New and proven solutions in joint and bone surgery

Replacement of knee and hip joints is still on the rise in Germany. Infections can occur following the surgical procedure, which are caused by germs in various ways. They can enter the surgical field from the outside via the patient's skin during the surgical procedure or reach the implant from other parts of the body through the bloodstream (haematogenous infection). Revision, i.e. replacement of the affected implant, is almost always unavoidable in such cases. With bone fractures as well, there are complications in up to 10% of cases, which are usually caused by the patient's risk factors (pre-existing diseases, lifestyle, etc.).

The medical possibilities for the diagnosis and therapy of periprosthetic infections and reconstruction of the bone defects involved have steadily improved in recent years.
In their therapy, the treating surgeons are able to call upon a broad combination of proven approaches such as antibiotic-loaded bone cements and new, innovative techniques like stem cell therapy. Bone cement tested in joint replacement is also used for therapeutic approaches in bone reconstruction, such as the Masquelet technique. Established methods are under further development in diagnostics and the combination options for diagnostic methods are becoming more sophisticated. This allows patient-specific treatment regimes to be derived, which lead to far better medical outcomes and chances of healing. The risks of recurrences can also be minimised accordingly, which in turn leads to a lower financial burden for the healthcare system in the long term – despite the increasing number of patients requiring joint surgery.

At this year's German Congress for Orthopaedics and Trauma Surgery (*DKOU*) in Berlin, Dr. med. Akos Zahar (Helios Klinikum Emil von Behring, Berlin-Zehlendorf), Prof. Dr. med. Gerhard Schmidmaier (Heidelberg University Hospital) and Dr. Christof Berberich (Heraeus Medical GmbH) discussed the use of new and established methods for the diagnosis and treatment of implant-associated infections and bone defects.

Diagnosis of bone and joint infections

The diagnosis of periprosthetic bone and joint infections is complex – there is no fail-safe diagnostic test with 100% sensitivity and specificity. Nevertheless, the targeted combination of different diagnostic test methods allows an accurate diagnosis. The components of the medical history include the clinical and imaging examination, an analysis of the blood parameters and the synovial fluid (puncture), as well as microbiological testing of tissue extracted pre- and intra-operatively. Investigation in the lab of the microbial colonisation of a removed implant following sonication can also deliver useful information about the germs present. The various investigations are carried out on the basis of a clearly defined diagnostic step-by-step plan presented by Dr. Akos Zahar.

The aim is to reduce false positive and false negative results to a minimum. According to Dr. Zahar, it is essential that surgeons and microbiologists work together regularly and closely in a multidisciplinary team. Only on the basis of the results of multidisciplinary team meetings is it possible to clarify all relevant questions, e.g. whether one-stage or two-stage prosthesis replacement is performed, as well as which cement and antibiotics should be used.

Based on the outline for a therapeutic algorithm, Dr. Zahar explained the decision-making process in which the insights developed by the multidisciplinary team contribute to arriving at a treatment plan.

While two-stage prosthesis replacement is accepted as the gold standard and can be applied for almost all patients, one-stage replacement requires intact soft tissue and bone substance, and especially a precisely known colonisation with easily mastered germs and a relatively good state of health of the patient. With early detection of infection (< 30 days), intact soft tissue and solid anchorage of the prosthesis, the implant can also be preserved (DAIR – debridement, antibiotics and implant retention).

Finally, Dr. Zahar demonstrated that besides systemic antibiotic therapy, the use of bone cement with special combinations of antibiotics (e.g. gentamicin and vancomycin or gentamicin and clindamycin) has proven to be a useful measure in supporting all therapeutic procedures.

