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Extracorporeal Shock Wave Therapy (ESWT) as a treatment for recurrent Neurogenic Heterotopic Ossification (NHO)

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Abstract

Background/Objective

To describe the effects of extracorporeal shock wave therapy (ESWT) on a patient many years post traumatic brain injury (TBI) who suffered from recurring Neurogenic Heterotopic Ossification (NHO) around the hip joint.

Case Description

The case study describes a 43 year old female, who sustained TBI about 10 years before she had new complaints concerning recurrence of NHO at the hip joint. The patient was unwilling to walk more than 10 metres due to pain and limited movement. Pain was rated as 9 out of 10 on the Visual Analogue Scale (VAS).

Intervention

Four applications of ESWT using a Minispec™ Extracorporeal Shock Wave Lithotripsy machine (Medispec Int. USA) administered over six weeks to the anterolateral aspect of the patient’s (R) hip.

Outcome

Following treatment, pain was reduced to 0 on the VAS scale; there was increased range of motion at the hip joint, increased step length and improved walking. At five month follow-up, without further ESWT intervention, these results were maintained.

Conclusion

This case study suggests that ESWT may be a non-invasive, low risk intervention for the management of NHO.
Introduction

Neurogenic heterotopic ossification (NHO) is the term used when heterotopic ossification is associated with central nervous system (CNS) injury or disease. NHO is a localized and progressive formation of pathological ectopic bone mainly located in the soft tissue at major synovial joints [1-4]. It occurs more commonly in patients with traumatic brain injury and spinal cord injury than in patients with stroke [1, 3-5]. The reasons for which have not yet been confirmed [6].

NHO was reported as early as 1918 in the joints of patients with spinal cord injury [7]. In the following decades its connection with spinal cord injury and other CNS injuries became well established [1-5]. The reported overall incidence of NHO in spinal cord injured patients varies from 11-53% [8] and in closed head injury from 10-20% [1] depending upon patient population, diagnostic method and research methodology [1-3]. The hip joint is the most common location followed by the knee and elbow. A single joint is affected in 40% of patients; in another third, two joints are affected. NHO begins within two months of a neurological injury and the process is usually complete by two years [1, 9].

The aetiology of NHO is still largely unknown. McCarthy and Sudaram [4] maintain that four factors are necessary for its pathogenesis: i) trauma ii) a signal from the site of injury, most probably a protein secreted from cells in the injured tissue iii) a supply of non-specific mesenchymal cells and iv) an appropriate environment conducive to the continued production of heterotopic ossification. Chauveau et al [10] demonstrated that significant differences exist in genetic expression patterns between cells from normal and heterotopic bone. Overexpression of osteocalcin, osteonectin and type 1 collagen mRNA levels could be associated with the high activity of this pathological bone [10]. Other factors which may also contribute to the formation of NHO include microtraumatic lesions, immobilisation, infection, pressure ulcers and vasomotor disturbances [11]. Passive manipulation of joints has been suggested as a possible cause [12, 13] with the implication that forcible ranging of joints can cause microtrauma and haemorrhages, which may increase NHO formation [5, 14]. Other studies have, however, shown a favourable effect of active and passive exercising of joints within the pain free range [6, 9, 15].
NHO can result in a variety of complications, including nerve impingement, joint ankylosis, complex regional pain syndrome, osteoporosis, and soft tissue infection. The associated decline in range of motion may greatly limit activities of daily living, such as positioning, transferring and maintenance of hygiene, thereby adversely affecting quality of life [2, 7].

According to van Kuijk [9] the pathophysiology of NHO is so poorly understood that early identification and adequate treatment of the presumed risk factors may be considered the best management. Prevention and/or reduction of bone repletion might be gained by using pharmacological intervention in the form of non-steroidal anti-inflammatory drugs (NSAIDs) [16-18]. This may also be followed by radiation therapy [19]. Surgical excision has also been performed but carries with it many unwanted complications such as infection, joint dislocation and pain [2, 20].

Extracorporeal shock wave therapy (ESWT) is an intense, but short, energy wave travelling faster than the speed of sound [21]. The basic mechanism of ESWT is analogous to lithotripsy, the technology that uses acoustic shockwaves to break up kidney stones without surgery, a treatment approach which has been used successfully for more than twenty-five years[22]. ESWT has been used most extensively in Europe, particularly Germany, where the technology originated. It has also been found to encourage bone healing in stress fractures, avascular necrosis and delayed and/or bony non-unions [23-27]. ESWT has been used effectively to treat pain in a variety of musculoskeletal conditions [28, 29] and pain reduction has been shown to benefit both behavioural and cognitive dimensions[30]. Treatment of the musculoskeletal system using ESWT has been found to have virtually no serious side-effects; even mild side effects like tingling, aching, redness, or bruising are relatively rare, modest and short-lived [31].

