Reversal of Deep Tissue Injury using Intermittent Electrical Stimulation

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Abstract

Deep tissue injury (DTI) is a dangerous form of pressure ulcer as it causes substantial subcutaneous damage before being detected. There are currently no practical and reliable forms of early detection or reversal of DTI. We propose the use of intermittent electrical stimulation (IES) to reverse the injury before it reaches the skin. Adult rats with spinal cord injury were used to assess the effect of IES on early DTI. The rats were randomly divided into two groups, the experimental group which received IES and a control group that did not receive the intervention. A DTI was produced using 20kPa of pressure applied to the triceps surae muscle of one leg. Twenty-four hours later the experimental rats were treated with IES for 2 hours, with stimulation delivered to the triceps surae muscles every 10 minutes for 10 seconds through a nerve cuff. The control rats underwent the same nerve cuff implantation procedure but without IES. A visible trend of reduced edema was seen in the loaded muscles of the IES group; however, given the small sample size, this difference was not statistically significant from the control animals. This work offers direction for the use of IES in the reversal of DTI early on in its stages of development.

Keywords: deep tissue injury, intermittent electrical stimulation, reversal

Introduction

Pressure ulcers are a huge burden on the health care system and are a constant concern for those with reduced mobility. Pressure ulcers cause increased length of hospitalization, additional surgery and lead to secondary infections that can be terminal. In the United States there are an estimated 60,000 deaths a year due to complications related to pressure ulcers1. There are also fiscal concerns as a single pressure ulcer can cost from $15,800 to $72,680 to treat 2. Annually the treatment of hospital-acquired ulcers costs > $11 billion in the United States1. Pressure ulcers cause a large decrease in quality of life of the patient. Despite the seriousness of the problem, existing technologies have not changed the incidence rates of pressure ulcer over the past half century3. With the recent change in American insurance policies on pressure ulcer reimbursement there is a greater push to find a solution4.

There are two major categories of pressure ulcers. One form of pressure ulcers develops from the skin and works its way towards the bone and they are often caused by poor skin condition, moisture and friction5. The second form of pressure ulcer, deep tissue injury (DTI), is caused by pressure at the bone-muscle interface that leads to the degradation of the muscle with very little change in the skin condition6. The damage to the muscle is caused by both mechanical stress and ischemia-reperfusion, leading to apoptosis and necrosis of the muscle cells6. The populations at risk of contracting a DTI are those with reduced mobility and sensation including those with spinal cord injuries, stroke, as well as intensive care unit patients and those in long-term care7.

Current treatment of DTI does not occur until the injury has reached the skin. The area is completely relieved of pressure through weight shifts and specialized cushions until the wound is fully healed8. The wound is treated with various wound dressings to keep it moist, free of infections and encourage tissue re-growth9. In extreme cases debridement is performed and muscle flap surgery is used to reseal the wound9.

Recently our laboratory has demonstrated that electrical stimulation can be used to prevent DTI in loaded muscle when applied every 10 minutes for 10 seconds. Throughout the period of loading intermittent electrical stimulation (IES) relieves the pressure through pressure redistribution and increases blood flow to the tissue delivering important nutrients10. We hypothesized that IES may also be used to reverse existing DTIs before they had reached the surface using the same mechanisms.

Materials and Methods

Experiments were performed in 14 female adult Sprague Dawley rats (301g ± 20g). All procedures were approved by the University of Alberta animal care and use committee.

SCI surgery

Initially, the experiments were conducted in non-spinal cord injured rats; however, it was noticed that the leg movements of the rat were equivalent to the treatment of IES. The two hours of extra stimulation were not enough to create a significant difference relative to the 46 hours of free movement performed by the rats; therefore, experiments were repeated in rats with spinal cord injury (SCI). A complete transection of the spinal cord was performed 2 weeks before the initiation of the DTI reversal experiment. Under isoflurane (2%) anesthesia, a laminectomy was performed on the 7-8 thoracic vertebrae and the spinal cord was completely cut at T8-9. The muscle layers and skin were then sutured closed. Baytril (enrofloxacin, 5mg/kg), a bactericide, was used to prevent and treat urinary tract infections and Temgesic (buprenorphine, 0.05mg/kg), a strong opioid analgesic, was used to control any potential pain and discomfort associated with the procedure. Rats had their bladders manually expressed two to three times a day.

Reversal of DTI

The reversal of DTI experiments were conducted over 3 days after the muscles of the hind limbs had atrophied. A DTI was produced by delivery of 20kPa through a 5mm indenter to the triceps surae muscle of one leg. This pressure related to the maximal pressure at the sacrum seen when sitting on a hard surface10. Pressure was applied for 2 hours under isoflurane anesthesia.

