39. Pain

Authors

Mats Börjesson, MD, PhD, Associate Professor, Department of Medicine, Sahlgrenska University Hospital, Gothenburg, Sweden

Kaisa Mannerkorpi, PT, Department of Physiotherapy, Sahlgrenska University Hospital, Gothenburg, Sweden

Stein Knardahl, MD, PhD, Professor, National Institute for Working Life and Psychology, Oslo University, Oslo, Norway

Jon Karlsson, MD, PhD, Professor, Department of Orthopaedics, Sahlgrenska University Hospital/Mölndal, Gothenburg, Sweden

Clas Mannheimer, MD, PhD, Professor, Pain Centre, Department of Medicine, Sahlgrenska University Hospital/Östra, Gothenburg, Sweden

Summary

Physical activity is of great significance for the treatment and rehabilitation of patients with long-term pain. There are three distinct effects of physical activity:

1) The "direct" pain-relieving effects of physical activity; 2) other "non-direct" effects on fitness and mood, reduced stress sensitivity and improved sleep, with potentially even greater effects on the pain situation of the patient; and 3) the positive effects of physical activity on lifestyle-related diseases in patients who tend to be inactive.

The physical activity must be regular and consistent to give direct or indirect pain relief. The physical activity should be carried out for at least 10 minutes, preferably for a much longer duration, and be of at least moderate intensity (> 60% of VO_2 max). Fitness and endurance training in the form of walking, jogging, cycling and swimming are often suitable activities. However, the type of physical activity the patient benefits from depends on his/her pain status and initial physical fitness. The physical fitness of patients with long-term pain is often very low and, consequently, the intensity of their chosen activity should ideally be gradually increased, starting at a low intensity level.

Introduction

Pain is a significant clinical problem. Studies show that up to 50 per cent of the population in Sweden and England suffer from chronic pain (9, 10). 13 per cent of the individuals questioned reported that their pain had led to reduced functional capacity (11). Only 40 per cent had been given a definite diagnosis (10). The most common clinical pain condition was chronic lumbago, i.e. chronic back pain (9). It has been described in the literature how individuals manage to continue with a particular sport without feeling any pain despite having suffered a stress fracture (1) or an acute heart attack (2). The importance of coping with pain in order to achieve success in endurance sports has also been the focus of much discussion (3). Elite swimmers have been shown to tolerate pain better than people who swim for the sake of exercise (4), and athletes who play contact sports appear to cope even better with pain than non-contact sport athletes (5). It has also been discussed whether sensitivity to pain in itself could be a predisposition for future physical inactivity (6).

The exact association between physical inactivity and long-term pain is still not fully known. Clinically, physical activity is considered to be of a great indirect and clinical importance in various chronic pain conditions. Aside from pain relief, physical activity may also contribute to increased functional capacity (by increasing fitness) in these patients. Expectancies may affect pain (12) as may improvement in the state of mood (13), which further reduces the pain experienced.

Definition

The International Association for the Study of Pain (IASP) defines pain as "an unpleasant experience that we primarily associated with tissue damage or describe in terms of tissue damage or both" (7). Accordingly, pain is a subjective experience that is not always related to the extent or even existence of tissue damage. Pain is a psychological phenomenon that must be described based on the behaviour and experience of the individual. Nonetheless, it is possible to assess pain using several methods.

Pain is either *acute* or long-term (*chronic*). Acute pain seldom gives rise to serious therapeutic problems and generally responds well to analgesics or cause-related treatment. Acute musculoskeletal pain usually responds well to analgesics or physiotherapy aimed at restoring function. Traditionally, the person administering the treatment (health professional) is normally active and the patient passive.

Chronic non-malignant pain (defined as pain that persists 3 months or more) is more complex, however, and often very difficult to treat. In such cases, ideally the patient should play a more active role while the person administering the treatment should act as an adviser, including encouraging the patient to be more active.

Pain analysis is used to assess whether the pain is *nociceptive*, i.e. stems from the skin, muscles or similar; *visceral*, i.e. stems from the inner organs; or *neuropathic*, i.e. caused by a nerve damage or dysfunction. Complex regional pain syndrome is often characterised by allodynia, which is painful hypersensitivity to stimuli that should normally not cause pain.

The definition of *pain threshold* is "the least stimulus intensity at which the patient perceives pain" (8). *Pain tolerance* is defined as the greatest level of pain that a patient is prepared to "tolerate". Two individuals can have the same pain threshold but a different tolerance for the same painful event. These two definitions are critical in the pain analysis and for the treatment required.

