REVIEW ARTICLE

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The use of low-intensity ultrasound system in Orthopedics for treatment of fractures

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INTRODUCTION

The treatment of non-union or delayed union of fractures includes a growing number of approaches and techniques, one of which is bone growth stimulation using low-intensity ultrasound (LIUS). The treatment is effective, painless and safe. Currently, Exogen is the only device marketed worldwide that uses LIUS to influence the fracture healing process.

THE HEALING PROCESS OF THE FRACTURED BONES

All the fractured bones have to go through a healing process. This is true in cases of surgery or injury. The process of bone healing has three stages. The first stage is inflammation. This starts when the bone has been fractured. Bleeding always takes place in the area of the fracture. This leads to clotting of blood and inflammation in the area. This provides the framework of a new bone. The second stage is bone production. With time, the clotted blood formed in the inflammation stage is replaced by cartilage and fibrous tissues. As the healing continues, the hard callus replaces the soft callus. This can be seen by x-rays some days after the fracture [1, p 20]. The last stage is bone remodeling. This stage goes on for months. In this stage, the bone continues to become compact and returns to its original shape and structure. The blood circulation in the area of the fracture improves. Once some bone healing has taken place, weight bearing encourages the bone remodeling stage [2, p 99].

THE EXOGEN ULTRASOUND BONE HEALING SYSTEM

This is an approved and clinically tested system for treatment of bone fractures. Exogen makes use of the painless ultrasound waves in order to activate the cells that are near the site of the fracture. This speeds up the natural repair process [3, p 1999].

Clinical studies have shown that the system accelerates the healing process of the fractured bones by 38 % in acute fractures [4, p 655] and 86% in non-union or delayed union. It has been shown that Exogen can improve the fracture healing process of older people, those who take tobacco and those who are obese, cases in which the healing process might be delayed. Exogen system can accelerate the process of healing as much as 50 % for the patients who smoke [6, p 254].

The picture below offers a basic explanation of how Exogen works at the cellular level.

To enhance bone healing, Exogen releases low intensity pulsed ultrasound waves at the point of the fractured bone. This jump-starts the natural healing process of the body. The waves move through the skin and the soft tissues to stimulate the critical cells

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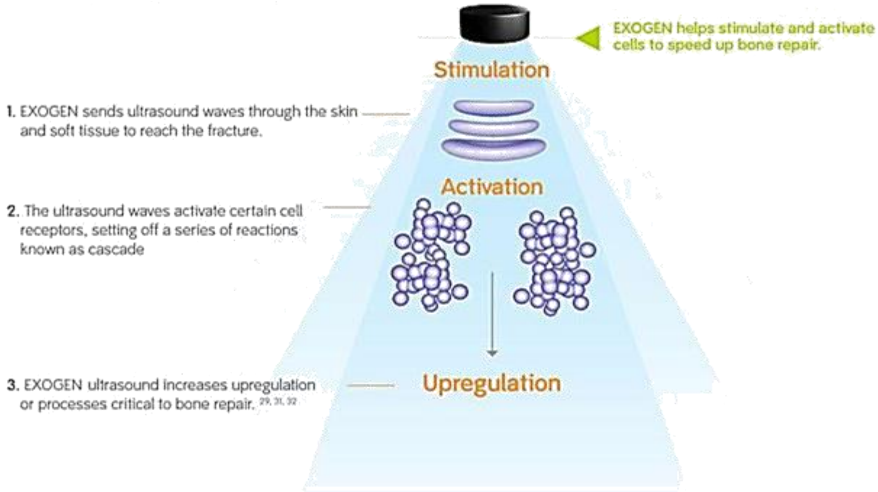
involved in bone healing.

Figure 1: The way Exogen Accelerates the Healing Process of a Fractured Bone [14]



In order to understand the role that the ultrasound plays in healing of the fractured bones, there is a need to understand what it is and how it works. It uses transcutaneous acoustic energy. The piezoelectric crystal produces sound waves which are transmitted through the various body tissues to make a number of changes which are implicated in the tissue healing [8, p 1098]. The density of the tissue is directly proportional to the sound waves that the tissue absorbs. The bone possess high density which makes the ultrasound waves to target the areas which may be affected or have bony abnormalities.

