebral disc disorders, and other non-traumatic joint disorders). The primary outcome of this study was the proportion of consultations that concerned these diagnoses. The authors did not establish the pain scores, so no information is known about the patients' presenting condition, simply what they sought help with. Overall, just under one in five outpatient visits occurred on rainy days (n = 2 095 761; 18.0%). There was a significant difference in the proportions of patients seeking help on rainy days and on non-rainy days (6.23% *vs* 6.42%; adjusted, 6.35% *vs* 6.39%). However, it appears that not only are the differences small, but that they are also in the unexpected direction, with patients needing less input for their musculoskeletal woes on rainy days. The authors also looked at the number of rainy days that week, in order to ensure that the patients did not stay at home when it rained due to their musculoskeletal pain. Again, they drew a blank. It appears that, for the present time, the largest study on the topic suggests that there is no link between consultation and weather for musculoskeletal pain. However, it is important not to misunderstand the result of this paper, in that only the cause of the consultation was established, and not the degree of pain.

Digital photography accurate for measuring range of motion of the shoulder and elbow?

■ This study from **Houston, Texas (USA)** investigated the potential and feasibility of digital photography to measure the range of motion within the shoulder and elbow.[6] Given the importance of examination on musculoskeletal pathologies, it is an interesting concept to be able to receive accurate measures of range of motion via telemedicine. The authors here did more than just investigate the use of digital cameras – they also evaluated infrared motion capture visual estimation, goniometry, and digital photography. For reasons that escape us, instead of using real patients, they undertook their investigation in cadavers. The authors measured shoulder motion (flexion/abduction/internal rotation/external rotation) and elbow motion (flexion/extension) using ten fresh frozen cadavers. The measurements were repeated by three physiotherapists and three orthopaedic surgeons. In short, the authors were unable to establish a clinically significant difference between the three motion-capture measures. There were, however, statistically significant differences with higher precision for digital photography and goniometry than for visual estimation. It certainly seems that the simple method of digital photography may be of use for telemedicine and, specifically, in follow-up that is not face-to-face, or in screening patients for referral with conditions such as frozen shoulder.

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