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Our Conception About Possibilities of Distraction Osteogenesis Stimulation in Limb Lengthening

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Abstract

Background: In recent years, many authors have noted slow formation of distraction regenerate during limb lengthening.

Aim of study: is to develop a concept involving various methods of osteogenesis stimulation for decrease of treatment time in limb lengthening by transosseous osteosynthesis method.

Material and methods: According to data from the experiment on 120 adult animals and the clinical experience mechanical, pharmacological, biological and biomechanical methods of osteogenesis stimulation in zone of bone lengthening were developed and introduced in nowadays practice.

Results: Applying of these methods of stimulating osteogenesis has significantly reduced time of patients' treatment. As a result, mean osteosynthesis index decreased from 35 to 16 days/cm and mean fixation index decreased from 25 to 10 days/cm. Desire results of distraction osteogenesis stimulation in limb lengthening were observed in 76% of animals with combined methods of stimulation. Effect of separated methods of stimulation was observed in 24% of experimental animals.

Discussion: In recent years, cases with slowing formation of distraction regenerate during bone lengthening have been increased. Such effects were found in treatment of systemic skeletal diseases (achondroplasia, rickets deformities of extremities, cosmetic bone lengthening), which needed to produce reoperations for stimulation of bone regeneration and/or correction of deformity. In such cases, there were indications for using one of stimulation methods or combination of them.

Conclusion: Use of methods of osteogenesis stimulation helps to eliminate possible complications and to decrease time of patients' treatment during limb lengthening and correction of deformity. We recommend using combination of methods for distraction osteogenesis stimulation in limb lengthening.

Keywords: Bone Lengthening; Distraction Regenerate; Ilizarov; Stimulation; Transosseous Osteosynthesis

Introduction

More than 50 years ago G.A. Ilizarov developed method for limb lengthening using the author's apparatus. Since that time these operations have moved from the category of exclusive to routine ones. However, with the widespread use of this method, especially with systemic skeletal diseases (achondroplasia, rickets deformities, cosmetic limb lengthening), we can often observe decrease of osteogenesis activity in the regenerate zone. The aim of this study is to develop concept about the possibilities of osteogenesis stimulation in limb lengthening. Currently, the lengthening technique is widely used in medical hospitals and in cosmetic private practice. The requirements of today are reduction of regeneration osteogenesis time and treatment time. Therefore, according to these requirements new technologies have been developed for limb lengthening including lengthening on two levels of two or more segments simultaneously [1-4]. Result of distraction produced in postoperative period is formation of several gradually increasing interfragmental diastasis. Organism mobilizes internal reserves, which are depleted under this load, which leads to attenuation or complete cessation of osteogenesis. In fracture

cases this process is much easier to compensate for, because injury is applied simultaneously. After immobilization of this bone, flow of pathological impulses gradually stops, process of bone consolidation occurs.

During bone lengthening operative trauma becomes chronic because after its application process of distraction begins. The organism mobilizes ontogenetic reserves to restore integrity of bone. But artificial growth of tissues produced by us occurs much more intensively than natural growth. As a result, organism capabilities dwindle and regeneration in zone of lengthening slows down or fades away completely. Therefore, it became necessary to stimulate osteogenesis during limb lengthening for which we developed the concept of regenerative processes stimulation, including mechanical, pharmacological, biological and biomechanical methods. To improve understanding of this situation we will give an example. Mean height of newborn child from European race is 50-52 cm. Natural growth continues until the age of 15. During this time, mean height achieves 165-175 cm, i.e. it increases by 3-3.5 times. Thus, annually general growth increases by 11-12 cm or per month by 1 cm. The overall height is sum of head size, height of spine and lower extremities. Mean length of newborn shin is 12 cm and adult one is 34 cm. Mean gain per 15 years is 22 cm or 1.5 cm per year and 0.125 cm per one month. During usage of external fixators lengthening rate is 3-4 cm per month, i.e growth rate increases by 24 times. It is clear that with such growth rate potential organism capabilities are quickly depleted. Therefore, organism needs help and carrying out stimulating procedures.

