

# **Nitric oxide mediates osteogenic factors in shockwave-promoted bone healing of long bone non-union**

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## **Device and producing company:**

Ossatron (SANUWAVE, USA)

## **Introduction:**

The mechanism of shockwaves in treating non-unions remains unknown. Many studies demonstrated that nitric oxide (NO) may play an important role in mediating shockwave-stimulated bone healing. This study investigated the biological role of NO in mediating shockwave-promoted osteogenic signals in long bone non-unions.

## **Methods:**

Thirty-three patients with 34 non-unions of long bones were included in this study. There were 18 men (19 non-unions) and 15 women (15 non-unions) with an average age of 36.5 years. Each non-union bone was treated with 6000 shockwave impulses at 28 KV ( $\approx$  0.62 mJ/mm<sup>2</sup> energy flux density) applied in 2 planes with equal dosage on each plane. The source of shockwaves is an Ossatron (Sanuwave) device. Evaluations included clinical assessments and radiographs of the affected bone. Ten milliliters of peripheral blood were obtained before treatment and at 1, 3, 6 and 12 months after treatment for measurements of NO levels and osteogenic markers including TGF- $\beta$ 1, VEGF and BMP-2.

## **Results:**

The union rate was 15% (4 of 27) at 3 months and 69% (18 of 26 cases) at 6 months. At 6 months, 18 unions and 8 non-unions were confirmed. The serum levels of NO, TGF- $\beta$ 1, VEGF and BMP-2 between unions and non-unions were analyzed. Statistically significant differences in serum NO level, TGF- $\beta$ 1, VEGF and BMP-2 were noted between patients with bony union and patients with non-union at 1 month ( $p < 0.05$ ). It demonstrated NO modulation of systemic osteogenic factors in shockwave-promoted bone healing in long bone non-union.

## **Discussion:**

Recent studies showed that shockwaves induce NO to promote proliferation and differentiation of human osteoblasts. The results of this study demonstrated that shockwave-promoted bone healing was associated with significant elevations of systemic NO, TGF- $\beta$ 1 and VEGF and a trend of increase in BMP-2.

## **Conclusion:**

Extracorporeal shockwaves are effective in promoting bone healing in non-union of long bones. Nitric oxide (NO) appears to play an important biological role in mediating osteogenic signals in shockwave-promoted bone regeneration in long bone non-union.