Clinical Use of Mononuclear Fraction of Autologous Bone Marrow in the Treatment of Closed Fractures of Long Tubular Bones

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ABSTRACT

The article presents achievements of modern traumatology and orthopedics in using mononuclear fraction of autologous bone marrow in the treatment of closed fractures of long tubular bones.

Key words: cellular technologies, traumatology and orthopedics, stem cells, mononuclear fraction of autologous bone

INTRODUCTION

Investigation of new, up-to-date methods of affecting reparative regeneration of bone tissue is necessary for further progress of our capabilities in the treatment of injuries and diseases of human musculoskeletal system. In the recent years traumatology and orthopedics specialists reached a significant success in surgical treatment of bone fractures, especially with the use of minimally invasive intramedullary osteosynthesis with blocking screws.

However, failure of fracture union and non-satisfactory outcomes of long-term treatment of false joints may occasionally occur even with the use of modern surgical techniques. Different methods that improve reparative regeneration of human locomotor system are traditionally used for prevention of these complications; they include auto- and allografts as well as different biocomposite materials.

However, the use of bone autografts considered to be a “gold standard” is hampered mainly by shortage of plastic material as well as by possible disadvantages, such as pain syndrome arising from additional injury and complications such as formation of postoperative hematoma and infection.

The use of allogenic tissues is also related to a number of problems and difficulties, such as harvesting grafts from dead bodies, need for preservation or reliable sterilization and storage of grafts under specific conditions.
Disadvantages of the use of allografts are also known: these include allergic reactions, infectious complications and slow graft remodeling.

Finally, a problem of deontology may also arise: the material is obtained from a dead human body. This unusual material may cause a sense of disgust and mistrust, as well as a fear of complications and even mental stress in patients [3].

In the recent years greater attention has been paid to innovative cellular technologies in our country and abroad.

It should be noted that the basics of teaching of osteogenic cells of bone marrow was introduced at the beginning of the XX century by A.A. Maximov – the founder of blood and connective tissue concept who discovered the “stem cells”.

Feasibility of using cultures of autologous bone marrow stromal stem cells in lesions of long cylindrical bones was studied in animal experiments [1,2]. It was established that transplanted cultured of bone marrow stromal tissues possess clear inductive and promotional effect on the course of bone reparation processes. Moreover, according to the authors, investigations into optimization of osteogenesis in long cylindrical bone defects demonstrate a tendency of enhancement of reparative osteogenesis, even after injection of a stromal cell culture suspension [1].

This innovative area of scientific investigations is now at an initial stage. Many aspects of cell technologies remain underexplored despite promising results of experimental studies.

Study goal – to assess the effectiveness of transplantation of mononuclear fraction of autologous bone marrow (MFABM) used as a supplement to surgical treatment in patients with locomotor system injuries.

MATERIALS AND METHODS

The work was based on 8 patients treated at the Department of traumatology and orthopedics of Pokrovskaya Hospital of Saint Petersburg (Russia) in 2007 - 2008. The patients had the following locomotor system injuries: 1 patient with ununited fracture of tibia with marginal defect, 1 patient with closed comminuted fracture of femur between its upper and middle third, 4 patients with closed medial fractures of femur neck and 2 patients with subcutaneous rupture of heel tendon. There were 5 men and 2 women among the patients. Their age varied from 30 to 66 years with mean age of 47.7 years.

Causes of trauma included the following: catatrauma (fall from a height) (2), fall on a horizontal plane (fall from one’s own height) (4), overstrain of calf muscles (2).

The procedure of obtaining autologous bone marrow with the following transplantation of MFABM, as well as surgical treatment of lesions was performed after patients’ informed consent.

