International Journal of PharmTech Research
CODEN (USA): IJPRIF, ISSN: 0974-4304, ISSN(Online): 2455-9563
Vol.9, No.5, pp 46-52, 2016

Efficacy of Extracorporeal Shock Wave in the Treatment of Heterotopic Ossification in Burned Patients

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Abstract: Purpose: to determine the effect of extracorporeal shock wave therapy (ESWT) in the treatment of heterotopic ossification in burned patients. Methods of evaluation (Assessment of pain via the visual analogue scale and size of heterotopic ossification measurement via the computed tomography). **Methods:-** Thirty patients male and female with post burn heterotopic ossification participated in this study, their ages ranged from 30 to 50 years old, they were divided randomly into two equal groups (A and B) .Group (A) received extracorporeal shock wave therapy plus medical treatment every two weeks for three sessions, while group (B) received traditional medical treatment only. Both groups were assessed by visual analog scale to measure the level of pain and C.T to assist the size of heterotopic ossification before and after treatment. **Results and conclusion:-** Results showed that application of the extracorporeal shock wave therapy had a valuable effects on heterotopic ossification in burned patients as evidenced by the highly decreases of pain via the visual analogue scale and size of heterotopic ossification measurement via the computed tomography.
Key words (Extracorporeal shock wave therapy, Heterotopic ossification in burned patients , Visual analogue scale and Computed tomography).

Introduction:

Heterotopic ossification (HO) is the formation of new bone in tissue which do not normally ossify)when it occurs around a joint it is usually referred to as periarticular ossification. HO is a rare but well-known complication of burns, occurring in 1% to 3% of such patients. HO is defined as the formation of lamellar bone inside soft tissue structures where bone normally does not exist. Myositis ossificans refers rather to a condition in which ectopic bone is formed within muscles and other soft tissues. Three types are distinguished: myositis ossificans circumscripta, myositis ossificans progressiva and localized traumatic myositis ossificans. Ectopic calcification is a mineralization of soft-tissue structures, which usually follows chemical or physical trauma[1,2,3].

Myositis ossificans and HO are fundamentally different. An important step in the ossification process is fibroblastic metaplasia. Histological studies clearly demonstrated a zone of fibroblastic proliferation, followed by chondroblasts, which eventually transformed into osteoblasts with blood vessels and Haversian canals. In HO mature lamellar bone is observed peripherally, surrounded by a capsule of compressed muscle fibres and connective tissue. Oedema, hypersensitivity, muscle necrosis, and osteoporosis around HO are consequences rather than causes of HO. It is suggested that bone forms in connective tissue between muscle planes and not in the muscle itself. The new bone may be contiguous with the skeleton, but does not involve periosteum. Mature HO shows cancellous bone and mature lamellar bone with blood vessels and bone marrow, with only a small amount of haematopoiesis [4,5].

The precise pathophysiology behind heterotopic ossification is still unclear but is thought to be related to both local and systemic factors causing osteoblastic differentiation of pluripotent mesenchymal stem cells. The most recent work has focused on BMP signaling and identification of progenitor cells responsible for ectopic bone formation. Much of our understanding has come from the work of Drs. Eileen Shore and Frederick Kaplan investigating fibro dysplasia ossificans progressiva, a rare genetic disease characterized by heterotopic bone formation. Patients with this congenital disorder have a mutation in the ACVR1 gene that causes constitutive activation of BMP type-I receptor activity and formation of ectopic bone. In those who have sustained a thermal burn, the elbow appears to be the most commonly involved joint resulting in marked limitation of movement which is often associated with compression of the ulnar nerve. Physical therapy has been shown to benefit patients suffering from heterotopic ossification. Pre-operative physical therapy can be used to preserve the structures around the lesion. Range of motion and strengthening exercises help in preventing muscle atrophy and preserve joint motion[6,7].