This case study examines the effect of ESWT in a case of recurrent femoral NHO following traumatic brain injury (TBI.)
Case Study

History

GA is a 43 year old female living in Israel. At the time of this intervention she was more than 10 years post severe TBI following a road traffic accident. Her Glasgow Coma Score on admission was three (3). She was unconscious for more than three months following her injury. Throughout the time she was unconscious she was treated in intensive care, where she had chest physiotherapy and passive movements daily. Also at this time, one month of inhibitory casting was applied to the right elbow, in an attempt to reverse tightness in her right elbow flexors. Following her slow return to consciousness she was moved from intensive care to a rehabilitation ward where physiotherapy, occupational therapy and speech therapy were provided on a daily basis. At this stage, psychological treatment was also introduced, because GA had sustained a severe diffuse axonal injury and had many behavioural issues and cognitive deficits, as well as physical injuries.

After more than 12 months hospitalization with intensive rehabilitation, GA was discharged to live in the community with her parents. Her residual impairments included spasticity and weakness on the right side and ataxia on the left side. She had a mild contracture of the right elbow (5° flexion) and limitation of wrist and finger movements in the right hand due to spasticity and weakness. She was right side dominant. Deep and superficial sensory disturbances were present on the right and left sides of the body. GA walked independently with a walking frame. Her two children lived with their father and his new wife but visited their mother regularly. Over the years there had been substantial improvement in her functional level and abilities and GA now, ten years post injury, was able to live in her own apartment with a 24 hour caregiver.

GA’s behavioural disturbances, as well as limited insight, were noted from the earliest days of her return to consciousness, so she required full supervision during most of her daily activities. During the intervening years she continued to receive rehabilitation in the form of physiotherapy, riding therapy, hydrotherapy and art therapy. She continued to suffer from cognitive, behavioural and motor deficiencies. During the last three years, i.e. from seven to ten years post injury, physiotherapy treatment concentrated on strengthening and mobilizing her right upper and lower limbs, improving balance reactions in sitting and
standing and improving all gait parameters. Although she had regained much movement in her right upper
limb and used it during dual tasks, she still had a preference for using the left hand.

During GA’s initial hospitalisation (2001) it was noted that she had a developing NHO around her right hip
which resulted in decreased range of motion and pain around the hip joint with consequent loss of
function. One year post injury (2002) GA underwent successful surgery for the removal of NHO around the
right hip. Post surgery she resumed physiotherapy, hydrotherapy with the result that the hip joint
movement returned to within normal limits. Pain was between 1 and 2 on the Visual Analogue Scale (VAS).

GA maintained good functional mobility of the right hip over the next six years, but in 2008, (eight years
post injury) she began again to complain of pain around the right hip joint and severe movement limitation
was noted (As seen in table 1). Plane x-rays and MRI revealed that NHO had recurred (As seen in figure 1).

Due to the number of complications that may arise following surgery [20], GA’s treating orthopaedic
surgeon did not consider her to be a suitable candidate for further surgical intervention. Pharmacological
intervention was also not considered since it was well known that GA was not compliant in taking
medication. As a result of the increased pain, GA became unwilling to walk long distances and her low
psychological tolerance levels were causing frequent violent outbursts as observed by her treating
physiotherapist and reported by her caregivers. Since the pain was reducing her functional level to that of a
non-walker, ESWT was considered to be a reasonable treatment option. With the approval of GA, her legal
guardians (parents) and her treating orthopaedic surgeon, a decision was made to apply a novel treatment
approach with ESWT.

Outcome measures

Goniometric measurements of all right hip movements were taken with the patient in supine. The level of
pain experienced by GA was assessed using the visual analogue scale (VAS), and the number of steps
required to cover a distance of 28 metres (the length of the driveway from GA’s car to the physiotherapy
clinic), were counted. All measurements were taken immediately prior to the administration of ESWT and at weekly intervals throughout the six week intervention. Plain radiographs of the hip joint were taken prior to treatment and post treatment. GA’s walking pattern and social behaviours were observed but not formally assessed.

Method

A Minispec™ Extracorporeal Shock Wave Lithotripsy machine (Medispec Int. USA) was used to deliver four applications of ESWT over a six week period to the area of the right hip joint corresponding to the underlying position of the NHO. Treatments were given by YA at the Department of Orthopaedics, Assaf Harofe Hospital. Three thousand shock waves were delivered at each treatment to the anterior aspect of the right hip at the intensity level of 5-6. During the period that GA was receiving the ESWT, all other treatments, including physiotherapy, hydrotherapy, riding therapy and psychology, continued as usual.

Results

Following four treatments of ESWT to the right hip, GA gained range of movement in all planes in the right hip and a longer step length on the right, as demonstrated by a reduced number of steps over a set distance (As seen in table 1). The longer right step length appeared to lead to improved symmetry in GA’s walking pattern compared to her pre-treatment walking pattern. Pain was reduced from 9 to 0 on the VAS following the first application of ESWT. As a result of these improvements, GA was able to walk more efficiently, at a faster speed, for a greater distance and with more stability.

