ULTRASOUND FOR TREATMENT OF PAIN FROM VARIOUS SOURCES

Literature Review – prepared by NanoVibronix

Background

Pain is one of the most common conditions that hinder quality of life of vast populations of patients on a regular basis. Pain related complaints are the most common reason patients seeking treatment from physicians. There are two major types of pain: acute and chronic. Acute pain plays an important role as the body's alarm system sending signals alerting the patient to possible injury or malfunction, (e.g inflammation).This adaptive mechanism protects an individual from further injury (1). Unlike acute pain, chronic pain serves no useful purpose and may cause disability and distress to sufferers and their families. Estimates of the number of people with chronic pain vary widely depending on severity and whether medical help is sought. According to Bennett (2) incidence of common types of neuropathic pain in the United States alone stands approximately at 3.8 million sufferers.

Because 40% to 50% of patients in routine practice settings fail to achieve adequate relief, chronic pain is now considered to be a public health concern of major proportion (3). The annual cost of chronic pain within the USA including medical expenses, lost income and lost productivity, is an estimated $100 billion (4). Many types of chronic pain disorders, also referred to as neuropathic pain syndromes, have been identified. These may be classified as either peripheral or differentiation in origin. The former type is of particular relevance to the scope of this brochure and includes diabetic peripheral neuropathy (DPN), postherpetic neuralgia (PHN), anti-neoplastic therapy–induced or HIV-induced sensory neuropathy, tumor infiltration neuropathy, phantom limb pain, postmastectomy pain, complex regional pain syndromes (reflex sympathetic dystrophy), and trigeminal neuralgia (5).

While pain alleviating medications may provide relief for certain pain disorders their use is often associated with serious disadvantages including drug dependency, side

effects, drug interaction, liver and gastroenterological damage. In addition, according to a recent review, analgesics are useful when there is a specific nociceptive component, but are often of limited usefulness in non-specific or chronic widespread pain (**6,7**).

Alternatively, there are a large number of non-pharmacological pain treatment modalities available, such as Ultrasound (US), transcutaneous electric nerve stimulation (TENS), low level laser therapy, pulse electromagnetic treatment and radiotherapy. Physical modalities are an integral part of inpatient and outpatient treatment of neurological and musculoskeletal injuries and disabilities. They also can assist with and augment the care of patients with cardiac, pulmonary, and developmental disorders.

Ultrasound Diathermy

The term diathermy means "induced heat" and it is a method of heating tissue electromagnetically or ultrasonically for therapeutic purposes in medicine. The Ultrasound Diathermy devices utilized are comprised of a transducer that is applied to the body and an electrical box that the transducer attaches to. The transducer is held over the area of the body that is being targeted for ultrasound diathermy therapy. A physical therapist is usually the one administering this therapy by holding the applicator or transducer over the intended area of therapy. US produces sound waves transmitted to the affected area through a handheld probe using conductive gel, thought to penetrate deep tissues and improve healing. Modifying the application parameters (i.e., intensity, wavelength, duty cycle, and frequency) provides a variety of local effects on tissues. US may be applied in continuous or pulsed mode. Ultrasound provides therapeutic benefit via thermal (continuous ultrasound) and non-thermal (pulsed ultrasound) effects (**8,9**). In the continuous setting, US convert non-thermal energy into heat, which increases deep soft-tissue extensibility and acts as a counter-irritant stimulus, thereby temporarily reducing pain. Pulsed US is thought to promote deep soft-tissue healing by improving blood flow, altering cell membrane activity, and vascular wall permeability to the applied region.

There is essentially no major variation in the technique of administration of this modality. Ultrasound diathermy is usually applied for up to one half hour at a time however time alone is not a limiting factor as amount of energy and the potential resultant bioeffects are the real determinants of length of application

High frequency ultrasound waves treat superficial tissues such as patellar tendons. Lower frequencies penetrate deeper to treat deep muscle bruising, spasms, and strains (**8**). Superficial heat is thought to temporarily reduce pain by acting as a counterirritant stimulus, increasing soft-tissue extensibility, and reducing muscle tone and spasm; these effects are noted mostly in superficial structures (**9**). Selection of ultrasound application parameters is based on the desired effect and the location and density of the tissue to be treated. These decisions are best made by a therapist experienced in performing therapeutic ultrasound.

