ROUNDUP360

Research

x-ref *For other roundups in this issue that cross-reference with Research see: Knee roundup 5; Foot & Ankle roundup 3; Shoulder & Elbow roundup 3; Trauma roundup 2; and Children's orthopaedics roundup 9.*

Intraoperative irrigation a balance of toxicities x-ref

There is no doubt that one of the most catastrophic complications in any kind of implant surgery is infection. Despite ongoing attempts to reduce infection rates with better surgical techniques and newer technologies, there remains a small but significant infection rate in all branches of orthopaedic and trauma surgery. There has been quite a focus in recent years on the potential for intraoperative antiseptic irrigation to reduce infection rates in both the arthroplasty and trauma settings. However conflicting research exists, with some suggesting a cytotoxic effect on cells (particularly chondrocytes), such that this practice is dangerous with the counter argument that reduced infection rates cannot be ignored. Researchers in **Amsterdam (The Netherlands)** took a fresh perspective on this argument and designed a study with the aim of establishing the optimal antiseptic solution (and concentration) to maximise bactericidal effects whilst minimising cytotoxic effects to human tissues. They designed a basic science study in which cultures of human cell lines and two bacteria (Staphylococcus aureus and S. epidermidis) were exposed to a variety of antiseptics in a variety of concentrations.[1] They tested the effects of polyhexanide, hydrogen peroxide, octenidine dihydrochloride, povidone-iodine, and chlorhexidine digluconate at different concentrations all for a standardised two minutes. The effect of the antiseptic was assessed through the quantitative suspension method and cytotoxic effect on human fibroblasts and mesenchymal cells measured through changes in metabolic activity (WST-1 metabolic activity assay). Unsurprisingly all of the antiseptics aside from polyhexanide were bactericidal at commercially available concentrations. In addition when diluted, only povidone-iodine was bactericidal whilst not completely cytotoxic. The results of this nice experiment suggest that Povidone-iodine diluted to 1.3 g/L is likely the ideal concentration for intraoperative irrigation.

Ibandronate effective in bone marrow oedema x-ref

Bone marrow oedema is not a difficult radiological diagnosis to make, the characteristic high signal on a T2 MRI makes that easy. What is far from clear is if there any effective treatment options. The appearance of 'bone bruise' or bone marrow oedema is seldom accompanied by any more effective treatment advice than rest and analgesics. Researchers in **Hamburg (Munich)** have investigated the potential efficacy of intravenous ibandronate in alleviating the symptoms of bone marrow oedema and stress fractures. They report a series of 25 high performance athletes (60% European soccer players and 40% international level athletes). All of the patients had MRI proven bone marrow oedema and received a combination of high dose vitamin D and intravenous ibandronate therapy. As is often the case with diagnoses of bone marrow contusion, there was a considerable delay of over 3 months between onset of symptoms and diagnoses. Pain scores were reduced and improved mobility was reported within two weeks of ibandronate therapy in over half the treatment cohort (n = 16/25 64%) and time from first treatment until return to competition was on average three months.[2] It is difficult to know what the therapeutic effect of this case series is – with no comparator group the only conclusion that can really be drawn is what outcomes can be expected with this therapy, not how it compares to the natural history. This said, it is an interesting paper – ibandronate slows bone turnover and reduces the activity of osteoclasts if it does have an effect on bone marrow oedema this could be the start of some interesting basic science studies into the evolution of bone marrow oedema and the pathophysiology.

Risk stratification in damage control surgery x-ref

There has been much in both the research literature and general trauma literature concerning the general physiological response to trauma and in particular the management of the badly injured patient without provoking the systemic inflammatory response syndrome (SIRS). Investigators chiefly in Europe have investigated a range of factors from genetic propensity through to serum IFN-γ levels. The transfer of pre-clinical knowledge to updated management strategies happened very rapidly and suddenly most patients were managed with so-called damage control surgery. But is this really the best option for every patient? We know the propensity to develop SIRS and the effectiveness of the compensatory anti-inflammatory response syndrome (CARS) response is different from patient to patient and very much dependent on the injury as well as the patients' make up. Researchers in **Cologne (Germany)** have utilised the German trauma registry in an attempt to validate their 'risk-adapted' approach where those at high risk of SIRS are treated with damage control and the others are not. [3] They undertook an analysis of the results of 42,248 patients entered onto the German trauma registry and identified bilateral femoral fractures as the signature (index) injury. Patients with polytrauma and bilateral femoral shaft fractures were risk stratified according to their management. The study population consisted of 379 patients who had been managed in one of four ways (no operation 8.4%, bilateral temporary external fixation 50.9%, early total care bilaterally 25.1% and a mixed approach. Despite the range of treatment options, there were no significant differences in mortality rates between the different groups when adjustment for injury severity was taken into account, although the incidence of multiple

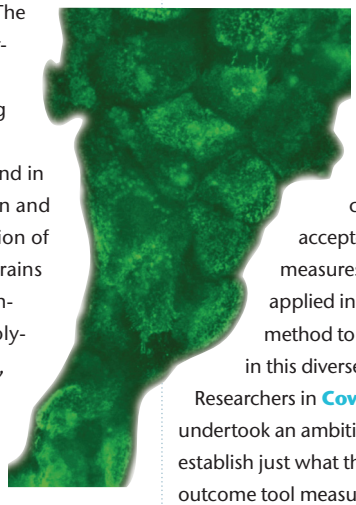
organ failure was higher in the damage control group.