The term "shock wave" denotes a high-energy sound wave that terminates in a bursting of energy similar to a mini-explosion. It is essentially the same as a super-sonic jet breaking the sound barrier and creating an energy force strong enough to shatter windows. ESWT utilizes a high peak pressure ranging from 5 to 130 Mpa, with a Physical properties of the extracorporeal shock wave. Of this unique form of energy is the rapid initial rise in pressure amplitude (500 bar) over short life cycle of less than 10 ns. Radial extracorporeal shock wave therapy rESWT has been introduced into medicine as an effective and easy method to apply shock wave technology. It represents an alternative to focused shock wave treatment, allowing for a broader application. Radial shockwaves are generated ballistic ally by accelerating a bullet to hit an applicator, which transforms the kinetic energy into radially expanding shock waves compared with these radial shock waves, the focused shock waves show deeper tissue penetration with significantly higher energies concentrated to a smaller focus[8, 9].

In an effort to decrease patient morbidity and health care costs, the use of noninvasive methods, such as the extracorporeal shock wave therapy (ESWT), seems to be a valuable alternative in the treatment of delayed union and nonunion. ESWT has been suggested for the treatment of various musculoskeletal disorders such as plantar fasciitis, lateral epicondylitis, calcifying tendinitis, and avascular necrosis of the femoral head. The exact pathway by which ESWT may exert its effect on bone healing remains the subject of ongoing experimental investigations. The aim of this article is to provide a concise review of the basic science of ESWT on fracture healing and to systematically review the current evidence in the literature for the use of ESWT in the treatment of fractures and delayed union/nonunion[10,11].

The effect of ESWT on fracture healing in vivo has been investigated in numerous studies using different animal models. Although some investigators did not observe any positive effects of ESWT on bone healing in their in vivo models, numerous authors reported a stimulating effect of ESWT on bone formation in vivo using different animal models. Further investigations using fracture models in rats, rabbits, and dogs showed increased callus formation, decreased healing time, and increased mechanical strength of broken bones with exposure to ESWT[13,14].

Radiography, magnetic resonance imaging (MRI) and computed tomography scan (CT) have low specificity in the early stage of HO. Before surgery, MRI and CT are valuable to assess the relation with blood vessels and peripheral nerve structures. Angiography is rarely used for the diagnosis of HO, but may aid in delineating important vessels in case of massive HO. Early identification of patients with heterotopic ossification can be difficult. The natural history of heterotopic bone formation is not well defined and depends largely on etiology. Usually, heterotopic bone will begin limiting joint range of motion in the first two months after injury or surgery but can also first present over a year after original insult. The most common clinical signs are fairly nonspecific, such as pain, erythema, swelling, and warmth of the affected joint. Because many of these patients have suffered neurologic insult, their cognition may be impaired, further obscuring the clinical diagnosis. In patients with impaired levels of consciousness, the clinician is often obligated to rule out other diagnoses such as infection, deep vein thrombosis, and osteomyelitis. Nonetheless, the diagnosis of heterotopic ossification should be considered in those patients with known risk factors for development[15,16,17].

Material and Methods

Subjects:

This study was carried out on thirty patients male and female with post burn heterotopic ossification participated in this study, their ages ranged from 30 to 50 years old, they were divided randomly into two equal groups (A and B) .Group (A) received extracorporeal shock wave therapy plus medical treatment every two weeks for three sessions, while group (B) received traditional medical treatment only. Both groups were assessed by visual analog scale to measure the level of pain and C.T to assist the size of heterotopic ossification before and after treatment.

Instrumentation:

In this study the measuring equipment and tools were the visual analogue scale to assess pain level and the computed tomography to measure size of the heterotopic ossification, while the therapeutic equipment was the extracorporeal shock wave therapy (ESWT), that generated by the two electro-hydraulic systems, Evotron or Ossatron (Milano, Italy) OSA 140by HMT srl, in according with the guidelines of the Inter-national Society of Medical Shock Waves Therapy (ISMST)[18,19,20].