Pain physiology

Pain, as experienced in the central nervous system (CNS), is the result of a complex processing of pain signals. Pain impulses usually transpire through the activation of peripheral pain receptors (nociceptors, from the Latin *nocere* = to injure). This activates primarily myelinated (A-delta nerve fibres) and thinner unmyelinated (C nerve fibres) neurons. The pain fibres reach the dorsal horn of the spinal cord via several segments. As a result, secondary neurons are activated and the pain signal is transmitted via the *spinothalamic fasciculus* up through the nervous system. Via the thalamo-cortical pathway, the signals reach the somatosensory cortex. Following a cortical processing, the activation typically gives rise to a sharp, well-localised feeling of pain ("it hurts"). Other fasciculi reach deeper and more diffuse subcortical areas (e.g. gyrus cinguli, prefrontal areas), also via the thalamus, for emotional processing. This gives rise to the emotional components of pain ("discomfort"), which are very important from a clinical standpoint.

In addition, there are a number of systems that process pain impulses before they give rise to the perception of pain. The spinal cord includes mechanisms that can both enhance and inhibit pain. Constant stimulation of the nociceptors may lead to central sensitisation, i.e. a heightened sensitivity to stimulation, which is of significant importance to long-term pain.

Descending pain-inhibiting systems from the *periaqueductal grey area* (PAG) and *nucleus raphe magnus* affect the sensory afferents of the spinal dorsal horn. Opioids play a dual role in these systems by activating the descending pain-inhibiting systems and inhibiting the ascending pain impulses of the spinal cord. Opioids can also lead to peripheral modulation of pain at the receptor level in connection with inflammation.

Psychological factors such as expectancies and experiences seem to influence the sensitisation of neurons (11) and, as a result, research into the mechanisms that underlie the placebo effect has intensified over the past few years.

The difficulties with experimental studies on physical activity and pain are the various types of pain-inducing stimuli used and the individual differences in pain sensitivity. In addition, there are methodological issues regarding the type of physical activity, duration and intensity. Experimentally induced pain is not comparable to clinical pain. For example, study subjects are usually less apprehensive/anxious since they know that the pain stimulation can be stopped at any time, which is not the case in real life situations.

The effects of physical activity on experiences of pain

Acute effects

Studies have shown that physical activity has a modulating effect on pain, i.e. it affects the way in which we experience induced pain, both during and after exercise. There are many indications that pain relief is an integral part of physical activity. An integration of behaviourial and cardiovascular reactions as well as pain inhibition take place via the PAG (14). In addition, the pressure receptors of the cardiovascular system appear to have an effect on the pain system (15).

During exercise. Experimental studies indicate that the pain threshold for different forms of pain stimulation increases *during* physical activity. For example, this applies to dental pain (16), electrically induced finger pain during a cycle test (17), and pressure-induced pain in the quadriceps muscle during static load (18).

After exercise. Evidence suggests that different forms of physical activity lead to pain relief *using a broad range methods* of assessment, as well as different pain stimuli (e.g. electrical stimulation, heat, pressure and ischaemia) (6, 19–21). Both experimental and "natural" physical activities have been tried (22). A high-intensity activity seems to increase the pain threshold, which then gradually decreases once the activity is finished (see "Prescription" below). Running, for example, has a pronounced effect on one's pain threshold. In a trial using thermal provocation, the analgesic effect of 45 minutes of high-intensity running corresponded to approximately 10 mg of intravenous morphine (19).

Paradoxal effects of physical activity on pain threshold. Experimental studies on fibromyalgia have shown physical activity to have the opposite effect. Unlike in healthy individuals (in whom the pain threshold decreases), the sensitivity to pain *was found to increase* during and after physical activity (23). This may render it more difficult for patients with fibromyalgia to be physically active, as part of their everyday clinical treatment.

Long-term effects

Do physically active persons *have a higher pain tolerance* than inactive persons? People who are physically active on a regular basis appear to have a higher *pain tolerance*. However, it does not necessarily mean that they have a higher pain threshold (24). Whether this potential difference in pain tolerance is due to the training itself, or simply individual/genetic, is currently subject to debate. However, the effect of physical activity on pain seems to be similar for both active sportsmen and untrained individuals (16, 20). A possible explanation for why certain runners are able to continue running despite an injury (1) could be that they have a high pain tolerance to begin with, which is then boosted by the extra physical load. Pain inhibition is an integrated part of the active pain control system (14). Also, by focusing on other signals from the body, attention is diverted away from the pain.

