THE IMPORTANCE OF STEM CELLS AND REGENERATIVE MEDICINE- INTERNATIONAL VS INDIAN SCENARIO IN VETERINARY FIELD

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ABSTRACT

The stem cell is an “undifferentiated cell of a multicellular organism which is capable of giving rise to indefinitely more cells of the same type, and from which certain other kinds of cell arise by differentiation”. Regenerative medicine is the branch of medicine that develops methods to regrow, repair or replace damaged or diseased cells, organs or tissues. Regenerative medicine includes the generation and use of therapeutic stem cells, tissue engineering and the production of artificial organs.

KEYWORDS: *Multicellular Organism, Regenerative Medicine & Stem Cells*

Received: Aug 27, 2018; **Accepted:** Sep 17, 2018; **Published:** Oct 01, 2018; **Paper Id.:** IJBTROCT20182

INTRODUCTION

The late nineties have brought the storm in culture dishes with the development of embryonic stem cells first isolated in marine species by Evans and Kaufman in 1981. Stem cells having the property of self –renewal, can differentiate into specific cell types and hence offer the possibility of a renewable source of replacement if cells and tissues to treat diseases in human including Parkinson’s and Alzheimer’s. Preliminary research in mice and other animals indicated that the bone marrow stem cells transplanted into damaged heart can generate heart muscle cells and successfully repopulate the heart cells.

Although stem cells have wide application in human welfare, they have also a vast potentiality in animal science particularly on reproduction.

Beyond the problem of animal health, the injuries, in turn, generate considerable economic problems, since horses are animals that involve significant costs to their physical training and competition. Due to the easy collection and effectiveness, administration of cell therapy for horses was based on the use of bone marrow mononuclear fraction have been introduced (Koch et al 2009; Smith et al 2010).

Problems involving injuries of soft tissues, cartilage, and bones, as seen, are fairly common in animals subjected to high-impact sports, especially in horses. However, degenerative processes in these tissues also occur in companion animal, like dogs and cats.

The following information is shedding some light on the studies in field India and abroad.

Tendons are fibrous structures with function of connective tissue, with intertwined collagen fibers, and are

attached to bones by annular ligaments. The recovery of damaged ligaments and tendons occurs with large influx of cells and formation of new fibrous tissue, but with lower biomechanical property, leading to performance fade, as well as increased risk of new injury. It was also pointed out that *tendon-derived stem cells*, able to differentiate into other cell types, such as muscle or fat, present in the injury could be liable to aggravate the pathological situation and cause chronic tendinopathy (Filomeno et al., 2012). Horses and dogs are among the most clinically affected animals, with naturally occurring tendinopathies with histopathologic similarities to those observed in humans when analysed by MRI and ultrasonography. Due to the high presence of collagen, the injury promptly induces activation of the homing mechanism, which allows the tendon repair by stem cell injection. Moreover, there are an increasing number of experimental protocols describing improved outcomes after the use of a combination of stem cells and integrated genes to stimulate the tendon regenerative process showed by [Carvalho et al., 2013](#). Filomeno et al. showed that adult stem cells treated with platelet-rich plasma could also be promising for veterinary and human trials.

Sport activities are also able to cause damage in the cartilages, especially in joints and other articulations, and veterinary medicine has also been concerned with these injuries has been reported by Van Osch G. J. V. M. 2009. In fact, these structures have a regenerative capacity lower than other tissues. Traumas caused in these cartilages to lead to ligament desmitis, a form of lameness that affects performance, and osteoarthritis, a degenerative disease that may cause pain, stiffness, and reduced functionality of the joints. Even though these lesions cause stimulation of stem cells homing, physiologically the mechanism is weakly activated. In this context, it is known that the MSC has high potential for differentiation into osteogenic and chondrogenic cell lines Bornes et al., 2014. However, there is discussion about which cell type (from bone marrow or adipose tissue) would prove to be of most advantageous use in veterinary medicine.

Use of Regenerative Medicine in Companion Animals

In recent years, there has been great interest in the use of stem cells as therapy for a variety of diseases in domestic animals, mainly those of companion animals. Although the scientific literature features a marked disparity between the supposed benefits of stem cell therapies and their proven capabilities in human, as defined by rigorously controlled scientific studies, stem cells implanted therapeutically offer innovative treatment perspectives for diseases considered so far without a cure in companion animals.

Recently, the morphology and physiology of MSC isolated from bone marrow have been evaluated in different canine breeds (Border Collie, German Shepherd, Labrador, Golden Retriever, and the Hovawart) Bertolo et al 2015. Regardless of some variations, the MSC was isolated from the bone marrow and established in culture, where all the analysed breeds were able to be expanded *in vitro*, showing potential for proliferation and differentiation, and thereby becoming eligible for cell therapies.

As seen for the equines, the potential clinical use of adult stem cells aroused commercial interest from several companies, where the purified cells have been even tested in research protocols for treatment of canine bone arthritis. Thus, it is in the orthopaedic treatment of dogs that the bone marrow mononuclear cells have been more concerned as a therapeutic method.