The rats were then randomly assigned to one of two groups, one that received the IES treatment (n=5) and a control group that did not receive IES (n=5). IES was delivered through nerve cuffs placed on the tibial nerve. Nerve cuffs were used rather than surface electrodes.
because the movement between the skin and the muscle in rats is large which compromises the stability of evoked contractions. Twenty-four hours after the induction of the DTI, surgery was performed to implant the nerve cuff and the treated group was stimulated every 10 minutes for 10 seconds (50Hz, 100µs, charge balanced and constant current between 1-2mA) for 2 hours. The control group underwent the same surgery and was under anesthesia for the equivalent amount of time but electrical stimulation was not delivered. The rats’ legs were then sutured closed and the rats were placed in their cages for recovery.

MR Image Analysis

Twenty-four hours after the removal of the nerve cuff, the rats were anesthetized with sodium pentobarbital (intraperitoneally, 45mg/kg). The extent of edema, an early indicator of tissue injury, was examined using magnetic resonance imaging (MRI) in a 3.0T magnet, a custom-built 8 cm birdcage coil and a T2-weighted spin-echo sequence (TE 80ms)(Figure 1). Rats were then perfused and the triceps surae muscles were extracted and stored in formaldehyde for later histological analysis. The spinal cord tissue around the injury site was collected for analysis of injury level and completeness.

The edema in the muscle was determined from the MR images. Correlation between the edema and muscle injury was established in previous studies\(^\text{10}\). The percentage of edema within the MR muscle images was analyzed using a custom Matlab code. The contralateral leg was used as an internal control to calculate an average signal intensity (SI) of the muscle without DTI. The SI in the experimental leg’s image was then compared to the average SI in the contralateral leg. Any pixels with SI above the average plus 3 standard deviations were considered to contain edema. The extent of edema in the experimental leg was then expressed as a percent of the muscle volume (figure 2).

Figure 1. A sample of the MR images collected from a treated rat (4% edema) and a control rat (19% edema).

Figure 2. Diagram showing the anatomical position of the image slices collected by the MRI and used for the analysis (6 slices, 2mm each).

Edema from only IES

An experiment was also performed to ensure that the IES did not damage the atrophied muscle. The experiment, on 3 rats with SCI, followed the same IES procedure as above; however; there was no induction of a DTI. To ensure that a moderate amount of force was generated the foot pulled on a force transducer and the current was adjusted to get 50% of the maximum force.

Change in DTI edema over 24 hours

One non-spinal cord injured rat was used to collect preliminary data on the reduction of edema between 24 and 48 hours without any IES. A DTI was induced for 2 hours with a 3mm indenter, to mimic past experiments\(^\text{10}\), and then the rat legs were imaged 24 and 48 hours after DTI induction.

Results

Our goal was to determine if IES could reduce the extent of an existing DTI that had not developed into an open wound. Edema in the loaded muscles of the treated animals with SCI occupied 7.81 ± 2.12% (mean ± standard deviation) of the muscle volume. In comparison, edema was seen in 12.47 ± 9.18% of the muscle volume in control animals. Interestingly, high variability was seen in the extent of edema in the control animals (edema varied from 1.40% - 24.2%). A two tailed unequal variance t-test resulted in p=0.15, indicating a trend but no statistical significance in the extent of edema between the experimental and control rats.

Figure 3. The average percentage of muscle volume exhibiting signs of edema in the control and experimental hind legs of the rat. The bars represent the standard deviation.

The use of IES at levels producing moderate contractions (50% of maximal force) in 3 animals with SCI, but no DTI, did not cause any significant damage. The resulting “edema” was 1.1 ± 2.4%.

In an animal with intact spinal cord, 24 hours after the induction of DTI, edema was seen in 19.0% of the muscle; however; at 48 hours this dropped to 15.3%.

Discussions

The results show a trend towards IES decreasing the amount of edema in muscles with a DTI that has not reached the skin.

The rats treated with IES demonstrated a consistent level of edema; however, the control animals had a large variation in the level of edema within the muscle. The injury caused by 2 hours of pressure in the rats may heal without any intervention after several days since the loading is not persistent (unlike clinical scenarios). This is seen in the decrease of the edema between 24 hours and 48 hours in the intact
animal. Despite this decrease in edema the variation in the control groups was unexpected. It may be that individual muscle healing rates vary greatly even in a genetically identical population. Interestingly, with two hours of IES a more consistent healing rate appears to be produced, although the mechanism is unknown.

A moderate amount of IES was found to not damage the atrophied muscle, supporting the safety of IES for patients with reduced mobility.

The use of IES as a reversal method for early DTI is a part of a larger project in which early detection is also being investigated. The only current reliable way of detecting DTI is through MR imaging; however, this is cost prohibitive and time consuming to be a regular practice for those at risk. There has been investigation into the use of ultrasound and specific biomarkers from blood samples. We believe that if an early DTI is detected, treatment would be initiated early, likely using the IES system already in development, Smart-e-Pants.

**Conclusions**

Although the use of IES to reverse DTI is only in its early stages of investigation, it appears to be a promising technique to fill an otherwise large gap in the clinical practice of DTI treatment.

**References**


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