It is therefore likely that individuals with a high pain tolerance turn out to be the most successful in many athletic areas, such as endurance sports, where athletes often have to tolerate severe muscle pain (25). The training itself may have a positive effect on their sensitivity to pain (3). For example, it has been noted that the pain sensitivity of competitive swimmers varies depending on the intensity of training during a season (4).

When treating patients with *chronic pain,* increased physical activity is a key factor for improving the prognosis and alleviating the patient's suffering. Aerobic fitness and quality of life is gradually reduced in patients with chronic pain, with the risk of social isolation. Activity-induced pain combined with the anxiety and uncertainty that comes with the possibly unknown cause of the pain often leads to a reduced level of activity. Disaster thinking, i.e. expecting that the pain will increase and the prognosis is bad, may worsen the prognosis. Patients with chronic pain are often downhearted and sometimes depressed. This could make the pain situation even worse. In a small number of cases, negative attributes such as pain communication, inadequate and increased pain distribution, as part of the so-called "somatoform pain disorder", have developed.

Increased physical activity has a significant effect on patients with chronic pain. Not only does it reduce pain, but it also positively influences the patient's mood (13, 26), alleviates social isolation, and increases functional capacity (27). Physical activity may also lead to an improved perception of body image (28) and the person's self image of being a healthy individual (29). These effects also increase the possibility of the patient being able to handle and cope with pain. Secondary muscle tension caused by pain can be reduced through physical activity and mobility training.

Mechanisms

Physical activity as pain relief

Endogenous opioids

The most favoured theory behind the effects of physical activity on pain relief is based on endogenous opioids (beta-endorphins; the body's own opiates). These can act as pain inhibitors at different levels, as described above (24). The concentration of beta-endorphin in the blood increases with physical activity (30), although this is probably only partly responsible for the pain relief. According to a theoretical model, the activation of ergoreceptors in major muscle groups during physical activity can lead to increased central opioid activity through the activation of A-delta fibres (31).

However, it seems that physical activity of a high intensity is needed to release significant amounts of endorphins (corresponding to 75–80% of maximum oxygen uptake capacity; VO_2 max) (32, 33), i.e. an almost anaerobic workload (32). However, for physical activity at lower intensities, such as aerobic endurance training with stable lactate levels, a long duration is required (> 1 hour) in order to obtain an increased release of beta-endorphins (32). Some studies support the endorphin theory by showing that pain relief is reduced when patients are given naloxone (an antagonist to morphine and other opiates and opioids that obstruct the analgesic effect of opiates by blocking their receptors) (19, 21), whereas other studies have been unable to confirm these findings (17, 21). This may be explained by an undefined selectivity to naloxone. One study has also been able to show that low-intensity physical activity equivalent to 63 per cent of VO_2 max may indeed increase endorphin levels and tolerance to pain (27). Thus, there seems to be more than one explanation for the secondary effects that physical activity has on pain. According to another study, aerobic activity at 50 per cent of VO_2 max did not give any relief from pressure induced pain (34), which may be an indication that there is a lower limit of intensity to achieve pain-relief.

Other descending pain-inhibiting systems that use different neurotransmitters (e.g. serotonin and noradrenaline) may potentially also be involved in pain relief secondary to physical activity.

Increased activity in non-pain transmitting sensory fibres

Activation of large afferents (sensory fibres) could, in theory, lead to reduced pain via the activation of pain-inhibiting interneurons (Gate Control Theory) (35). This effect is not mediated through increased opioid activity, but possibly through the transmitter gamma-aminobutyric acid (GABA).

Distraction

A distraction or diversion has been proven to change the experience of pain (36) and can contribute to alleviating pain during and after an activity (37). A sports activity may distract an individual from pain, as also illustrated historically by injured and fleeing soldiers. Consequently, the analgesic effects of physical activity demonstrated in laboratory tests may be underestimated due to insufficient exterior influences (38).

Expectations

It can be difficult to differentiate between the effect that the stress experienced before a competition/activity has on pain and the effect the physical activity itself has on the same pain. *Expectations* prior to a physical activity, in addition to *trepidation*, could in themselves act as pain inhibitors or enhancers/triggers (39). One study showed that more than 50 per cent of study subjects who were told that they might get a headache from electrical stimulation did in fact get such a headache, despite not being exposed to any such electrical stimulation (expected or nocebo pain) (40).

Adaptive reactions – stress

Regulation of pain sensitivity is an integrated part of our adaptive reactions to stress (14). *Acute stress* is usually associated with pain relief (41, 42), while *chronic stress* is usually associated with an increased sensitivity to pain (43).

