INFLUENCE OF SHOCK WAVES ON FRACTURE HEALING*

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ABSTRACT—During the last decades the influence of physical factors on fracture healing has been widely described. With the use of shock waves for the treatment of urolithiasis, a new mechanical medium has been introduced into medicine. For the first time the influence of shock waves on fracture healing was studied in rats. With fractioned shock-wave treatment (5 times 100 shock waves at 14 or 18 kV) an enhancement in healing could be achieved.

During the last twenty-five years, it has been shown that healing can be not only retarded but also improved by physical influences. Most of the physical factors, such as electrical stimulation,[1] electromagnetic fields,[2,3] piezoelectricity,[4,5] ultrasound,[6,7] or mechanical influences such as intermittent tension,[8,9] effects of immobilization and continuous passive motion,[10] and micromovement[11,12] were tested in biologic systems involving bone growth or fracture healing. Although the actual mechanism(s) involved in the stimulation of the wound repair by the aforementioned factors are not understood, several hypotheses have been suggested. Cell proliferation, the activation of cells with enhanced deposition of macromolecules by these cells, and also faster remodeling of the treated tissue may explain these effects. These hypotheses include the effect of the transduced physical energy on the structural and functional changes of molecules at the plasma membrane level (cAMP, cGMP, ATPase, etc.), which by a second messenger mechanism promote cell mitosis and enhance cell activity to synthesize structural macromolecules. It can well be an induced effect of physical forces on the mediators or activators of cell activity, such as release of serotonin or histamine by mast cells.

A new mechanical factor, shock waves (Extracorporeal Shock-Wave Lithotripsy [ESWL]), was introduced into medicine for the treatment of urolithiasis.[13,14] A shock wave is a single-pressure impulse which can be created by a high voltage spark discharged under water causing an explosive evaporation of water. The shock waves are focused by a semi-ellipsoid and therefore can be concentrated on rather small regions. Because of similar acoustical characteristics, shock waves can be transmitted into a human body.

The ability to control the number and intensity of shock waves, thus the actual effect of shock waves on the tissue structure, allows us to test the hypothesis that shock waves (similar to other physical factors) at low-energy levels would stimulate the cells of the wound and consequently enhance wound-healing. Whereas with high-energy shock waves, we would expect destruction, necrosis, and scar formation.

In a previous study this hypothesis was proved to be true for the healing of split thickness wounds in a pig model.[15] The purpose of the present study was to evaluate the influence

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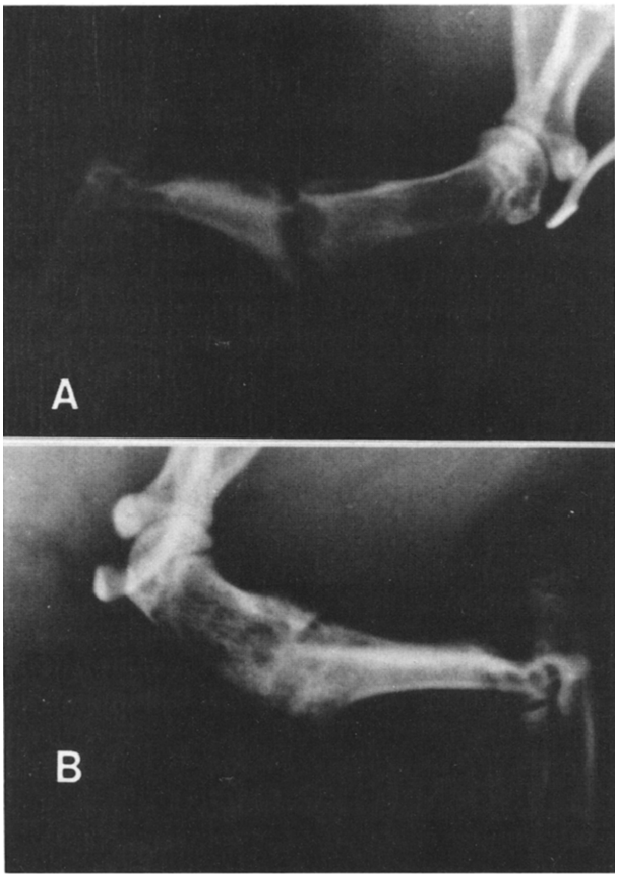

FIGURE 1. *X-ray films: (A) control rat three weeks after fracture, and (B) 18-kV-treated rat three weeks after fracture.*

of shock waves on the healing of fractures in Sprague-Dawley rats.[16]

Material and Methods

Forty Sprague-Dawley rats with a body weight of 200 to 230 g were used. With digital pressure diaphyseal fractures of the left humeri were inflicted. Five treatments were performed on days 2, 5, 9, 14, and 19 after infliction of the fracture, using the experimental Dornier XL-1 lithotriptor. Fourteen rats served as control with sham treatment, the others were treated with 100 shock waves per application, with either 14 or 18 kV. The actual focus pressure in the XL-1 is higher than in the lithotriptors of the HM series (both regular and modified). The analyzed parameters were bone weight, breaking strength, and x-ray films, calcium-45 uptake, and histology.

