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Keynote Lecture:

The Role of Shockwave Medicine in Pain Control

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Introduktion

Traditionally, ESWT is primarily oriented in the treatment of structural disorders, like tendinopathies, calcific deposits in tendons or bone defects. Pain relief is considered as a concomitant effect, although it is decisive for the patients.
In the newly developing application of ESWT for myofascial treatment, pain reduction has a higher value, as it is the main therapeutic aim and therefore directly influences the treatment decisions.

Pathophysiology of pain

Pain perception is started by the sensitization and activation of nociceptors. They consist of free nerve endings lying in between muscle fibers and run mostly in the neighborhood of vessels.
The stimuli are either mechanical (overload, trauma) or biochemical through endogenous inflammatory mediators (bradykinin [BK], prostaglandin E2 [PGE2], serotonin), which are mostly released from vessels in case of ischaemia or tissue lesions.
After stimulation, the nociceptors themselves release substance P (SP) and calcitonin gene-related peptide (CGRP).
The afferent nociceptive information is transported to the central nervous system (CNS) via unmyelinated, slow conducting C-fibers (group IV fibers).

SP and CGRP are neuropeptides with various biological functions, including pain transmission. They are synthesized in the spinal ganglion cells and localized in capsaicin-sensitive axons. They are released at peripheral terminals (nociceptors) and central terminals (dorsal root ganglia) of sensory nociceptive neurons.
Centrally they act as co-transmitters and contribute to a central sensitization of pain. In the periphery, where they are released from nociceptors, their major role is trophic and not nociceptive: Induction of neurogenic inflammation and stimulation of different cells (fibroblasts, osteoclastic and osteoblastic cells).
The neurogenic inflammation is due to the stimulation of target cells by SP and CGRP. Here they induce a local inflammation releasing BK and PGE2, which sensitize the nociceptors even more. In addition they induce a local tissue oedema by dilating the local blood vessels and increasing their permeability. This finally leads to a painful swelling in the target area.

A long-lasting influx of nervous impulses from nociceptors into the spinal cord increases the excitability of posterior horn neurons. This overexcitability of nociceptive neurons in the CNS is considered the main cause of allodynia and hyperalgesia in patients with chronic pain.
The endpoint of chronification consists of structural remodelling processes in the CNS that open up new pathways for nociceptive information and cause pain to persist over the long term.
One of the clinical results is the creation of the “referred pain”.

The referred pain is a clinical phenomenon, where pain is felt in an area, where nociceptors are not primarily activated. It is the result of an opening of ineffective synapses, so that the nociceptive

information is reaching somatotopically inappropriate dorsal horn neurons, and the patient is mislocalizing the pain in his brain. The referred pain is characteristic but not specific for myofascial trigger points.

Pain research in ESWT

The analgesic effects of ESWT were discovered by chance during its application for urolithiasis (Chaussy C., 1982). A frequently cited hypothesis in the past was Melzack's concept of hyperstimulation analgesia, although it has never been proven.

A different working mechanism has been validated during the last 10 years in various animal studies to clarify the pain reduction after ESWT: the degeneration of CGRP- and substance P-positive nerve fibers.

The degeneration of nerve fibers has been proven as well in the periphery, at the treatment site (Ohtori S., 2001; Maier M., 2003; Takahashi N., 2006; Hausdorf J., 2008a), as centrally in the dorsal root ganglia (Takahashi N., 2003; Ochiai N., 2007; Hausdorf J., 2008b). The pain reducing effects start 6-24 hours after the treatment. It lasts 2-6 weeks, the time reinnervation of the nociceptive nerve fibers need. Achieved temporary denervation can also lead to a reduction of the neurogenic inflammation and therefore decrease the local tissue inflammation and the concomitant pain (Hausdorf J., 2008a).

Multiple applications of ESWT provide a longer-lasting antinociceptive effect in the periphery, as reinnervation occurs slower in the repeated-treatment group, showing a cumulative effect on nerve fibers (Takahashi N., 2006).