Fig. 1. Patient K., X-ray: a – before operation; b, c – after operation of intramedullary splintage with a nail with blocking screws.
RESULTS AND DISCUSSIONS

Cells that take part in osteogenesis arise from mezenchymal (stromal) bone marrow cells and can be found in endosteum and periosteum [4]. The number of these cells is controlled by biochemical signal molecules during bone tissue remodeling and reparation of bone defects; local cellular microenvironment determines differentiation of osteogenic cells into osteoblasts and chondroblasts [5]. High degree of bone tissue vascularization is determined by the need for oxygen and nutrients required in large amount for normal bone growth and development. Beneficial dual role of blood vessels in osteogenesis is undisputable – this is their transport function (delivery of nutrients) and development of osteoblasts and osteocytes from endothelial cells. Blood vessels develop as a primary event and tend to grow towards

Fig. 2. Patient Sh., X-ray: a – before operation; b, c – after operation of intramedullary splintage with a nail with blocking screws.

Fig. 3. Comparative X-ray images in 6 weeks after operations: a) X-ray of the patient K.: well-differentiated elements of endostal and periostal bone callus; b) X-ray of the patient Sh.: poorly differentiated elements of periostal bone callus.
necrobiotic area. Their orientation in this direction is determined by enzymes. Primary bone plates are formed along blood vessels; they are connected to each other and to endothelial cells by cytoplasmatic processes. “There is no regeneration without vascularization” - this statement of a famous Russian orthopedist V.D. Chaklin (1935) is truly reasonable. According to the author, the growth of bone tissue depends on nutrition and shape formation – an obscure genetically predetermined bone capacity to restore its shape when it is partially lost.

Fig. 4. Comparative X-ray images in 12 weeks after operations:
a) X-ray of the patient K.: clearly seen elements of bone callus, fracture line can be traced only partially;
b) X-ray of the patient Sh.: elements of endostal and periostal bone callus. Clear line of the fracture.

Fig. 5. Comparative X-ray images in 24 weeks after operations:
a) X-ray of the patient K.: complete consolidation of the fracture;
b) X-ray of the patient Sh.: the line of the fracture is partially visible with the elements of periostal and endostal bone callus.
We attempted to optimize the process of reparative regeneration of bone tissue in an acute fracture by using autologous bone marrow mononuclear fraction. The following extract from the medical records of the patient K, male, 30 y.o., is presented as an illustration: on 27.08.07 the patient received a high-energy trauma (catatrauma) and was admitted to the Department of traumatology and orthopedics of the Saint Petersburg City Healthcare Institution Pokrovskaya Hospital. On admission the patient was diagnosed with a dislocated closed comminuted fracture of the right femoral bone between its upper and middle third (fig. 2a). After examination on 25.10.07 intramedullary osteosynthesis with a nail with blocking screws was performed under electro-optical converter control and spinal anesthesia (fig. 2 b, c). The site of femoral bone fracture was also not exposed open during this procedure. No external immobilization was used.

Control X-ray examination in 6 weeks after surgery revealed the following results: in patient K who received mononuclear fraction of autologous bone marrow well-differentiated elements of periostal and endostal bone callus were clearly marked (fig. 3a). Also absence (lysis) of the cortical bone fragment previously observed at the site of fracture of the femoral bone is notable (fig. 1). In patient Sh. (who did not receive mononuclear fraction of autologous bone marrow) only poorly differentiated elements of periostal bone callus are visible (fig. 3 b).

A comparative X-ray examination in 12 weeks after operation demonstrated that in patient K. the elements of bone callus were well-differentiated, and the line of fracture could be only partially traced along the external surface of the femoral bone. Marked sites of ossification were also observed along the external surface of the femoral bone (fig. 4a). Only elements of periostand and endostal bone callus were observed on the X-ray of the patient Sh., and the complete line of fracture could be clearly traced with a bone fragment at the external surface of the femoral bone (fig. 4 b).

When X-ray images taken in 24 weeks after surgical treatment were analyzed, a complete consolidation of the femoral bone fracture was found in the patient K. (fig. 5a). The line of the fracture could be traced in the patient Sh with the elements of periostal and endostal bone callus (fig. 5 b).

CONCLUSION

In such a way, the first results of clinical use of autologous bone marrow mononuclear fraction
clearly demonstrated that, when transplanted to the fracture site, it renders a marked osteoinductive and promoting effect over the processes of bone tissue reparative regeneration and can be used as a supplement to surgical treatment of patients with lesions of musculoskeletal. It enables to increase the effectiveness of the main mode of treatment and to shorten terms of rehabilitation after a trauma.

REFERENCES