X-ray films were taken weekly with industrial high-resolution film. The radiographic signs of healing were graded blindly on an objective scale from 0 to 4 by four professionals in an independent manner. In addition, the callus volume was digitally evaluated. Twenty-four hours before termination, 18 of the animals (6 per group) were injected with 10 μCu calcium-45 per 100-g body weight. After thirty-five days the rats were sacrificed and both humeri were dissected, carefully cleaned, and weighed. The breaking strength of the wet, fresh humeri was measured by longitudinal extension with a tensometer (Instron table model). The calcium-45 uptake was evaluated with a gamma counter. Histologic evaluation with hematoxylin eosin, safranine-o, and trichrome staining was performed in two samples of the control group and in the 18-kV treatment group. Duncan's[17] multiple range test was used for the statistical comparisons.

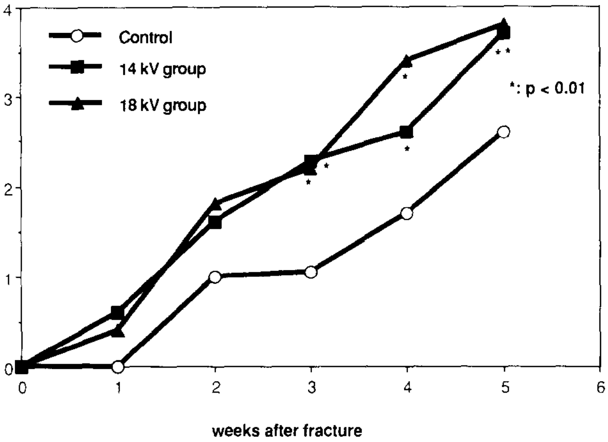

FIGURE 2. *X-ray readings.*

Results

No significant differences were found in the body weight or in the wet bone weights of both humeri between the groups. The fractured bone was uniformly 80- to 110-μg heavier than the normal bone in the treatment and the control groups. The fractured humeri in the control group broke at an average stress of 12.7 kg (standard deviation 4.2). The breaking strength of the fractured humeri in the treated groups was 12 percent and 30 percent, respectively, higher than in the control groups. However, this did not prove to be significant.

Representative x-ray films for the control group and the 18-kV-treated group are shown in Figure 1. The x-ray readings revealed radiologic signs of faster healing in the treated groups (Fig. 2). These were performed individually and blindly by two trained radiologists and two other physicians, with only minor differences

TABLE I. *Calcium-45 uptake* of the broken and contralateral humerus: average (Av) and standard deviation (S.D.)*

Bone		Control	14 kV	18 kV
Broken	Av	624	386	465
humerus	S.D.	51	204	214
Normal	Av	503	367	449
humerus	S.D.	66	197	198

*Counts/μg bone.

noted among the four readings. The radiographic differences are significant after three or more weeks ($p<0.05$ in first experiment, $p<0.01$ in second experiment). The average calcium-45 uptake in the fractured bones was 124 percent of the uptake in the normal humeri in the untreated group, but only 105 percent in the 14-kV and 104 percent in the 18-kV-treated groups (Table I).

Histologically no striking differences could be found between the two groups, some findings should be noted: while in one of the treated humeri the fracture was completely healed, the other treated humerus still revealed more fibrous tissue at the fracture site and partly immature bone. In neither sample was hemorrhage or necrosis found. One of the control humeri showed an inconspicuous, almost completely healed fracture, while the other one represented an immature phase of fracture healing with considerable amounts of cartilage and fibrous tissue. In summary, neither control nor treated samples showed hemorrhage or necrosis, nor significant decreases of hematopoietic cells. Showing only slight differences, the treated samples appeared to heal better.

Comment

The results indicate a positive effect of shock waves on fracture healing. Significantly better radiologic healing, stronger mechanical stability, and some morphologic indices in the treated groups suggest enhanced fracture healing. After five weeks the peak of remineralization is passed. The lower calcium-45 uptake results of the treated bones shown on x-ray film may be interpreted as already normalized remineralization, while in the control group these are still in a phase of higher mineralization activity. The histologic readings prove that neither necrosis, hemorrhage, nor bone marrow suppression are visible five weeks after inflicting the fracture or two weeks after the last shock wave treatment, negative effects, which might have been expected after shock wave treatment.

Although these are encouraging results, there is some criticism. Due to the method of fracture infliction the reproducibility of the fractures is not optimal. This leads to greater variability in the results, especially in the breaking strength. Also it was difficult to define and isolate the callus macroscopically after sacrifice of the animals. We believe that this reflects the difficulty of obtaining similar volumes of callus. Therefore, further studies should define a model that provides a homogeneous, highly reproducible and stable fracture, which allows secure isolation of the callus.

Since these first experiments, especially in the radiologic findings, strongly suggest there is improvement of fracture healing by shock waves, two questions arise: what is the optimal dosage with reference to timing and number of treatments, as well as number and generating voltage of the shock waves, and what mechanisms are responsible for the enhancement of fracture healing by shock waves. The dosage and mechanism questions shall be addressed with a new model in future investigations. However, the present method has been granted a U.S. patent,[18] and the first clinical applications for the treatment of pseudarthrosis in our and other institutions have been successful (80% improvement, 50% complete healing).[19]

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