The application of a local anaesthesia (LA) in order to prevent the treatment pain from ESWT results in less good clinical results (Rompe J., 2004, 2005; Labek G., 2005). As an explanation it was stated, that LA prevents the release of neuropeptides, which is normally provoked by ESWT and therefore would counteract the beneficial effect of increased metabolism in bradytrophic tissues, thus altering the biological responses to ESWT (Klonschinski, T., 2011). As a consequence, no LA should be applied prior to ESWT.

Clinical application in tendinopathies

Tendinopathy is an ongoing degenerative process, not a “leukocyte-driven” inflammation. The transition to the symptomatic phase is usually marked by characteristic histological changes: the invasion of vessels, which is followed by a nerve proliferation. Neural in-growth accompanying the neovessels leads to overexpression of glutamate, SP and CGRP, triggers a neurogenic-mediated inflammation and therefore explains the occurrence of pain (Abate M., 2009).

Under these circumstances the pain reducing effect of ESWT can be twofold: First by the aforementioned degeneration of sensory, unmyelinated nerve fibers and the reduction of the neurogenic inflammation (0-6 weeks), second by an induced tissue regeneration after 4-12 weeks (Wang C.J., 2003).

Clinical application in myofascial pain

Muscle nociceptors are sensitized and activated by strong mechanical stimuli (trauma, overload), endogenous inflammatory mediators (BK, PGE2), adenosine triphosphate (ATP), and acidic tissue pH (chronic ischaemic states, tonic contractions or spasms, myofascial trigger points).
Especially the increased muscle tension and the myofascial trigger points lead to difficult treatable pain and result often in referred pain patterns. In both situations the local ischaemia is crucial.

Applying ESWT on muscles is normally well tolerated by patients. But it can be quite painful on trigger points, as it elicits here a sharp local pain and often a referred pain too, especially with focused shockwaves. Accordingly ESWT can be used as a diagnostic tool in the search for the origin of myofascial pain. After detection of trigger points the treatment is added immediately. The radial ESWT is suitable for the treatment of large muscle areas (Gleitz M., 2012).
Attention should be paid to the fact, that high muscle pain needs low ESWT energy levels, otherwise the pain will be increased significantly. Adaptation of the energy level of ESWT is needed. Starting off with high pain levels during ESWT is a sign for a longer healing period (Gleitz M., 2011).

Relating the findings of proven working mechanisms of ESWT to the current theoretical framework of muscle pain and trigger point development (Mense S., 2001), several explanations can be given for the muscle pain reduction after ESWT:

- Degeneration of sensory, unmyelinated nerve fibers and reduction of the neurogenic inflammation after ESWT (aforementioned)
- Reactive hyperaemia and neovascularization after ESWT (Wang C.J., 2003)
- Reduction of muscle tension after ESWT (Amelio E., 2010; Kenmoku T., 2012). Latter is due to an immediate degeneration of acetylcholine receptors with a temporary impairment of the neurotransmission at the neuromuscular junctions. This effect lasts up to 56 days.

And in analogy to standard trigger point treatments:

- Breaking of Actin-Myosin-Links (Travell, J.; 1983; Shah J.P., 2008)
- Dilution of vasoneuroactive substances (Mense S., 2001; Shah J.P., 2008)

Conclusion

This overview shows that ESWT should not only be considered as a treatment of structural deficits but also as a primary pain treatment and as a diagnostic tool, especially for myofascial pain.
The aim of shockwave therapy is an immediate to mid-term reduction of peripheral and central pain mechanisms, including the reduction of the neurogenic inflammation. The long-term pain reduction is achieved by the tissue regeneration.
Regarding these pain mechanisms after ESWT and the fact, that long-lasting pain in the periphery will result in chronification, it is recommended to start shockwave treatment as early as possible.