Regular physical activity may *reduce sympathetic activity*, which in turn can lead to pain relief by way of reduced ischaemia in conditions such as angina pectoris, peripheral vascular disease and dysmenorrhea (see below).

Sensitisation and previous experiences with pain

Persons with previous pain experiences may feel less pain than persons without such experiences (44). However, other studies seem to suggest the opposite, possibly due to various circumstances. Patients with fibromyalgia experience *hyperalgesia*, i.e. increased pain sensitivity during a similar form of stimulation and activity. This could be explained by sensitisation (23) as part of he development of chronic pain. Direct pain-relieving effects are noted in patients with fibromyalgia who are able to do the same type of moderate to high-intensity exercise as healthy individuals (45), whereas other patients with fibromyalgia doing only lower intensity training see bigger improvements in their general health status and mood state (29, 46).

Indirect effects

Effect on depression and anxiety

According to one study, 8 weeks of physical activity (walking or jogging) led to reduced symptoms of depression and anxiety (13). This has also been shown in other studies (47, 48). Depression may lead to increased pain and a reduced capacity to cope with the pain situation. Consequently, increased physical activity may have a positive effect on the pain situation by boosting the patient's self-esteem and mood state. This positive effect of physical activity appears to be mediated partly through its effect on the central serotoninergic system (49). Patients with fibromyalgia report being less depressed and anxious following a period of physical activity. These effects may be achieved with both low-intensity and high-intensity exercise (50, 51).

Effect on sleeping

Regular physical activity of a moderate intensity has been shown to improve the quality of sleep (52). This should, in theory, also contribute to a better pain situation, as the patient feels more rested and content.

Prescription

Duration. Available studies suggest that it is possible to achieve pain relief through short sessions of physical activity, though a minimum duration of 10 minutes is needed (34, 38). However, a further increase in the pain threshold can be expected if the physical activity continues for longer than 10 minutes. Thus, 50 minutes of running increases the ischaemic pain threshold more than 15 minutes of running on a treadmill (38). The effect on pressure-induced pain lasts for at least 5 minutes after exercise (18). The pain thresholds revert to normal within approximately one hour after the physical activity has finished (17).

Type of activity. Almost all data on physical activity and pain relates to aerobic fitness training. A small-scale study showed that 45 minutes of strength training at 75 per cent of an individual's 1 RM (1 RM = Repetition Maximum, i.e. the maximum amount of weight one can lift in a single repetition for a given exercise) resulted in a significantly heightened pain thresholds and reduced pain intensity compared with control groups (53). The alleviation of pain lasted for 10 minutes, i.e. a considerably shorter effect than after fitness training (53). However, according to another study, pain tolerance did not increase after 12 weeks of strength training (3). Hence, the effect of strength training on the release of beta-endorphins is still unclear (33). More studies are needed to determine whether strength training does have an alleviating effect on pain.

Intensity. High-intensity fitness training, such as cycling at a minimum of 75–80 per cent of VO_2 max (which increases beta-endorphin levels), has shown to alleviate pain (19, 54). However, even low-intensity fitness training (63% of VO_2 max) increases pain tolerance (27). According to a study using pressure induced pain, fitness training at 50 per cent of VO_2 max did not alleviate pain (34), which appears to indicate that there is a low-intensity limit. Yet, the fact that submaximal exertion seems to have an alleviating effect on pain does have important therapeutical implications, as this means that more patients may be able to alleviate their pain through physical activity. Persons with chronic pain often have low functional capacity (55) and, as a result, may find it difficult to engage in relatively high-intensity activities. A simple activity such as walking could therefore be of sufficient relative intensity for an unfit person in this context.

Continuity. The prescribed physical activity has to be regular for continuous effect.

Summary of prescription

A physical activity must be regular and consistent to give direct or indirect pain relief. The physical activity should be carried out for at least 10 minutes, preferably much longer, and be of at least a moderate level of intensity (> 60% of VO_2 max). Aerobic fitness and endurance training in the form of walking, jogging, cycling and swimming are often suitable, but the type of physical activity the patient benefits from most depends on his/her pain status and initial fitness. The physical capacity of patients with chronic pain is often very low and, consequently, the intensity of their chosen activity should be gradually increased, starting from a relative (individual) low intensity.

Clinical indications

Physical activity as pain relief in patients with various diseases

Unspecified Chronic Pain (UCP) and Chronic Pain Syndrome (CPS)

Whatever the initial cause of the pain, physical activity plays a very important role and is perhaps the most important part of the patient's treatment programme. The patients regularly show a low functional capacity (reduced fitness) and are often passive. Breaking this vicious circle is vital, as is to gradually and carefully increase the patients' level of physical activity. At the same time, the patients are often in a primary or secondary state of dejection or even depression. If this is the case, then physical activity could act as a positive complement to traditional medical treatments (13).