Common indications for high frequency ultrasound therapy include treatment of tendon injuries and short-term pain relief. (**11-13**) Ultrasound has also been shown to promote healing of some acute bone fractures, venous and pressure ulcers, and surgical incisions (**8,9,14,15**). However, therapeutic ultrasound can cause burns or endothelial damage if applied incorrectly (**8,9,16**)

High frequency US diathermy can be contraindicated in use over malignant lesions, pregnant abdomens, plastic implants, hemorrhagic regions, cemented areas of prosthetic joints, ischemic regions, insensate areas, infected lesions, electronic implants (including neurostimulators), areas that have been exposed to radiotherapy within the past 6 months, fractures, epiphyseal growth plates in skeletally immature patients, thrombotic areas, orbits of the eyes, gonads, and spinal cord after laminectomy.

Low frequency Ultrasound Diathermy

High power, high frequency Ultrasound is define as an Ultrasound of 0.5-10 MHz and up to 1500W/cm^2 while low power, low frequency Ultrasound is define as an Ultrasound of 20-120 kHz and 0.05-1.0 W/cm^2). Low frequency/low intensity US is mainly reflected in the skin or wound surface. Only a small portion of the energy transmitted by the probe reaches deeper tissue layers and the major effect is

mechanical effect, which is the opposite for high frequency US that combine mostly thermal with mechanical effects.

During the recent years, low frequency ultrasound based devices were tested and introduced to the market. The motivation of looking for alternative ultrasound parameters was due to the fact that application of high-frequency US is limited in vivo due to tissue heating. Thus, using low-frequency US with less tissue heating act as a "slow release" mechanism may become the standard care in treating slow-to-heal lesions, pain from musculoskeletal sources, skin ulcers and nonunion fractures. In addition it may be able to facilitate protein secretion and enzymatic reactions.

There is growing evidence-based information that shows the various clinical impacts following low frequencies US treatments.
Common indications for such therapy include treatment of tendon injuries and short-term pain relief. (**17**), chronic low back pain (**18**), sinusitis (**19**), venous and pressure ulcers (**20, 21**). Moreover, low frequency Ultrasound has also been shown to promote healing of some acute bone fractures (**22**) and blood thrombolysis (**23**)

In addition extensive in-vitro studies suggest other effect of low frequency US including activation of plasminogen (**24**), Nitric oxide (**25**) and other molecules that are of important in different biological mechanisms. There is a growing body of evidence demonstrating correlation between nitric oxide increased and pain relief (**26,27**), and this increase can be accelerated by ultrasound therapy (**28**). Therefore, induction of nitric oxide by ultrasound may play a key role in pain control therapy.

REFERENCES

1. Galluzzi K.E. Management of neuropathic pain. *JAOA* 2005; Supplement 4, 105(9):S12-S19
2. Bennett G.J. Neuropathic pain: an overview. In: Bosook D.,ed. Molecular Neurobiology of Pain. Seattle, Wash: IASP Press; 1997:109-113
3. Glajchen M. Chronic pain: treatment barriers and strategies for clinical practice. *J Am Board Fam Pract* 2001; 14:211-218
4. Chronic pain in America: roadblocks to relief. Survey conducted for the American Pain society, The America Academy of Pain Medicine, and Janssen Pharmaceutica. Hanson, NY:Roper Starch Worldwide, 2000
5. Dworkin R.H. An overview of neuropathic pain: syndromes, symptoms, signs, and several mechanisms. *Clin J Pain* 2002;18:343-349.
6. Bergman S. Management of musculoskeletal pain. *Best Pract Res Clin Rheumatol* 2007; 21(1):153-166
7. Chen H., Lamer T.J., Rho R.H. Marshall K.A., Sitzman B.T.,Ghazi S.M., et al. Contemporary management of neuropathic pain for the primary care physician. *Mayo Clin Proc* 2004; 79:1533-1545
8. Cameron MH. Thermal agents: cold and heat, ultrasound, and electrical currents. In: Cameron MH. Physical Agents in Rehabilitation: From Research to Practice. 2nd ed. St. Louis, Mo.: Saunders, 2003:133-259.
9. Guide to Physical Therapist Practice. Part 1: A description of patient/client management. Part 2: Preferred practice patterns. American Physical Therapy Association. Phys Ther 1997;77:1160–656.Brosseau L, Welch V, Wells G, DeBie R, Gam A, Harman K, et al. Low level laser therapy (classes I, II and III) for treating osteoarthritis. Cochrane Database Syst Rev 2004;(3):CD002046.
10. Kibler WB, Duerler K. Electrical stimulation and application of heat. In: DeLee J, Drez D, Miller MD. DeLee & Drez's Orthopaedic Sports Medicine: Principles and Practice. 2nd ed. Philadelphia, Pa.: Saunders, 2003:349-51,356-9.
11. Casimiro L, Brosseau L, Robinson V, Milne S, Judd M, Well G, et al. Therapeutic ultrasound for the treatment of rheumatoid arthritis. Cochrane Database Syst Rev 2002;(3):CD003787.