Material and Methods

The main guidelines of the concept were formulated after conducting experiments on 120 adult animals and clinical approbation. The final decision was made after conducting comprehensive complex morphological and electron microscopic, biochemical, biomechanical and other studies of internal environment condition of organism and organism as a whole. Neurophysiological examination of neuromuscular apparatus of lengthened extremities, blood circulation and microcirculation and psychological examination of the patients were produced clinically. The following measures for reducing of patients' treatment time have been developed in clinical practice. After end of distraction period and achievement of planned lengthening rates, control X-ray was performed. After that external fixator was switched to fixation mode for 10 to 12 days, which were necessary for adaptation of soft tissues to new physical dimensions of extremity segment. After examination of X-rays pictures, condition of distraction regenerate was determined. Attention was paid to shape of regenerate, height of its middle layer, density of bone regions of regenerate at ends of bone fragments. Indication for using one of the methods for osteogenesis stimulation was formation of regenerate in the form of a sandglass, height of the middle layer 10 mm or more, the low mineralization of bone sections during ultrasound examination.

All ways for osteogenesis stimulation in limb lengthening received permission from the Ministry of Health of the Russian Federation.

Results

As a result, the high efficiency of the developed methods was proved. Mean osteosynthesis index decreased from 35 to 16 days/cm and mean fixation index decreased from 25 to 10 days/cm. Desire results of distraction osteogenesis stimulation in limb lengthening were observed in 76% of animals with combined methods of stimulation. Effect of separated methods of stimulation was observed in 24% of experimental animals. The simplest method is the method of mechanical stimulation, including simultaneous compression of the regenerate by 7-10 mm with a force of 7-14 kg. This leads to connection of ends of bone regenerates (Figure 1).

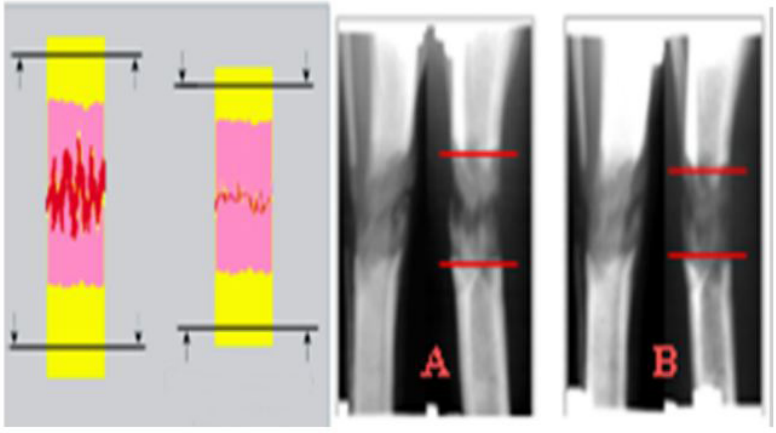

Figure 1: Scheme of regenerate compression and X-rays of patient during limb lengthening: A- before compression, B - change of regenerate after one-stage compression.

After applying this method general integrity of interfragmental regenerate was restored, its diameter increases, and mechanical strength of regenerate were increased [5]. To increase the effectiveness of regenerate stimulation it is possible to use drugs. Typically, this is done using well-known drugs in our daily practice. These include bioactive additive Flexpro, Stimbone, Solcoseryl, Pectibon, Baclofen, Mydocalm, Perftoranum, vitamin therapy, etc. [6,7]. Some authors [8,9] consider that the therapy with biphosphonates (Zoledronic acid, Ibandronic acid, etc.) is indicated for treatment of weakening of osteogenesis. During this period hyperbaric oxygenation by oxygen is indicated. What role do drugs have during limb lengthening? It is known that during bone lengthening process soft-tissue apparatus resists change in size of segment. This resistance is less in post-traumatic and post-infections shortenings, because soft-tissues are adapted to real size of segment. In cases with congenital shortening there is a significant amount of connective (fibrosous) and cartilage tissues in muscle mass which have an expressed resistance for stretching. Therefore, process of lengthening is accompanied by a painful reaction which is associated with developing soft tissue ischemia. In these cases, use of baclofen was indicated to relieve muscle spasm and improve blood supply. During course of baclofen patients were resilient to process of distraction. Hyperbaric oxygenation by oxygen has the same effect [10]. Depending on range of distraction, one-two courses of hyperbaric oxygenation are indicated for 5-7 sessions. Oxygen treatment improves metabolic processes in tissues and restores blood supply, as evidenced by disappearance of edema.