Procedures

Evaluation:

1- Visual Analogue Scale (VAS): The pain level was assessed by visual analogue scale (VAS) before starting treatment (first record) then after one month and half (6 weeks) (as second final record). The visual analogue scale (VAS) consists of a line, usually 10 cm long, whose ends are labeled as the extremes of pain (e.g., no pain to unbearable pain). Patient was asked to place a mark at the point on the line which best represent his experience of pain between two "no pain" to "worst pain", then the operator measured the distance from the zero "no pain" in centimeters[21,22].

2- Computed tomography Scan (CTS): The role of CT in the diagnosis of soft tissue masses has been diminishing. CT is still widely used in the current clinical practice of some institutions depending on the referring physicians. This is probably due at least in part to the introduction of high speed multi slice CT, which has improved accessibility**.** CT of the affected elbow with three-dimensional (3-D) reconstruction was routinely performed in order to assess the site and extent of the HO, All the aforementioned parameters (VAS and the CTS) were measured 2 times; the baseline record that was taken before starting of the study, the second record was taken after one month and half (6 weeks) from the starting of the study (as second final record)[22, 23].

1- Treatment procedures of the ESWT:

The ESWT was generated by two electro-hydraulic systems, Evotron or Ossatron (Milano, Italy) OSA 140by HMT srl, in according with the guidelines of the Inter-national Society of Medical Shock Waves Therapy (ISMST). The skin region was put in direct contact with the shock waves generation tube, after applying ultrasound gel. Using an X-ray image in scale1:1, the area of ossification was outlined on the skin region and administered 100 impulses per cm2 of ossification, every 2 weeks for three sessions. The shock waves were performed without an aesthesia, the medium power was applied, so the pain was well tolerated (range from 0.13 to 0.23 mJ/mm2, mean 0.15 60.02 mJ/mm2), on the basis of the energy flux density (EFD) used in the treatment of calcified tendons[19,20,21,22].

Data analysis:

Visual analogue scale (VAS) and size of the heterotopic ossification via the computed tomography scan (CTS), were measured pre-treatment as a first record and after one month and half (6 weeks) as a second final record in both groups. Collected data were fed into computer for the statistical analysis; descriptive statistics as mean, standard deviation, minimum and maximum were calculated for each group. The t-test was done to compare the mean difference of the two groups before and after application and within each group. Alpha point of 0.05 was used as a level of significance[24,25].

Results

As shown in table (1) and figure (1), the mean value of the VAS before treatment was (8.633 ± 0.166) degrees in the study group, while after treatment was (2.200 ± 0.221) degrees. These results revealed a highly significant reduction in VAS ($P < 0.0001$). While in the control group, the mean value of the VAS before treatment was (8.630 ± 0.162) degrees, while after treatment was (8.628 ± 0.158) degrees. These results revealed non-significant difference in the VAS ($P > 0.05$).

Table (1): Comparison of the mean values of the VAS in degrees before and after treatment in the study and control groups

	Before treatment		After treatment		Mean difference	T-value	P.value	Level of significance
	Mean	SD	Mean	SD				
Study Group	8.633	0.166	2.200	0.221	6.43300	90.14	0.0001	Highly significant decrease
Control Group	8.630	0.162	8.628	0.158	0.002000	0.03	0.973	Non-significant

