ROUNDUP360

Research

For other Roundups in this issue that cross-reference with Research see: Foot & Ankle Roundup 3; and Trauma Roundup 6.

Passive smoking and bone substitutes

Bone defects, both acute and chronic, are increasingly commonly treated with grafting of bone substitutes (often ceramics) rather than using auto- or allograft. The effects of smoking on bone healing are well described, but little is currently known about the effects of passive smoking on bone graft substitute ingrowth. Researchers in **Sao Paulo (Brazil)** used a well described Wistar rat model of bone defects to establish the effects of passive smoking on bone graft substitute ingrowth. The study team used a critical size bone defect model in the distal femoral epiphysis of 20 healthy Wistar rats. In all cases the bone defect was treated with hydroxyapatite grafting. The rats were divided into smoking and non-smoking cohorts and, in addition, further randomised to the use of laser bone stimulation or control. The 'smoking' rats were submitted to an eight-month period of passive smoking to allow for the longer-term effects of smoking to establish themselves upon bone metabolism. Following surgery, the rats were killed at eight weeks and histological analysis undertaken to visualise the graft integration in all four groups. In the non-smoking rats, both with and without laser stimulation, there was good histological evidence of bony ingrowth into the porous ceramic implant. This was not seen in the smoking group either with or without laser stimulation. In all cases the ceramic implant was surrounded by fibrous tissue with little evidence of osseo-integration.[1] While not unexpected that passive smoking reduces the ability of ceramic bone substitutes to osseo-integrate, this finding does have some clinical significance, and in light of this in future we will certainly be using autograft when using bone void defect fillers in smokers.

Platelet-rich plasma and osteogenesis

Study of the osteogenic effects of biologic agents is fraught with difficulty. When studying a particular endogenous factor, knockout mice provide a convenient model and healing times can be easily compared with a simple standardised fracture model between knockout and normal groups. However, the same cannot be achieved for many biologic agents such as platelet-rich plasma (PRP) where a knockout model will never be appropriate. Researchers in **San Sebastián (Spain)** used an excellent model of distraction osteogenesis which is both controlled and reproducible to study the effects of PRP in an ovine femur fracture model. The study team used 20 sheep aged four months and produced a standardised distraction osteogenesis model using a distal femoral cortical osteotomy and subsequent controlled distraction osteogenesis. The research team randomly assigned ten sheep to the intervention and control groups. The intervention group received injection of PRP at days 0, 10 and 20. All sheep were killed at day 40 and the femora evaluated using CT and histology to objectively and subjectively assess callus and bone quality and quantity in the two groups. Histological evaluation included assessment for presence of osteoblasts, osteoclasts, vascular lumen, trabeculations and the quantity of cartilage and fibrous tissue present. Despite this thorough evaluation in an excellent model of bone regeneration, the investigators were unable to establish any differences whatsoever in bone or callus quantity and quality between the two groups. The only measurable difference was an increased diaphyseal width in the PRP group, but no changes were noted at the site of the regeneration.[2] There are, of course, two possible explanations. With such a thorough evaluation it seems unlikely that PRP has any positive osteogenic effects, however, we must always acknowledge that the model itself may not have been suitable to measure the therapeutic effects of the intervention. This seems a much less likely explanation in this case to us.

Plantar fasciitis and platelet-rich plasma: a match made in heaven?

As far as platelet-rich plasma (PRP) is concerned, it appears nowhere is sacred, as researchers in **Milan (Italy)** have cranked up their centrifuges and set about assessing the potential efficacy of PRP in the treatment of chronic plantar fasciitis. A small pilot study is reported of 14 consecutive cases of plantar fasciitis treated with three injections of PRP with follow-up over a 12-month period. Patients were assessed with a VAS score for pain and the Roles and Maudsley score. By the end of the follow-up period the research team had established a statistically significant drop in the VAS score (from 7.1 to 1.9) in favour of the treatment group, although this dramatic improvement wasn't mimicked in the Roles and Maudsley scale, where only two thirds of patients reported excellent results. The research team concluded that they had established the safety and efficacy of what amounts to an experimental treatment in their uncontrolled case series.[3]

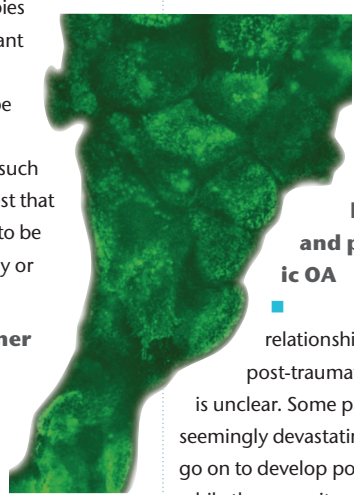
MRSA decolonisation decreases infection rates

Operative intervention in patients colonised with MRSA is always a relatively high risk strategy. A quick unscientific straw poll round 360 HQ found that we all prefer (when possible) a comprehensive programme of decolonisation and negative post-decolonisation swabs for MRSA infections, but rarely insist on the same deconoinisation regime, for staphylococcal colonisation. In a slightly more scientific manner, researchers in **Iowa (USA)** conducted a comprehensive meta-analysis and review of the evidence for (and against) bundling nasal decolonisation and glycopeptide prophylaxis in both orthopaedic and cardiac surgery. The review included a thorough search of all widely recognised indexing services including

contacting the original study authors for additional information when required. Gold standard Cochrane-style methodology was applied, with all randomised controlled and quasi-randomised controlled trails included in the review, and two independent reviewers involved in assessment for risk of bias, study quality and data extraction. Analysis was conducted using a random effects model, and corrections were made for the homogeneity of the results. There were 39 studies included and the pooled results of 17 studies showed that nasal decolonisation had a significantly protective effect against surgical site infections (relative risk 0.39) when all patients and just carriers underwent decolonisation (relative risk 0.36). The meta-analysis included 15 studies reporting data concerning glycopeptide prophylaxis. This was found to be significantly protective against MRSA infections (relative risk 0.40), however, this was a non-significant risk factor for the development of MSSA infection (1.47). Seven studies included enough data to assess the bundle of decolonisation and glycopeptide prophylaxis for patients colonised with MRSA with meta-analysis, yielding a protective effect (relative risk 0.41).[4] This paper is conclusive to our minds: decolonisation is effective, as is glycopeptide prophylaxis. Individual surgeons will have to make a clinical decision in light of the slightly increased risk of MSSA infection with glycopeptide prophylaxis. In the MRSA patients we feel the message is clear: a bundled approach can reduce infection rates to about one third of the expected level.