At final stages of distraction period, therapy with intravenous injection of Perftoranum was indicated. Well-known that Perftoranum is an active carrier of oxygen, which it quickly donates to tissues. In the presence of vasospasm, smaller particles of Perftoranum penetrate deep into the tissues, which leads to an increase of metabolic processes and activation of osteogenesis. Recently, a biological method of stimulation has been widely used, including the implantation of bone marrow, introduction into the zone of the middle layer. Of blood plasma taken from a patient or the introduction of whole blood. A method is known as stem cell therapy. Bone marrow is usually taken from iliac or from metaphysis of unoperated femur or tibia. After preparing of bone marrow cells, they are introduced into the middle zone of the regenerate. As a rule, after 2 weeks thereafter, a noticeable compaction of the regenerate is determined, which allows us to remove apparatus. The complex of experimental studies which were carried out by us [11,12] indicated a stimulating effect of autologous bone marrow, introduced into the connective tissue layer of distraction regenerate, on bone formation processes. It should be noted that by the end of distraction mean height of the layer reached 8-10 mm, its share in the regenerate was 26%. After 7 days of fixation (after stimulation) in half of the experiments the regenerate lost its zonal structure, which allowed removing external fixator after 14 days (Figure 2).

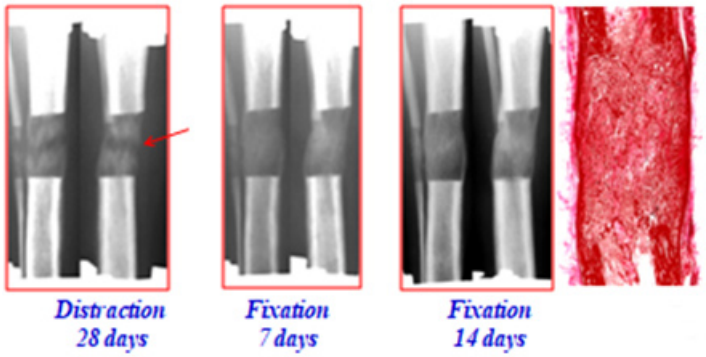

Figure 2: Stimulation of regenerate maturation by introduction of bone marrow into the middle layer.

In (Figure 2) change of regenerate condition before and after 7, 14 days after the introduction into the middle layer of bone marrow is shown. Before bone marrow introduction non-mineralized structures occupied 26%, poorly mineralized - 19% and medium mineralized - 55%. After two weeks of injection of bone marrow, these indicators were changed markedly and amounted to 6, 16% and 77% respectively. By this time, highly mineralized structures were appeared in the amount of 1%, which made it possible to remove apparatus. Other authors have also reported on the use of bone marrow and mesenchymal cells in clinical practice [13-15]. The blood is taken from a vessel on the operating table, it is centrifuged. Plasma in the amount of 7-10 milliliters is got from special device (centrifugate). If there is no centrifugate in the operating room, you can enter the same amount of whole blood (hemotherapy effect).

The biomechanical method includes automatic lengthening and the introduction into the intramedullary canal of lengthening segment of two flexible wires coated with hydroxylapatite [16-18]. Currently, surgical intervention with intramedullary wires is often mandatory in limb lengthening. The introducted wires enhance the fixation of bone fragments, which excludes the possibility of their secondary displacement at level of distraction. In the process of lengthening, hydroxylapatite degrades from wires into the surrounding tissues, thus accelerating the process of mineralization of the regenerate. Currently, the introduction of the wires into the intramedullary canal of lengthened bones of segments is main and most frequently used method of stimulation. Clinical example of limb lengthening by combined osteosynthesis you can see in (Figure 3).

