EDITORIAL

Bridging Large Bone Defects

Bridging a large bone defect remains one of the challenging problems in Orthopaedic Surgery. Options include using non-vascularised autografts, pedicled autografts, free vascularised bone transplants, allografts, ceramics and custom-made prostheses.

Recently, the rapidly progressing new field of tissue engineering is looked upon for providing the "ultimate bone substitute". Adult mesenchymal stem cells could now be cultured from bone marrow and from adipose tissue and could be primed to differentiate into osteoblasts. These osteoblasts could be transplanted into an appropriate scaffold to bridge the defect. However, before this could be achieved, several issues still need to be resolved. Firstly, Stem Cell Specialists have still not shown whether it is better to use undifferentiated MSCs or differentiated osteoblasts. Secondly, quality control systems must be established to ensure delivery of pure MSCs or pure differentiated osteoblasts for implantation. When using MSCs, the cells implanted could be contaminated by some cells which have differentiated into other cell types. Likewise, when using differentiated osteoblasts, the cells transplanted could be mixed with some undifferentiated MSCs which are pluripotential and could develop to other unwanted cell types such as chondrocyte, myocyte, tendoncyte, adipocyte or fibrocyte. In both situations, undesirable effects could arise. Thirdly, tissue engineers have yet to use protocols for culturing MSCs that do not use materials/media of xenogeneic origin. Fetal calf serum should no longer be used and should be replaced by human serum instead. Likewise, carriers for the cells to be transplanted into scaffolds must not be from animal origin. Bovine collagen should be replaced by human collagen. Fourthly, the facilities used in tissue culture laboratories producing MSCs for clinical application must be of high standard, including the use of Class 100 laminar flow laboratories. The quality system that must be set in place and the standards that should be adopted must follow the strict discipline and principles of clinical good manufacturing practice already applied to tissue banks for bone allograft transplantation. Finally, the scaffolds used must have the appropriate biological and biomechanical properties for a bone substitute replacing such a large bone defect. The scaffolds currently worked upon, including chitin and polycaprolactone, are grossly inadequate in terms of biomechanical strength.

Whilst tissue engineering has come a long way, it could take another decade or more before the answers to all these issues could be found and the technology be made available for safe cell transplantation practice in clinical practice following all the requirements of clinical good manufacturing practice.

On the other hand bone allografts remain a readily available, viable and good option for large bone reconstruction provided bone allografts of good quality could be provided by a tissue bank complying to all the requirements of clinical good manufacturing practice to ensure safe clinical allograft tissue transplantation. Such a bank must conform to the standards set by the American Association of Tissue Banks and the European Association of Tissue Banks to minimize the risk of disease transmission. It must follow strict procedures according to the banks' procedure and quality manual and the bank's operations must be audited on a regular basis by the relevant regulatory authorities. Such quality control systems have been established for tissue banks since the last two decades. Surgeons should not use bone allografts from banks who do not comply to such strict quality control measures. The other options of using ceramics and custom-made prostheses are not popular in the Asia Pacific region as they are not readily available and incur large costs compared to bone allografts.

Being inert, allografts should not be used alone. They are best used as allograft-autograft composites including allograft-live fibular bone composite. Even with the advent of tissue engineering, bone allografts would continue to play an important role. They are ideal as "natural carriers" for mesenchymal stem cells with biological and biomechanical properties most similar to the patient's own bone and therefore best suited for bone reconstruction. The allograft-osteoblast composite could improve the biology and biomechanics of the healing of bone allografts. Bone allografts could also be used as allograft-growth factor composites including allograft-bone morphogenetic protein composite and allograft-platelet rich plasma composite. The addition of such growth factors could enhance the biological and biomechanical function of bone allografts. Basic research is currently undertaken by some research scientists to evaluate the value of such allograft composites.

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