Ryu 2012 reported that despite the benefits obtained with the use of cells isolated from peripheral blood, depending on the animal state of health and age, the response of these cells can be weaker in relation to other cell types such as the MSC. Nevertheless, older dogs present common problems involving the circulatory system dogs and cats may

present bone problems, either hereditary or caused by some malformation or inadequate diet. The main problems are the rickets, osteomalacia, osteoporosis, osteofibrosis, and another skeleton malformations. Considering the bone repair and lengthening (*osteogenesis*), the MSC is also a good therapeutic option. Interestingly, in addition to its intrinsic activity, this cell type may also serve as gene carriers (*ex vivo* gene therapy) of pharmacological agents that, in turn, can assist in the osteogenic process Knight et al 2013. Even in view of the use of multipotent stem cells in regenerative veterinary medicine, Park et al. isolated and used MSC isolated from amniotic membrane of dogs reported by Park S.-B., 2012. Horie et al. 2012 tested the implantation of synovial-derived MSC to treat rabbit knees with partial meniscectomy. After 24 weeks, the implanted cells adhered to meniscal defects and activated the tissue regeneration, where they differentiated into type-I and type-II collagen-expressing cells. Bone diseases such as osteoarthritis and problems in cartilage and joints also affect domestic cats. Analysing and considering the information regarding age and pathological conditions, most adult stem cell protocols, as those used in dogs, may also be extrapolated to cats. Nevertheless, some of these diseases are also found in farm animals, destined for slaughter.

Use of Regenerative Medicine in Farm Animals for Slaughter

Nowadays, one of the major concerns is obtaining agricultural and cattle inputs for the nutrition of world population. In this way, there is a great concern for cattle destined for slaughter, where the husbandry environment (confine or pasture) and physical development to obtaining of better meat and reproductive potential should be considered. Although stem cells are still little explored in this field, there are already some caprine models for treating cartilage injuries and cell types, as the iPS, being studied.

The cattle creation, where it aims to develop fat to obtain tender meat, sometimes by their highest weight, may induce cartilage and bone problems. Further, especially when in grazing, this may influence their locomotion. Nam et al. 2013 proposed the identification and establishment of MSC for repair of caprine chondral injuries. The bone marrow was aspirated from the iliac crests and MSC were established *in vitro*. Histological and immunohistochemical analysis demonstrated hyaline-like cartilage regeneration and glycosaminoglycans synthesis in the transplanted sites of the group that received 1×10^7 MSC compared to control or bone marrow-treated goats. The intra-articular injection of MSC may provide superior cartilage repair outcomes and that could be extrapolated to other farm species.

The bovine mastitis, an inflammatory disease in the mammary gland, causes a drastic decrease in milk production and economic problems. The disease directly affects the farmer's income by decreasing milk production, reduced milk quality, and reduced animal value, while leading to costs with drugs, risk of culling of animals, and possible death. Besides, bovine mammary epithelial cells and their stem cells are very important in milk production and bioengineering. Thus, Sharma and Jeong demonstrate the possibilities of bovine mammary stem cell therapy, offering significant potential for regeneration of tissues that can potentially replace or repair the diseased gland suggesting differentiation of stem cells isolated into epithelial, myoepithelial, and/or cuboidal/columnar cells decreasing risks after reinjection reported by Sharma et al 2013. The authors also believe that the iPS cells could be used in this kind of approach.

There are several studies which use Induced pluripotent stem (iPS) (differentiated cells that have been experimentally reprogrammed to pluripotent cells), to achieve an embryonic stem cell-like state.. Both MSC and fibroblasts may be used for these purposes and there are studies already for the obtaining of iPS to buffalo, cattle, goats, pigs, sheep, and other farm animals reported by Kumar et al 2015. In this way, a study was also conducted to assess the effect of supplementation of different growth factors in embryonic stem cell culture of buffalo reported by Puri et al 2012..

Authors showed efficiency of blastomere attachment, formation of embryonic stem cell-like colonies, and their propagation *in vitro* and characterization, concluding that these buffalo cells presented high potential of pluripotency (Thesis Mehere et al., IVRI 2005). In addition, the stem cell manipulation is already a reality with regard to improving reproductive health. However, the use of stem cells to increase the clonogenic potential still lacks many studies.

CONCLUSIONS

When it comes to Indian scenario and clinical parts of stem cell therapy and regenerative medicine, although a lot of laboratories are ready to provide stem cells for animals and stem cell banks are available due to financial constraints many owners are not able to afford these therapies for companion animals.

When it comes to research part of stem cell therapy and regenerative medicine in India one can observe that it is not controlled as per guidelines.

This may be for several reasons, but the major reason for this is financial constraints and the laws and legislation of Indian Government towards the use of stem cell therapy in animals.

As there are a lot of antibiotic resistance stories which we can hear now a days, we have the alternative of regenerative medicine and stem cell therapies for which is emerging field and need about an hour in veterinary medicine in India.

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