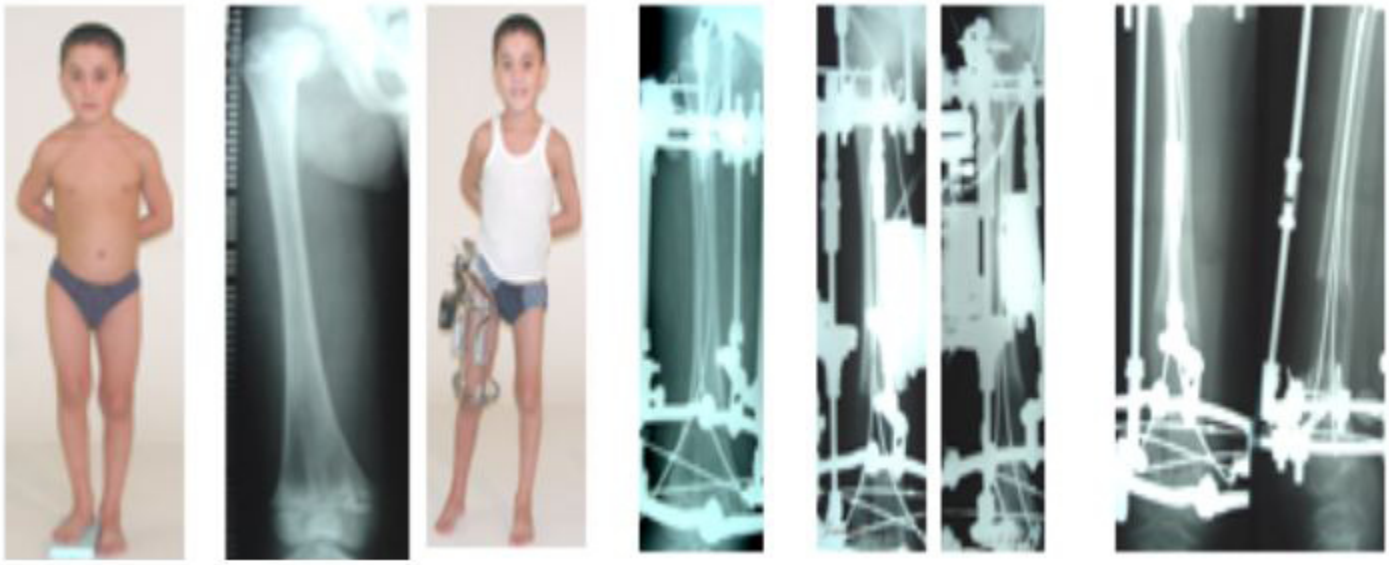

Figure 3: Photo and X-rays of patient 7-years-old with consequences of hematogenous osteomyelitis, 5 cm shortening of right leg before and during treatment

A 7-year-old patient was admitted with a shortening of the right leg by 5 cm. The extension was performed automatically using two intramedullary wires. The average rate of distraction was 1.1 mm/day. Duration of external fixation was 70 days.

Result of the treatment - the planned limb lengthening was achieved (Figure 4). The osteosynthesis index was 17.5 d/cm, while other authors report an osteosynthesis index of 30 days or more per cm of lengthening. This message is interesting because during the lengthening two types of stimulation were used: the lengthening in the automatic mode and use of intramedullary wires. Even in the process of lengthening the function of adjacent joints was restored. Lengthening in automatic mode is already one of the methods of regeneration stimulation, since it proceeds smoothly without periodic jerks [19,20]. Patients in the process of lengthening, as a rule, do not complain about pain, they get exercises with full functional weight-bearing on operated leg.