Before choosing a passive treatment method such as weak analgesics for a non-depressed patient, the patient should reach a basic level of physical activity (walking). More specific training programmes are also of significant importance, not least to show the patient that it is possible to remain active, i.e. to eliminate unconstructive thoughts relating to the pain.

Chronic lumbago

Indication and prescription

Individualised functional training combined with information about the underlying disease, with the aim of increasing the person's level of physical activity, is considered essential for patients with chronic lumbago. Women with lumbago have a lower aerobic fitness level compared to male subjects of the same age (56).

A training programme may incorporate stability training, graded endurance and strength training, as well as stretching of shortened torso and leg muscles. Studies have shown that strength and an increase in training gives improved back function and reduced pain when comparing a group of training patients to an untreated control group (57, 58). Also fitness training has been shown to have positive effects on pain intensity and pain frequency (59). This patient group may even benefit from everyday physical activities (60). Cycling was shown to have an effect on the quality of life and mental capacity of older patients with lumbago (61). In addition, a Pilates-based approach to training seemed to have a better effect than standard treatments (62).

It is recommended that the training begin under the supervision of a physiotherapist who will adapt the various exercises to the patient's functional limitations and pain, and gradually increase the physical load. The long-term effects of supervised training surpass the effects attained from self-training at home (58).

In the case of acute back pain without a known pathologic cause, everyday physical activities seems to be most beneficial (63). The risk of prescribing physiotherapy is that it may enhance the patient's perception of disease rather than improve the situation.

Fibromyalgia

Indication

Many patients with fibromyalgia are physically inactive due to an overall feeling of tiredness and diffuse pain. Inactivity is considered one of the most important reasons for these patients having reduced functional capacity, as well as reduced muscle strength and aerobic fitness (64). However, the ability of the patients to train their muscles does not appear to be affected (65).

Prescription

Numerous studies have shown that patients with fibromyalgia benefit from physical training in that their physical functioning improves and the severity of their symptoms is reduced, which boosts their frame of mind. The feeling of general well-being is further enhanced if the training takes into account the patient's current level of functioning and pain tolerance (29). It is worth noting that the intensity of a physical activity is always relative. In other words, it must be prescribed in relation to the individual capacity of the patient.

Low-intensity training

Patients with fibromyalgia whose level of activity have been low for a longer period of time are often despondent or frightened of experiencing increased pain as a result of physical activity. The initial training should therefore be of a low intensity and gradually increase at a rate that the patient feels comfortable with. If the training is beneficial or manageable, the patient is more likely to feel motivated to continue training. For these patients, regularity is more important than the intensity of the training. Studies have shown that walking (46, 66, 67) and low to moderate-intensity training in a heated pool (50, 68–71) improves physical functioning and lessens the severity of symptoms and feelings of despondency. Patients who are unable or do not have time to exercise for an uninterrupted duration of 30 minutes may divide the training into two 15-minute training sessions daily (72).

Body image therapy and self-care training may be vital for those patients who need to improve their knowledge of their bodies and physical limitations (29, 73).

Moderate to high-intensity training

Patients who are able to do fitness training for at least 20 minutes 2–3 times a week, at an intensity of 55–90 per cent of their maximal heart rate have been shown to have improved fitness and pain situation (45). The types of exercise carried out include cycling (74), combined with fitness training, strength training and stretching (75). Because of the problematic pain situation, not all patients manage to achieve a (relatively) moderate to high-intensity level of training (76). However, most untrained patients with a low aerobic fitness level are able to achieve moderate-intensity training by simply walking on flat ground!

Strength training

Patients who begin strength training at 40–60 per cent of their maximum capacity and gradually increase the resistance to 60–80 per cent have been shown to have improved muscle strength.

In short, fitness training, walking, exercising in water and strength training are generally considered to have a positive influence on the physical functions, symptoms and despondency of patients with fibromyalgia. Since pain often leads to muscle tension and possibly shortening of the muscles, stretching after a training session is considered beneficial. Training that is carried out at an adequate level seems to give patients added self-esteem and a more positive view of their bodies. Many patients prefer training in a group as it offers them the social support needed to continue training regularly.

Neck pain/whiplash

For patients with chronic neck pain, a structured training programme that focuses on the neck area may alleviate pain and increase physical functioning and muscle strength (79). A combination of strength training and stretching is recommended (80). Neck training exercises may also lead to reduced muscle fatigue (81).