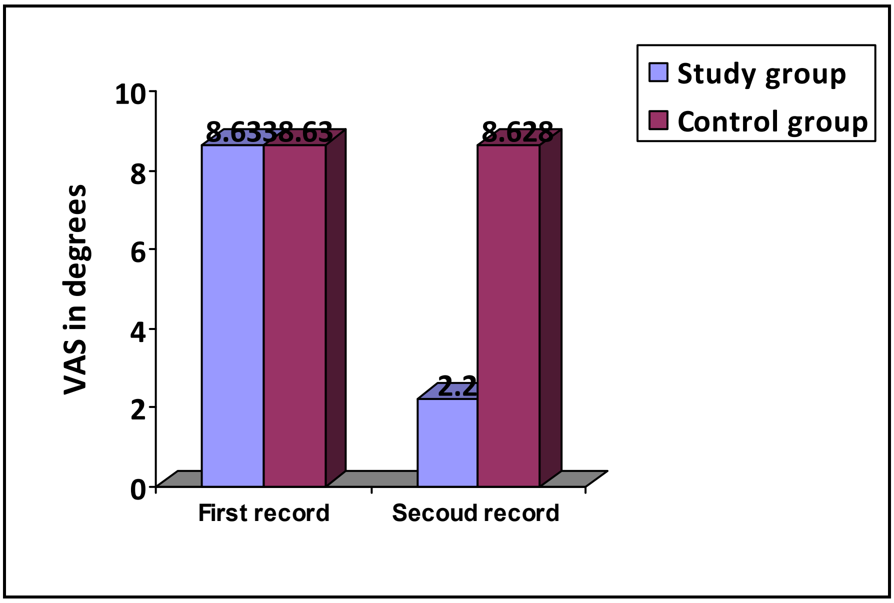

Fig (1): Mean values of the VAS before and after treatment in both groups.

As shown in table (2) and figure (2), the mean value of size of the heterotopic ossification via the computed tomography scan (CTS) in cm before treatment was (1.98 ± 0.34) cm in the study group, while after treatment was (0.88 ± 0.19) cm. These results revealed a highly significant reduction in size of the heterotopic ossification ($P < 0.0001$), while in the control group, the mean value of size of the heterotopic ossification via the computed tomography scan (CTS) in cm before treatment was (1.99 ± 0.36) cm, while after treatment was (1.96 ± 0.34) cm, these results revealed non-significant difference in the size of the heterotopic ossification via the computed tomography scan (CTS) in cm ($P > 0.05$).

Table (2): Comparison of the mean values of the size of the heterotopic ossification via the computed tomography scan (CTS) in cm before and after treatment in the study and control groups

	Before treatment		After treatment		Mean difference	T-value	P.value	Level of significance
	Mean	SD	Mean	SD				
Study group	1.98	0.34	0.88	0.19	1.10000	10.94	0.0001	Highly Significant decrease
Control group	1.99	0.36	1.96	0.34	0.03000	0.23	0.816	Non-significant

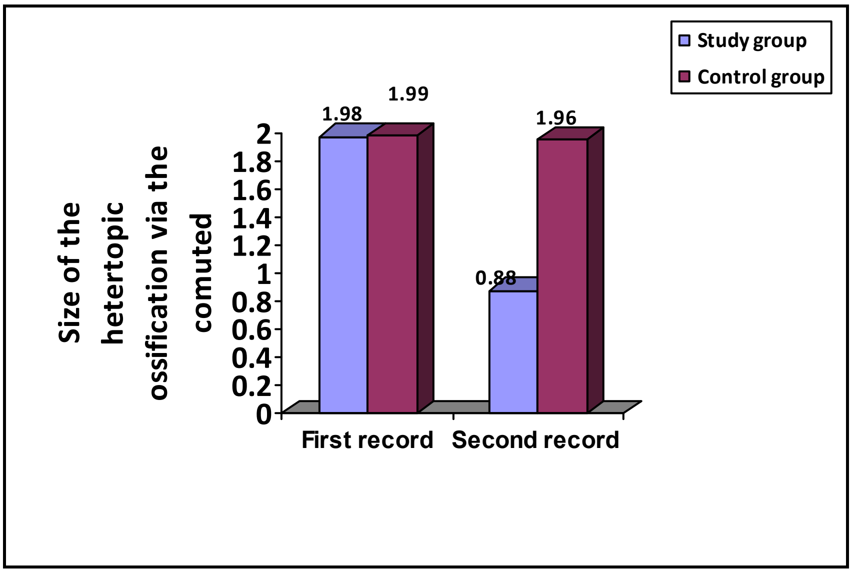

Fig (2): Mean values of size of the heterotopic ossification via the computed tomography scan (CTS) in cm of the 2 records in both groups.