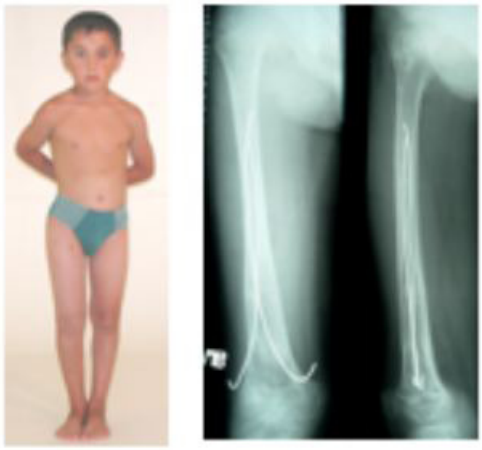

Figure 4: Photo and X-rays of patient 8-years-old as the result of limb lengthening by combined osteosynthesis.

Discussion

The article presents mechanical, pharmacological, biological and biomechanical methods of stimulation, accelerating the formation of distraction regenerate. This is due to the fact that in recent years the number of extermity lengthenings has noticeably increased. The procedure was transferred from the medical into cosmetic area to increase growth. The characteristic changes of recent times are the lengthening of the bones on two levels of two or more segments of the human body simultaneously. This is due to the fact that patients raise the question of reducing the time of treatment. This is especially important during lengthening in systemic diseases (achondroplasia, rickets), as well as increasing growth. Simultaneous lengthening of two or more segments, especially when re-lengthening, depletes the internal capabilities of the body and this leads to a slowdown or complete attenuation of the regenerative process. In such situations, osteogenesis stimulation is shown in the elongation zone. For this purpose, different variants of stimulation are used. The simplest is compression of distraction regenerate by 5–7 mm. It seems the value is quite small, but for this procedure the patient's consent should be obtained. Patients are struggling for every millimeter of elongation and it is not easy to compress the regenerate without prior extension to the indicated value. To perform this method, G.A. Ilizarov proposed a gradual compression of the regenerate in ¼ mm 4 times a day for 8-10 days. He called it the "regeneration upbringing." With further improvement of bone lengthening technologies in order to reduce the time of fixation, V.I. Shevtsov and A.V. Popkov proposed a single-stage acute compression of a distraction regenerate (RF patent No. 2071740 of the Russian Federation). Practice has shown that single-stage compression is much more effective than gradual.

Further development of the stated technology of bone lengthening has undergone some changes. Paley D. [21], Popkov D. [22], Shapovalov V.M. [23] modified this technology and they used combined osteosynthesis: during the operation a lockable rod is inserted into the bone marrow channel. The locking screws were inserted only into the holes of the proximal part of the rod. Next, the Ilizarov apparatus was applied, bone osteotomy was performed, and after 5–7 days, distraction began on the rod. Upon reaching the planned extension, lockable screws were inserted into distal part of the rod and the device was removed. With this technology, the time of osteosynthesis with the device was reduced, the contractures of the joints were not observed and their mobility was restored in the shortest possible time. A number of authors propose new constructions for bone lengthening [24,25]. But at the same time, only the appearance of the constructions on which the technologies developed by G.A. Ilizarov and his school created by him changes. Issues of osteogenesis were described in modern paper, which confirm the findings of Ilizarov [26]. Jauregui JJ etc. [27] analyzed the literature data about effect of ultrasound (physiotherapy method) for stimulation of distraction osteogenesis, which we also consider useful.

Conclusion

Thus, the integrated use of these methods of stimulating osteogenesis can significantly reduce the time of treatment of patients. The time has come when patients want not only to get rid of their existing defect, but also to achieve this in short time period. Therefore, the process of lengthening cannot be approached in a pattern, formally. It is necessary to use the whole arsenal of technologies aimed at improving the efficiency and performance of the applied techniques. We recommend using combination of methods for distraction osteogenesis stimulation in limb lengthening.

Conflict of Interest

There are no conflicts of interest.

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