In a randomised controlled trial on patients with a "whiplash-associated disorder" (WAD), physical activity carried out in addition to standard treatment had the greatest effect on pain and on functionality in patients with the most pronounced symptoms (82). There are considerable geographical differences in the prevalence of WAD, and it is much more common in Scandinavia/Canada than, for example, Lithuania/Greece (83). This indicates that other factors, such as the expectation of chronic pain, are of importance. Physical activity plays an important role in showing the patient that it is possible to be physically active despite the pain.

Urogenital pain

A 3-month fitness training programme reduced symptoms of primary dysmenorrhea (84). Whether this is due to a reduced sympathetic tone or endorphins has been discussed (85).

A double-blind randomised study examined the effects of fitness training in men with refractory chronic prostatitis/chronic pelvic pain compared with placebo/stretching. The results showed that 18 weeks of aerobic fitness training reduced the pain as well as improving depression and anxiety (86).

Rheumatoid arthritis/osteoarthritis

Reduced functional capacity, restricted movements and pain are common problems among patients with rheumatoid arthritis (RA), the characteristics of which are inflammation of the joints, tendon sheaths and bursae, with subsequent destruction of cartilage and bone. The pain experienced in connection with RA is usually nociceptive, due to inflammation or destruction, or neurogenic, due to compression of peripheral nerves or nerve roots. When putting together an exercise programme, the joint and muscle function of the patient must be taken into account, and the exercise programme be individualised accordingly.

Flexibility training for the prevention of restricted flexibility should be carried out daily, especially during periods of aggravated joint inflammation. If the patient experiences localised pain, with restricted flexibility, muscle fatigue and pain, the flexibility may have to be addressed separately before the patient can commence strength and aerobic fitness training. Patients with RA are able to improve their muscle strength (87) and fitness (88) through strength and fitness training. A number of scientific studies have used endurance/strength training at 50–80 per cent of Maximal Voluntary Contraction, and fitness training at 60–85 per cent of Maximal Heart Rate (88).

Some of the studies reported a reduction in pain subsequent to group strength and fitness training (88). No increased inflammation activity or symptoms (87, 88) were reported following an adequately planned training programme.

Ischaemic pain – vascular disease

An association between physical activity and pain has been noted in various forms of *ischaemic pain situations*, such as angina pectoris and claudication (claudicatio intermittens). In the case of claudication, physical activity has been shown to alleviate pain and lengthen the walking distance (89, 90). The improvement can be attributed to both the improved physical health and increased functional capacity (91).

In the case of a coronary artery disease, the appropriate dose of physical activity has been shown to increase the functional capacity for a given exercise (92). A lower heart rate reduces the oxygen consumption in the heart muscle, which in turn reduces ischaemia (93) and delays the onset of angina pectoris (92). Patients participating in a cardiac rehabilitation programme usually have a low level of fitness at the start of the programme (94), which further reinforces the need for participating in such programmes. These programmes can potentially affect the patients' physical activity levels and quality of life for a number of years (95).

Interactions

Analgesics or other pain-modulating substances, such as non-steroidal anti-inflammatory drugs (NSAID), are normally used to alleviate pain. Products such as NSAIDs are able to modify the pain experience by influencing both the spinal and peripheral receptors, for example, through reduced sensitisation. NSAIDs should not be prescribed to individuals with risk factors for or established cardiovascular disease. However, low-dose NSAIDs are non-prescription drugs. Analgesics are sometimes indicated for minor traumas that do not affect the general activity level, e.g. a toe fracture in a football player. However, by using analgesics, the protective aspects of the sensation of pain itself are partly eliminated, entailing a risk of making the injury worse.

Contraindications

Pain is not altogether a bad thing. Humans are equipped with a pain system that, among other functions, acts as a defense mechanism against trauma and other damaging impacts on the body. It is important to remember that high-intensity training in connection with *fibromyalgia* is usually contraindicated at first (see above), while acute pain may be a sign of injury, whereupon physical activity should be avoided.

Always listen to the body. The treatment of acute pain due to distortion of the knee ligaments or a collision-induced fracture rarely poses a problem. However, the gradual onset of pain, often the result of an overuse injury, can be a bigger problem, while long-standing pain remains the greatest treatment challenge.