Comparison of X-rays taken pre- and post-treatment showed no major radiographic changes.

(As seen in figure 1)

Five months after treatment, during which time GA had minimal therapy intervention, movements at GA’s right hip were re-measured. She had retained the gains she had previously made, there was no recurrence of pain and her step length continued to increase. The changes in range of movement, pain and function over time are reported in table 1.
Anecdotally, her carers reported an improvement in social behaviours and a decrease in her violent outbursts.

Discussion

The only known, definitive, currently available treatment for NHO is surgical excision. This is a major procedure with numerous associated complications and post-operative recurrence is common [20]. Identification of a non-surgical (invasive) treatment method would, therefore, be valuable in this patient group.

As there were no radiological changes following the four treatment sessions with extracorporeal shock waves, it is possible that the immediate improvement in GA’s ROM and function were related to pain reduction and/or microscopic changes in the ossification and/or fibrotic changes. Wang, in his studies on treatments for osteonecrosis of the hip in 2005 and 2008, also found that there were significant improvements in pain and function of the hip without changes on MRI [26, 27]. Since ESWT has been shown to effectively reduce pain [26-29] and reduction in pain can positively affect behavioural and cognitive responses[30], it is possible that GA’s behavioural responses became more manageable due to a reduction in her pain this in turn leading to an improvement in function.

If the actual size of the mass of bone had not been reduced, what then caused the reduction in pain and allowed an increased range of motion? Since anti-inflammatory medication has been shown to have a positive effect on the signs and symptoms of NHO [16, 32-34], it is possible that the ESWT may exert an anti-inflammatory effect on NHO, which might explain the reduction in pain observed in our case study. In future studies bone scans would be useful in assessing this effect.

Maier et al. [35] reported an increase in the release of substance P within the first 24 hours after application of shock wave therapy, and a decrease six weeks later. This time course closely approximates that of the clinical time course of an initial increase in pain followed by a later reduction after application of shock wave therapy. Although Haake et al. [36] showed no effect of EWST on the spinal nociceptive system, a later study in rats showed that ESWT reduces the expression of calcitonin gene-related peptide (CGRP), a marker of sensory neurons involved in pain perception in dorsal root ganglia [37]. ESWT applied to the rat
footpad caused degeneration and reinnervation of sensory nerve fibres innervating the skin [38]. Murata et al. [39] showed that EWST induced injury of sensory fibres, followed by rapid regeneration. Although both small and large diameter fibres were damaged, a greater proportion of large-diameter fibres were affected. Activity in large-diameter axons modulates nociceptive signals transmitted by small-diameter axons in the dorsal horn [40]. These observations may help explain the analgesic effect of ESWT. Moreover, subsequent applications of EWST have a cumulative effect on sensory fibres, thus providing a longer-lasting effect on pain [41]. Wess [42] has suggested that EWST may disrupt the neural circuitry giving rise to chronic pain and thereby lead to pain relief.

In addition to its anti-nociceptive effect, EWST induces new blood vessels in the region of application, with angiogenic markers being expressed within a week, and vascularisation commencing four weeks post-treatment and continuing for 12 weeks [43]. While angiogenesis promotes healing and pain relief in conditions such as chronic tennis elbow [29] or non-union of long bone fracture [25] the effect of angiogenesis in the case of NHO is yet to be elucidated.

ESWT has been effective in reducing both acute and chronic pain in a variety of orthopaedic pathologies [23-25, 28, 29]. Buselli [44], in a recent paper on the treatment of myositis ossificans with ESWT in sportsmen, concluded that it is the reduction of pain which leads to an increase in function. These findings are supported by our study. Since spasticity was not evaluated quantitatively it is not possible to discern if the effect of ESWT was directly on the pain and/or through reduction of spasticity around the treated joint.

This report actually raises more questions than answers:

1. Why was there a small, yet noteworthy, increase in the range of motion around the hip joint, without reduction of bone mass?

2. What was the mechanism underlying reduced the pain post ESWT?

3. What was the effect post-ESWT that allowed the gains to last for a long time without any further intervention?
The very promising results presented here warrant further investigation with a larger sample of spinal cord and brain injured patients who have developed NHO.

Caption for table: Results

Measurements pre and post treatment

Captions for figures:

Figure 1  X-ray of bilateral hips pre-treatment
Figure 2  X-ray of right hip pre-treatment
Figure 3  X-ray of bilateral hips post-treatment
Figure 4  X-ray of right hip post-treatment
Table 1

Results:

Measurements pre- and post treatment.

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<th>Post-treatment</th>
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<td></td>
<td>Number of Steps over 28 metres</td>
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</tr>
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</table>
Radiographs taken before and after treatment with ESWT

Figure 1
Pre Treatment

Figure 2

Figure 3
Post Treatment

Figure 4