Osteoblast like cells potentially safe

Cellular therapies are all the rage across the whole of the orthopaedic spectrum from the laboratory desk to the operating theatres and beyond. It seems at times like no stone is left unturned in the search for a cell line, protein molecule or scaffold that might yield scar free musculoskeletal healing. Bone regeneration appears to be next in the sights of the cellular biologists, with researchers in **Nagoya (Japan)** publishing a safety study this month in Bone & Joint Research which examines the *in vivo* biodistribution of locally and systemically transplanted osteoblasts. The research team harvested osteoblast-like cells generated from bone marrow derived mononuclear cells harvested from Sprague-Dawley rats. The harvested cells were cultured and directed towards an osteoblast-like differentiation. The cultured cell lines were transplanted in two ways both locally with a collagen scaffold and systemically as an intravenous infusion into rats with a critical bone defect model. Outcomes were assessed with flow cytometry and histology for cellular tracking. The locally transplanted donor cells were seen to stay in the vicinity of the transplant and not migrate to neighbouring organs, whilst those administered a systemic infusion were seen to clear the transplanted cells within three days and there were no adverse effects of the transplanted cells on any end organ.[4] This early pre-clinical study demonstrates key biodistribution data that opens the way for further animal studies on monoclonal osteoblasts as a potential therapy in bone healing. The clinical application however may need a little more proof. This study does however represent an important message regarding biological distribution.

Better wear and antibacterial? x-ref

One of the lesser sung innovations in total joint replacement recently is the advent of the vitamin E infused polyethylene. Whilst not as exciting as the newer ceramic articulations or indeed as controversial as metal-on-metal, vitamin E infused polyethylene offers a tantalising compromise between improved wear characteristics and a reliable safety profile. There may also be another potential benefit. Researchers in **Turin (Italy)** assessed the effects that vitamin E infusion may have on bacterial adhesion (a key part of biofilm formation). The research team undertook a quantitative *in vitro* analysis using the most common bacterial species found in arthroplasty infection and measured the adhesion of biofilm producing strains to standard ultrahigh-molecular weight polyethylene (UHMWPE), vitamin E infused UHMWPE and cross linked UHMWPE using a standard laboratory analysis technique (sonication). The results were surprising. The research team established that both Staph. Aureus and E. Coli strains had a significantly lower adhesion to the vitamin E infused UHMWPE as compared with the standard polyethylenes.[5] Given the catastrophic effects of infection, any potential to reduce the biofilm formation that is key to overcoming prosthetic infection must be seen as an extremely positive step. Vitamin E infused polyethylene may offer the killer combination of better wear characteristics and lower infection rates. Here at *360* we are watching developments with anticipation.



Assessing outcomes in hip fracture x-ref

Whilst not widely regarded as the most glamorous research topic, hip fractures are here to stay, and indeed not just stay but escalate. Successful management of these fractures and improving outcomes will likely rely on a carefully orchestrated research programme with ongoing stepwise improvements in the treatments available and outcomes. The current difficulties predominantly surround making that assessment. Due to the unique nature of the hip fracture population there are no currently widely accepted outcome measures that can be applied in a standardised method to assess outcomes in this diverse patient group. Researchers in **Coventry (UK)** undertook an ambitious study to establish just what the optimum outcome tool measure was in a group of hip fracture patients. The research team measured responsiveness and associations between the Oxford Hip Score (a hip specific measure: OHS), ICEpop CAPability (a measure of capability in older people: ICECAP-O) and EuroQol EQ-5D using data previously collated from two studies. The three outcome measures were assessed concurrently at a number of fixed time-points allowing for direct assessment of change (responsiveness), inter-measure associations and validity. Surprisingly the research team established that the ICECAP-O was not responsive to change whilst both the EQ-5D and OHS were strongly correlated with each other. Additionally the EQ-5D was found to be a moderately good predictor of death and proxy reporting to behave similarly to self-reported scores. [6] The researchers' findings certainly seem to suggest that the EQ-5D could be an excellent tool for assessing outcomes in hip fracture research, and that in this patient group global indicators of quality of life may in fact be as appropriate as disease specific scores.

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