References

1. Colt EWD, Spyropoulos E. Running and stress fractures. Br Med J 1979;2:706.
2. Colt EWD. Letter to the Editor. N Engl J Med 1980;302:57.
3. Anshel MH, Russell KG. Effect of aerobic and strength training on pain tolerance, pain appraisal and mood of unfit males as a function of pain location. J Sports Sci 1994; 12:535-47.
4. Scott V, Gijsbers K. Pain perception in competitive swimmers. Br Med J 1981;283:91-3.
5. Ryan ED, Kovacic CR. Pain tolerance and athletic participation. Perc and Motor Skill 1966;22:383-90.
6. Janal MN, Glusman M, Kuhl JP, Clark WC. Are runners stoical? An examination of pain sensitivity in habitual runners and normally active controls. Pain 1994;58:109-16.
7. IASP. IASP Subcommittee on Taxonomy. Pain terms. A list with definitions and notes on usage. Pain 1979;6:249-52.
8. Guyton AC. Textbook of medical physiology. 7th edn. Philadelphia (PA): W.B. Saunders; 1986.
9. Elliott AM, Smith BH, Penny KI, Smith WC, Chambers WA. The epidemiology of chronic pain in the community. Lancet 1999;354:1248-52.
10. Andersson HI. The epidemiology of chronic pain in a Swedish rural area. Qual Life Res 1994;suppl 1:19-26.
11. Matre D, Casey KL, Knardahl S. Placebo-induced changes in spinal cord pain processing. J Neuroscience 2006;26:559-63.
12. Finnis DG, Benedetti F. Placebo analgesia, nocebo hyperalgesia. Pain Clin Updates 2007;XV(1).
13. Sexton H, Maere Å, Dahl NH. Exercise intensity and reduction in neurotic symptoms. Acta Psychiatr Scand 1989;80:231-5.
14. Bandler R, Shipley MT. Columnar organization in the midbrain periaqueductal grey. Modules for emotional expression? Trends Neurosci 1994;17:379-89.
15. Rau H, Brody S, Larbig W, Pauli P, Vöhringer M, Harsch B, et al. Effects of PRES baroreceptor stimulation on thermal and mechanical pain threshold in borderline hypertensives and normotensives. Psychophysiol 1994;31:480-5.
16. Pertovaara A, Huopaniemi T, Virtanen A, Johansson G. The influence of exercise on dental pain thresholds and the release of stress hormones. Physiol Behav 1984;33:923-6.
17. Droste C, Greenlee MW, Schreck M, Roskamm H. Experimental pain thresholds and plasma beta-endorphin levels during exercise. Med Sci Sports Exerc 1991;23:334-42.
18. Kosek E, Ekholm J. Modulation of pressure pain thresholds during and following isometric contraction. Pain 1995;61:481-6.
19. Janal MN, Colt EWD, Clark WC, Glusman M. Pain sensitivity, mood and plasma endocrine levels in man following long-distance running. Effects of naloxone. Pain 1984;19:13-25.

20. Kemppainen P, Pertovaara A, Huopaniemi T, Johansson G, Karonen SL. Modification of dental pain and cutaneous thermal sensitivity by physical exercise in man. Brain Res 1985;360:33-40.
21. Haier RJ, Quaid K, Mills JSC. Naloxone alters pain perception after jogging. Psychiatr Res 1981;5:231-2.
22. Bartholomew JB, Lewis BP, Linder DE, Cook DB. Post-exercise analgesia. Replication and extension. J Sports Sci 1996;14:329-34.
23. Kosek E, Ekholm J, Hansson P. Modulation of pressure pain thresholds during and following isometric contraction in patients with fibromyalgia and in healthy controls. Pain 1996;64:415-23.
24. O'Connor PJ, Cook DB. Exercise and pain. The neurobiology, measurement, and laboratory study of pain in relation to exercise in humans. Exerc Sports Sci Rev 1999;27:119-66.
25. Cook DB, O'Connor PJ, Eubanks SA, Smith JC, Lee M. Naturally occurring muscle pain during exercise. Assessment and experimental evidence. Med Sci Sports Exerc 1997;29:999-1012.
26. Morgan WP. Affective beneficience of vigorous physical activity. Med Sci Sports Exerc 1985;17:94-100.
27. Gurevich M, Kohn PM, Davis C. Exercise-induced analgesia and the role of reactivity in pain sensitivity. J Sports Sci 1994;12:549-59.
28. Tucker L. Effect of weight training and self concept. A profile of those influenced most. Res Quart Exerc Sports 1983;54:389-97.
29. Mannerkorpi K, Gard G. Physiotherapy group treatment for patients with fibromyalgia. An embodied learning process. Disabil Rehabil 2003;25:1372-80.
30. Colt WD, Wardlaw SL, Frantz AG. The effect of running on plasma beta-endorphin. Life Sciences 1981;28:1637-40.
31. Thoren P, Floras JS, Hoffman P, Seals DR. Endorphins and exercise. Physiological mechanisms and clinical implications. Med Sci Sports Exerc 1990;22:417-28.
32. Schwarz L, Kindermann W. Review. Changes in beta-endorphin levels in response to aerobic and anaerobic exercise. Sports Medicine 1992;13:25-36.
33. Goldfarb AH, Jamurtas AZ. Beta-endorphin response to exercise. Sports Med 1997; 24:8-16.
34. Hoffman MD, Shepanski MA, Ruble SB, Valic Z, Buckwalter JB, Clifford PS. Intensity and duration threshold for aerobic exercise-induced analgesia to pressure pain. Arch Phys Med Rehabil 2004;85:1183-7.
35. Melzack, Wall D. Pain mechanisms. A new theory. Science 1965;150:971-9.
36. Miron D, Duncan GH, Bushnell MC. Effects of attention on the intensity and unpleasantness of thermal pain. Pain 1989;39:345-52.
37. Debreuil DL, Endler NS, Spanos NS. Distraction and redefinition in the reduction of low and high intensity experimentally induced pain. Imag, Cogn and Pers 1987;7:155-64.
38. Janal MN. Pain sensitivity, exercise and stoicism. J R Soc Med 1996;89:376-81.
39. Sternberg WF, Bailin D, Grant M, Gracely RH. Competition alters the perception of noxious stimuli in male and female athletes. Pain 1998;76:231-8.