Low intensity pulse ultrasound (LIPUS) specifically works as a potential noninvasive therapeutic in healing of fractures. The waves which are produced by LIPUS introduce micromechanical stress in the area that has been fractured. This stimulates the cellular and molecular responses that are involved in the normal fracture healing. The osteogenic and angiogenic effects caused by the administration of LIPUS are non-thermal. The effects are mechanical in nature with a temperature variation of less than 10C [9, p 802].

The optimum parameters used to archive the maximum benefits of LIPUS are: a pulse width of 200us, an intensity of 30 Mw/cm2 and a 1.5 MHz frequency repeated at 1 kHz every day for 20 minutes [6, p 254].

HOW ULTRASOUND EXERTS MECHANICAL STRESS

There are two mechanisms by which LIPUS induces the mechanical stress in tissues. First it achieves it by displacement of the ends that are fractured and secondly by cavitation.

Research shows that displacement of the fractured ends occurs in at Nano metric scale [9, p 802]. This then stimulates the cellular and the molecular pathways which are involved in the bone healing process [10, p 1022]. It has been shown that LIPUS causes micro motion at the hard and soft tissues interface also. This action produces a mechanical stimulus that is more salient to the integrin mechanoreceptors which take part in osteogenic differentiation and cellular signaling. However it is not yet clear through the available research which displacement mechanism is dominant [11, p 703].

The second mechanism involves the acoustic streaming and cavitation. This mechanism promotes the idea that the sound waves that are emitted from LIPUS allow the accumulation of gas bubbles in the tissues and the cells [12, p 411]. This creates a cavity which gives room for the acoustic streaming. The streaming leads to turbulence or circular flow in the fluids from the tissues as the sound waves move around the bubble of gases. The acoustic streaming produced increased cell permeability. Once this has happened, the blood pressure rises in the area where the fracture has occurred. The increase in the blood pressure leads to the acceleration of healing by ensuring that there is sufficient gas exchange and the delivery of nutrients to the site. When the cavitation is not stable, the bubbles burst and the resultant energy stimulates the surrounding tissues [13, p 2642].

THE EFFECT OF LIPUS ON CELLS AND MOLECULES

There have been studies that have demonstrated the ability of LIPUS to promote fracture healing through the alteration of molecular and cellular mechanisms which are involved in the process of healing. Integrins are crucial in signaling modulation involved in fracture healing [14, p 345]. They act as mechanoreceptors and are also reactive to pressure changes and vibration caused by LIPUS in the cells environment. The mechanical stimuli increase the clusters of integrin on the fibroblasts. They also up regulate the mRNA expression of the integrin in osteoblasts [15, p 284]. The changes that occur enhance the sensitivity of the respective cells to motion and increase the cells intercellular signaling capacity. An important outcome associated with the intercellular signaling induced in the osteoblasts is the increased activation of ocyclooxygenase-2 enzyme. This increases the production of prostaglandin which is critical in the mineralization during the process of endochondral ossification especially on the soft callus [16, p 660]. The endochondral ossification which is enhanced by LIPUS leads to formation of the bony callus by the process of augmented mineral deposition [17, p 77].

LIPUS also stimulates the differentiation of the cells which are involved in the process of fracture healing, chondroblasts, fibroblasts, mesenchymal and osteoblasts. Additionally, it increases the way aggrecan expresses itself [18, p 1957]. Aggrecan is a stimulator of chondrogenesis. Presence of aggrecan accelerates the differentiation of chondroblasts into chondrocytes. The production of chondroitin sulfate at the site of injury is accelerated by the presence of more chondrocytes.

Chondroitin sulfates are essential components in supporting bonny and cartilaginous structures. Because of the cavitation process aforementioned, LIPUS increases pressure at the site of injury due to the increase in the vascular permeability [19, p 727]. The increase in pressure has been associated with mesenchymal stem cells differentiation which enhances the development of fibro cartilaginous callous.

LIPUS increases the expression of the early osteogenic genes which include osteonectin, the insulin growth factor and osteopontin. These genes have an important role in making sure that proper osteoblast differentiation takes place [20, p 3190]. The osteoprogenitor cells from the bone marrow may also differentiate into the osteoblasts at a high rate when LIPUS is used. This will enhance the bone healing process and remodeling.

CONCLUSION

The use of low-intensity ultrasound system is a relatively new technology that has been proven to be safe and efficient in the treatment of acute fractures or in cases of non-union or delayed union. The effects at the cellular and molecular level demonstrate its efficacy.

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