Local antibiotics in bone cement

Dr. Christof Berberich then explained the preventive and therapeutic use of local antibiotics in bone cement. Compared with systemic administration of antibiotics, local antibiotics have the clear advantage that, despite high concentrations of the active substance, toxic side effects are very rare and the active substances are released at the site of surgery or infection. Moreover, the dosage in which the systemic antibiotics can be administered is often no longer sufficient for combating certain pathogenic strains, as was shown with the example of increasing MIC (minimum inhibitory concentration) values of Staphylococcus epidermidis. The effect of systemic antibiotics is also limited by the poor blood flow in bone tissue and joint compartment (insufficient vascularisation), moderate bone penetration and the fact that most bacteria live in biofilms, which makes it very difficult for antibiotics to penetrate.

Antibiotic-loaded cements can be administered in high and low dosages. While high-dose antibiotic cements (e.g. COPAL® G+C) usually contain specific antibiotic combinations and are used for special prophylaxis and to support the treatment of severe infections, low-dose cements (e.g. PALACOS® R+G) usually contain a broad-spectrum antibiotic and are used for routine prophylaxis.

In the case of revisions due to periprosthetic joint infections, the combination of several antibiotics in the bone cement, such as for spacers, has proven effective in preventing recurrent microbial colonisation of the prosthesis or new infections during revision, says Dr. Berberich. He underlined this statement using data from in-vitro and in-vivo studies.

The advantages of antibiotic combinations in bone cement are manifold. On the one hand, two different antibiotics cover a far broader spectrum of activity. At the same time, local antibiotic release is improved. The risk of antibiotic resistances can also be reduced because resistances against two active substances rarely form simultaneously.

Antibiotic combinations in bone cement are also helpful in certain situations for preventing infections following joint surgery interventions. As a reference, Dr. Berberich cited a study of more than 800 patients with femoral neck fracture who clearly benefited from the use of COPAL® G+C bone cement (gentamicin and clindamycin); here the infection rate in the COPAL® group was significantly reduced by almost 70%.

Finally, Dr. Berberich also gave some important practical information. Here he recommended the use of industrially manufactured bone cement. However, if an antibiotic still has to be added manually in exceptional situations in surgery, he discouraged adding active substances in liquid form, as they can impair the mechanical properties of the bone cement. Attention must also be paid to the stability and heat sensitivity of the antibiotics added in such cases. Dr. Berberich referred to a table in the PJI Pocket Guide from the Pro-Implant Foundation for an overview of suitable antibiotics.

New concepts for improving bone healing

Prof. Dr. Gerhard Schmidmaier then presented new regenerative approaches for improved bone healing following infection treatment. In 5-10% of all cases of bone fractures, complications arise such as insufficient biomechanics, soft tissue damage or impaired biology.
Risk factors include osteoporosis, diabetes mellitus, microangiopathy and macroangiopathy, polyneuropathy, smoking, alcohol abuse or certain drugs. Bone healing disorders and infections can lead to various forms of pseudoarthrosis.

The Diamond concept developed by Prof. Schmidmaier is a promising approach. It is used for bone healing disorders or defects, and encompasses various components of restorative medicine (e.g. scaffolds, growth factors, good blood flow, mechanical stability).

In recent years, surgeons have increasingly used stem cell-based therapies in applying the Diamond concept to stimulate cell proliferation and thus promote regeneration. Today, mesenchymal stem cells (MSCs) play a significant role in this process. They are obtained from the bone marrow and are a promising source of the cells necessary for regenerative methods. The use of MSCs is already established with pseudoarthrosis; only the time usually required to obtain the MSCs by standard centrifugation (approx. 2 hours working time) represents a restriction and can only be used in the case of two-stage replacement.

An attractive alternative – especially for intraoperative and one-stage interventions – is offered by innovative vertical centrifugation with HERAGEN®maxx, which can perform the process in just 60 seconds in a few simple work steps. The new method enables up to a 94% better and thus significantly higher yield of CD34+ cells and 7.8 times higher platelet concentration.

The method probably also offers advantages in the yield of growth factors and cytokines, but this still has to be investigated further.

Source: Heraeus Medical satellite symposium "Infekt – Defekt – Regeneration", 25.10.2018, German Congress for Orthopaedics and Trauma Surgery (*DKOU*) 2018, Berlin.