Discussion

Heterotopic ossification (HO) is defined as the anomalous formation of lamellar bone in extra skeletal nonosseous tissues such as muscle, fascia, or cartilage. This ectopic bone formation is thought to arise from the transformation of resident undifferentiated mesenchymal cells down an osteoblastic lineage**.** Clinically, HO can develop in several clinical scenarios of trauma, including blast and burn injuries. Although the overall incidence of HO in all burn patients is less than 5%, this number increases to more than 50% in major burn injuries and more than 60% of blast injuries[4, 12,21].

Thus, the size of the burn seems to influence heterotopic bone formation. Perhaps, more interesting is the fact that increased burn injury increases the amount of HO both in the region of the burn and remotely. Once this complication arises, patients experience severe pain, nerve entrapment, joint contractures, and stiffness. After HO is diagnosed by radiography, few treatment options exist and the criterion standard surgical treatments are inadequate, often leaving patients with residual contractures and a high rate of recurrence after surgical intervention[12, 19].

Despite advances in our understanding of the pathways involved in HO, few treatment options have resulted from these studies because these models require mutant mice that do not correlate with the true clinical development of HO from trauma. One of the limiting factors to improving treatment modalities has been the absence of animal models that mimic ectopic bone in the setting of inflammation or burn injury. Acquired HO models have focused on implantation of osteogenic compounds such as BMP-containing scaffolds or biomaterials with calcium phosphate[13,14,15].

Although much has been written about heterotopic ossification it is clear that as yet there is no clearly defined mechanism for its occurrence. It has a multi-factorial aetiology with several risk factors identified which pre-dispose to its formation. Trauma is a constant feature and in the case of head injury, traumatic damage to the brain. Other general factors have been identified from studies of patients undergoing total hip arthroplasty who have developed heterotopic ossification. It is uncertain whether these risk considerations play a significant role in patients with head injuries[1,6,17, 18, 19].

Extracorporeal Shockwave Therapy is used to treat a growing number of tendon, joint and muscle conditions. These include tennis elbow, where results in double blind studies are reported as excellent. Chronic tendinitis of the knee and shoulder rotator cuff pain**.** Achilles tendinitis, hamstring tendinitis**.** Plantar fasciitis are also treated successfully, the above conditions are often difficult to treat using other methods and can become chronic. With ESWT patients report reduced pain and faster healing, without significant adverse side effects. However, the treatment has proven challenging to verify categorically in large controlled studies, in part because the therapist and patient are aware whether or not they are in the treatment cohort or the sham cohort. ESTW is also used to promote bone healing and treat bone necrosis[18,19,20,21].

The findings of the present study showed non-significant differences in the pre-treatment records of both VAS and size of the heterotopic ossification via the computed tomography scan (CTS) in cm between the mean values of the study and the control groups.

Results of the study group revealed a highly significant decrease in the mean values of both VAS and size of the heterotopic ossification via the computed tomography scan (CTS) in cm, after application of the ESWT, when compared against the pre-application results.

Significant differences showed in the study and control groups were consistent with those observed and recorded by[4,5,6,5,9,10,11,13,21,22,25].

Results of this study support the expectation that application of the extracorporeal shock wave therapy (ESWT) had a valuable effects on heterotopic ossification in burned patients as evidenced by the highly decreases of pain via the visual analogue scale and size of heterotopic ossification measurement via the computed tomography.

Conclusion

Application of the extracorporeal shock wave therapy (ESWT) had a valuable effects on heterotopic ossification in burned patients as evidenced by the highly decreases of pain via the visual analogue scale and size of heterotopic ossification measurement via the computed tomography.

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