AFFECTING GROWTH ARREST BY ELECTRICAL CURRENT IN RABBIT GROWTH PLATES: A MODEL OF EPhipySEdiosIS

**Introduction**

Epiphysiodesis is a common orthopaedic procedure used to intervene when there is disproportional long bone growth. A technique invoking the open surgical ablation of the physis was described by Phemister more than 70 years ago and was the standard for decades. Since the early 1980’s, several alternative methods with efforts to reduce the invasiveness and surgical dissection appeared, such as epiphyseal stapling or percutaneous epiphysiodesis. Success of each method requires late growth stages and is irreversible. The use of staples has problems of asymmetrical fusion and or incomplete fusion. Currently, percutaneous epiphysiodesis is the method of choice. The percutaneous technique is limited in the amount of physeal plate to ablate under fluoroscopic control and in how to ensure the completeness of the ablation. This experimental study was designed to develop a simpler and more reliable method of epiphysiodesis with minimal trauma, which we believe can be achieved through electrically stimulated completeness of the ablation. This experimental study was designed to achieve this we used a rabbit model and inserted an electrode into the distal femoral growth plate and observed the changes after two weeks of no current, or constant 10 microamps, or 50 microamps. Comparisons were be made within each group between the operated and non operated, contralateral limb. We assessed bone growth by longitudinal length measurements, histological appearance and morphometric and volumetric analyses.

**Material and Methods**

The design of this project focused on developing a animal model of epiphysiodesis of the distal femur using implantable electrodes in the distal femoral physis. For this study we opted to use existing devices (EBI) where the electrode (cathode) and power source (anode) were both implanted. We had three groups of animals (4 New Zealand white rabbits of 10 weeks of age for each group) which were either control (sham operated and implanted with an inactive low current electrode), low-current (LC) group implanted with 10 uA power source similar to those currently available for clinical use (OsteoGen™, EBI), and a high current (HC) group implanted with a 50-uA power source. After a pre-anesthetic injection of Xylazine (4 mg/kg IM) followed after 10 minutes with Ketamine (50 mg/kg IM), a 1 cm long electrode was directionally placed from lateral to medial through the mid region of the distal femoral physis and the power source was implanted subcutaneously. After surgery, the rabbits were housed in an approved animal facility, where all three groups were given identical diet and water supplies and monitored daily. Voltage readings of actual current generated were assessed every three days. On the 14th day, the animals were sacrificed by Sleepaway (0.4 ml/kg IM), and electrodes were removed and both femurs were harvested from each group. Femur lengths were measured with a digital caliper three times at three locations, the medial femoral head to medial condyle, the middle (piriformis fossa to intertrochlear groove) and the lateral (tip of greater trochanter to lateral femoral condyle). The difference in length between right (unoperated) and left (operated) in each group were plotted. After decalcification and histologic staining with H & E and Safranin-O, we studied multiple sections for any changes in the microscopic characteristics of the distal femur, including narrowing of the growth plate or its possible closure, bony bridges, and the cellular arrangement of various zones in growth plate.

Using a computer-integrated microscope with image analysis software (Image ProPlus 4.5™, Media Cybernetics), the histomorphometric analysis of the dimensions of the growth plate was performed. Equivalent areas from full view micrographs at a magnification of 10 X were analyzed. Each zone (resting, proliferative and hypertrophic) was delineated and volumetric analyses were performed.

**Results**

In the high current group, all the three length measurements of the nonoperated limbs were consistently larger than those in control and LC group. The growth of the left, (operated) limb in the HC group was inhibited by ~200% in comparison to control or LC. (Fig. 1). Radiographs showed new bone formation at the site of electrode insertion with the LC and to a lesser extent with the HC groups. By radiographs no noticeable changes were observed in the growth plate and epiphysis, nor were there any signs of infection. This was consistent with the findings of the gross inspection. The most significant histologic finding was the appearance of putative bony bridges and some distorted internal structure of the growth plate in the HC group (Fig. 2). The HC group also showed disorganized columnar arrangement and decreased lengths in the proliferative zones. We could not detect bony bridges nor the same degree of disorganization in the LC group as in the HC group. Examining the zone of Ranvier, the HC group had an increased number of hypertrophic cells close to the electrode. This was not observed in the LC, and control group tissues. In the histomorphometric study, the volumes of whole growth plate, resting zone, and combined proliferative and hypertrophic zones in high current group were consistently smaller by ~20% when compared to all those of the other groups. (Fig. 3) The reduction in volume if these discrete zones was more distinct on the lateral side, near side of electrode.

**Discussion**

Electrical current made a marked change in the growth plate volume and characteristics in this rabbit model. Interestingly, the results demonstrate that only after a short 2 week period of treatment, the physical length can be measured as arrested in the HC group. No consistent, measurable difference was detected in the left and right femurs of either LC or control groups. The results were consistent within each group but since the number of animals per group was 4, statistics were not available. Results were reproducible and consistent between physical length measurements and morphometric analyses. Our findings support the use of electrical current to potentially achieve an epiphysiodesis. Since no complete closure of the growth plate is presented, the results suggest the effects may be reversible. Molecular events controlling growth arrest are currently being studied; additional animals for longer time periods are being planned.