Gums, bisphosphonates and orthopaedics

■ With an ever-increasing population taking bisphosphonate therapy, a wider and wider range of indications and a broadening range of suitable agents to treat patients with conditions as diverse as osteoporosis, hypercalcaemia, malignancy and myeloma, bisphosphonate-associated complications (including fractures, osteonecrosis and intolerance) will become more commonplace. A more in-depth understanding of the risks of such complications and the differences between agents in producing these complications is required. Researchers in **Kiel (Germany)** set out to investigate the effects of three different bisphosphonates (zoledronic acid, pamidronate and alendronate) on a model of osteoblastic cells, gingival fibroblasts and osteogenic sarcoma cells. The researchers cultured gingival fibroblasts, osteoblasts and sarcoma cells in various concentrations of each bisphosphonate, then both collagen and cell proliferation were measured. All of the tested bisphosphonates were associated with decreased collagen production and lowered cell proliferation of cultured cells. However, all concentrations of zoledronic acid had the largest inhibitory effect.[5] With a wider range of bisphosphonate therapies available, it is important that the side effect profiles continue to be assessed clinically, as basic science studies such as this seem to suggest that they are not all likely to be equal in either efficacy or side effect profiles.



PRAISE and partner violence

■ The largest study into non-accidental injury and intimate partner violence (IPV) has reported this month to the Lancet. PRAISE (PRevalence of Abuse and Intimate partner violence Surgical Evaluation) is the largest study to date aiming to evaluate the incidence and lifetime prevalence of IPV. The team of 80 investigators sampled a contiguous cohort of 2945 female participants presenting to 12 fracture clinics in Canada, USA, Denmark and India, using direct questions concerning all types of IPV (physical, emotional and sexual), and two previously validated questionnaires: the Women Abuse Screening Tool (WAST) and Partner Violence Screen (PVS). The study team were able to obtain responses from a whopping 85% of their sample size (n = 2344), of whom a very worrying one in six women disclosed IPV within the past year and one in three in their lifetime. While only a very small minority of patients had actually attended the fracture clinic as a direct result of IPV (1.7%, n = 49), of the 49 women who attended as a direct consequence of IPV, only seven had ever been asked about IPV in a healthcare setting.[6] The PRAISE researchers were able to identify risk factors of short-term relationships (OR 0.584), previous physical abuse and finally, North American origin, as significant risk factors for IPV. This is an extremely valuable study highlighting an increased risk that patients who present in an orthopaedic trauma department may be victims of IPV. This is something we should all be aware of.

Scuffed but not broken: blunt impact and post-traumatic OA

■ The precise relationship between post-traumatic OA and injury is unclear. Some patients with seemingly devastating injuries do not go on to develop post- traumatic OA, while the opposite can also be true. An area in which little research exists is that of cartilage impact without fracture. A research team in **Munich (Germany)**, reasoning that loss of cartilage viability and post-injury inflammatory state have been implicated as contributing factors to post-traumatic OA, set about establishing the chondrocyte response as distinct from the fracture response through application of a highly calibrated surface compressive strain model. The research team developed a model that allowed them to apply a blunt impact at precisely 70%, 80% or 90% surface-to-surface compressive strain and were able to induce, or not, an articular fracture in a cartilage explant model – a truly cunning experimental design. Outcomes were assessed following the mechanical loading, through measuring the production of a number of mediators (dsDNA, NF-κB and TLRs). The research team established that an impact at 70% strain resulted in a combination of apoptosis and necrosis in the cartilage, whereas impacts above 80% strain caused necrosis. At distant sites, chondrocyte viability was not affected.[7] This subtle but clear difference in chondrocyte fate following injury based on mechanical injury factors clearly establishes a potentially different pattern of inflammatory response. We would be very surprised if a number of papers don't emerge examining this interesting phenomenon more closely.

IDEAL research and implants

■ In the light of a number of recent 'scandals' concerning implant failures (hip resurfacing and breast implants), the BMJ has run a series of articles highlighting the use of the IDEAL principles to produce high quality research. The IDEAL collaboration is the result of a series of conferences between surgeons and methodologists in **Oxford (UK)**. Initially established to examine why high quality trials in surgery were difficult to conduct, IDEAL went on to study what could be done to address this. The working parties identified important differences in how research in surgery differs from that in medicine or pharmacology, and established a framework by which all 'interventional therapies' could be studied (this not only includes surgery, but also technical procedures such as cardiac catheterisation and physiotherapy, for example). The IDEAL framework was born and highlights a stepwise method by which research can be conducted (idea, development, exploration, assessment, and long-term study) and provides guidance for funders, editors and professional societies as to how the research environment can be improved. The three articles discuss each part of the ideal

framework in detail and highlight how it can be applied to each stage of research. Without these early 'case series' and 'surgical innovations' we will never develop new treatments, and here at 360 we are delighted to embrace the 'IDEAL' framework wholeheartedly.[8-10]

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