12. Robertson VJ, Baker KG. A review of therapeutic ultrasound: effectiveness studies. Phys Ther 2001;81:1339-50.
13. Van der Windt DA, van der Heijden GJ, van den Berg SG, ter Riet G, de Winter AF, Bouter LM. Ultrasound therapy for musculoskeletal disorders: a systematic review. Pain 1999;81:257-71.
14. Busse JW, Bhandari M, Kulkarni AV, Tunks E. The effect of low-intensity pulsed ultrasound therapy on time to fracture healing: a meta-analysis. CMAJ 2002;166:437-41.
15. Flemming K, Cullum N. Therapeutic ultrasound for venous leg ulcers. Cochrane Database Syst Rev 2000;(4):CD001180.
16. Brosseau L, Casimiro L, Robinson V, Milne S, Shea B, Judd M, et al. Therapeutic ultrasound for treating patellofemoral pain syndrome. Cochrane Database Syst Rev 2001;(4):CD003375.
17. Warden SJ. A new direction for ultrasound therapy in sports medicine. Sports Med. 2003; 33 (2):95-107.
18. Ansari NN, Ebadi S, Talebian S, Naghdi S, Mazaheri H, Olyaei G, Jalaie SA. randomized, single blind placebo controlled clinical trial on the effect of continuous ultrasound on low back pain. Electromyogr Clin Neurophysiol. 2006 Nov;46(6):329-36
19. Ansari NN, Naghdi S, Farhadi M, Jalaie S. A preliminary study into the effect of low-intensity pulsed ultrasound on chronic maxillary and frontal sinusitis. Physiother Theory Pract. 2007 Jul-Aug;23(4):211-8
20. Kavros SJ, Schenck EC. Use of noncontact low-frequency ultrasound in the treatment of chronic foot and leg ulcerations: a 51-patient analysis. J Am Podiatr Med Assoc. 2007 Mar-Apr;97(2):95-101.
21. Tan J, Abisi S, Smith A, Burnand KG. A painless method of ultrasonically assisted debridement of chronic leg ulcers: a pilot study. Eur J Vasc Endovasc Surg. 2007 Feb;33(2):234-8.
22. Rubin C, Bolander M, Ryaby JP, Hadjiargyrou M. The use of low-intensity ultrasound to accelerate the healing of fractures. J Bone Joint Surg Am. 2001 Feb;83-A(2):259-70.

23. Daffertshofer M, Fatar M. Therapeutic ultrasound in ischemic stroke treatment: experimental evidence. Eur J Ultrasound. 2002 Nov;16(1-2):121-30.
24. Pieters M, Hekkenberg RT, Barrett-Bergshoeff M, Rijken DC. The effect of 40 kHz ultrasound on tissue plasminogen activator-induced clot lysis in three in vitro models. Ultrasound Med Biol. 2004 Nov;30(11):1545-52.
25. Atar S, Siegel RJ, Akel R, Ye Y, Lin Y, Modi SA, Sewani A, Tuero E, Birnbaum Y. Ultrasound at 27 kHz increases tissue expression and activity of nitric oxide synthases in acute limb ischemia in rabbits. Ultrasound Med Biol. 2007 Sep;33(9):1483-8
26. Mackenzie IS, Rutherford D and MacDonald TM. Nitric oxide and cardiovascular effects: new insights in the role of nitric oxide for the management of osteoarthritis *Arthritis Research & Therapy* 2008, 10(Suppl 2):S3
27. Abramson SB. Nitric oxide in inflammation and pain associated with Osteoarthritis. *Arthritis Research & Therapy* 2008, 10(Suppl 2):S2
28. Altland OD, Dalecki D, Suchkova VN, Francis CW. Low-intensity ultrasound increases endothelial cell nitric oxide synthase activity and nitric oxide synthesis. *J Thromb Heamost* 2004 Apr;2(4):637-43


NANO VIBRONIX™
Curing through prevention