The use of microcurrent bioelectric stimulation to reverse erectile dysfunction: A randomized, double-blind, placebo-controlled trial.

Background:

Erectile dysfunction (ED) effects up to 20% of men, and an increasing problem with advancing age. There are many contributing causes of ED, including concomitant use of prescribed medications for health problems including hypertension, or causal diseases such as diabetes. The current treatment includes improved diet, exercise, stress reduction and sleep, but also the use of drugs that are inhibitors of the Phosphodiesterase pathway, which leads to vasodilation in the venous system of the penis to induce erections. These drugs have significant long-term side effects, and are very expensive, prohibiting their use by a large percentage of men with ED.

There are a number of electrical fields in the body, with examples including the electrocardiogram (EKG) and brain encephalogram (EEG). Bioelectric stimulation (BES) utilizes the delivery of precise microcurrents targeted to specific proteins in the tissue being treated that causes upregulation or increased local tissue expression of the protein(s) of interest. The identification of the precise signal for each target protein has taken decades to define and confirm, using quantitative measurements from tissues that were stimulated at various frequencies until the optimal signal was identified. The use of BES has been shown to be very safe, and in fact is being tested as a treatment for cancer. It has been used to induce organ and tissue repair and regeneration in many diseases and conditions, varying from accelerating tooth movement, reversing heart failure, traumatic brain injury and stroke, to enhanced breast milk production, and hair regeneration.

This study follows the very successful demonstration of the absolute safety, and remarkable efficacy, of using functional bioelectric stimulation to treat ED by Carboni and colleagues[1.] Dr Carboni will also serve as the Principal Investigator of this new follow up study. The previous study was a very well designed randomized, sham and placebo-controlled, trial that demonstrated 100 % success in reversing ED with no other intervention in the treatment cohort, while none of the control subjects experienced reversal of ED during the 4 week study period. The bioelectric signal used in the study targeted only a single protein, vascular

endothelial growth factor (VEGF), which has been shown to be one of the most potent inducers of the formation of new blood vessels and improve blood flow.

The goal of this study will be to examine the potentially additive effect of adding a third arm to the previous protocol to include the addition of 4 new target proteins to VEGF including endothelial nitric oxide (eNOS), which regulates endothelial vasoreactivity and should enhance venous vasodilation, stromal derived factor-1 (SDF-1) which stabilizes the blood vessels formed,), insulin-like growth factor (IGF) which is very decreased in ED, and follistatin, which is a potent stimulator of muscle function and contractility leading to enhanced erection, all leading to improved blood flow and reversal of ED.

Study Design: Randomized, double-blind, sham and placebo-controlled
Number of Study Subjects: 30, with 10 subjects in each of 3 groups
Number of Sites: one
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Principal Investigator: Cristiane Carboni, Msc, Physiotherapy
Study Enrollment: No subject will receive treatment until they have had all possible risks and benefits explained by the PI and the Consent Form signed.
Expected Duration of Enrollment: 3 months

Study Arms: 3

Gp I: Control. To receive the same duration of BES in a blinded manner as the other two groups, but no BES delivered.
Gp II: BES at the same current, duration, and frequency as the previous study, and other treatment groups, but targeted to only VEGF.
Gp III: BES of the same duration as all groups, but targeted to not only VEGF, but to 4 additional proteins (eNOS, SDF, IGF, and Follistatin).

Treatment:
Number of total treatments: 8
Frequency: twice/week for 4 weeks
Duration of treatment: 20 minutes/treatment
Stimulator to be used: Commercially approved stimulator, either the oneused in the previous study conducted by Carboni et al[1.] for this indication (Neurodyne), or

other commercial approved stimulator that is confirmed to be able to reach the signals required for the additional protein targets.

Method of Delivery of stimulation: Simple patch electrodes applied to the dorsum of the penis and connected to the bioelectric stimulator. The current will be slowly increased from zero to the specific current for each protein to be stimulated.
The stimulator will be controlled by a medical assistant who will prevent the subject from seeing any adjustment of current, with no presence of the PI or Co-PI's in order to maintain the double blind of the study design. Care will be taken to assure each subject receives the same duration of actual or pretend stimulation to maintain the blind for each subject in the study.

End Points:
1. Reversal of self-assessed ED compared to baseline on a scale of 1-5.
2. Adverse events including pain, local skin irritation, or difficulty with urination.
3. Serum Testosterone levels will be measured in 3 randomly selected subjects in each of the three treatment groups at baseline, one hour after a treatment following 2 weeks of study, and at the end of the study. These blood levels are to examine the potential role of BES in stimulating increased testosterone production, and a possible role in ED reversal.

Data Analysis:
Patients will be seen by the PI or sub-investigator at the time of study enrollment, the mid-point(2 weeks), and end of the study (4 weeks) to assess any adverse events. However each subject's self-assessment of the degree of reversal of ED will be collected by a person blinded to treatment assignment to prevent bias in data analysis.

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