40. Bayer TL, Baer PE, Early C. Situational and psychophysiological factors in psychologically induced pain. Pain 1991;44:45-50.
41. Millan MJ, Przewlocki R, Herz A. A non-beta andorphinergic adenohypophyseal mechanism is essential for an analgesic response to stress. Pain 1980;33:343-53.
42. Pitman RK, van der Kolk BA, Orr SP, Greenberg MS. Naloxone-reversible analgesic response to combat-related stimuli in posttraumatic stress disorder. Arch Gen Psychiatry 1990;47:541-4.
43. van Houdenhove B. Psychosocial stress and chronic pain. Eur J of Pain 2000;4:225-8.
44. Kemppainen P, Hämäläinen O, Könönen M. Different effects of physical exercise on cold pain sensitivity in fighter pilots with and without the history of acute in-flight neck pain attacks. Med Sci Sports Exerc 1998;30:577-82.
45. Busch A, Schacter C, Peloso P, Bombardier C. Exercise for treating fibromyalgia syndrome. Oxford: The Cochrane Library; 2002.
46. Valim V, Oliveira L, Suda A, Silva L, de Assis M, Barros Neto T, et al. Aerobic fitness effects in fibromyalgia. J Rheumatol 2003;30:1060-9.
47. Byrne A, Byrne DG. The effect of exercise on depression, anxiety and other mood states. A review. J Psychosom Res 1993;37:565-74.
48. LaFontaine TP, DiLorenzo TM, Frensch PA, Stucky-Ropp RC, Bargman EP, McDonald DG. Aerobic exercise and mood. A brief review 1985–90. Sports Med 1992;13:160-70.
49. Chaouloff F. Effects of acute physical exercise on central serotonergic systems. Med Sci Sports Exerc 1997;29:58-62.
50. Gowans S, deHueck A, Voss S, Silaj A, Abbey S, Reynolds. Effect of a randomized controlled trial of exercise on mood and physical function in individuals with fibromyalgia. Arthritis RHeum 2001;45:519-29.
51. Mannerkorpi K, Iversen M. Physical exercise in fibromyalgia and related syndromes. Best Pract & Res Clin Rheumatol 2003;17:629-47.
52. King AC, Oman RF, Brassington GS, Bliwise DL, Haskell WL. Moderate-intensity exercise and self-rated quality of sleep in older adults. JAMA 1997;277:32-7.
53. Koltyn KF, Arbogast RW. Perception of pain after resistance exercise. Br J Sports Med 1998;32:20-4.
54. Koltyn KF, Garvin AW, Gardiner RL, Nelson TF. Perception of pain following aerobic exercise. Med Sci Sports Exercise 1996;28:1418-21.
55. Bennett RM, Clark SR, Goldberg L, Nelson D, Bonafede RP, Porter J, et al. Aerobic fitness in patients with fibrositis. Arthritis and Rheum 1989;32:454-60.
56. Hoch AZ, Young J, Press J. Aerobic fitness in women with chronic discogenic nonradicular low back pain. Am J Phys Med Rehabil 2006;85:607-13.
57. Hayden J, Tulder M, Malmivaara A, Koes B. Meta-analysis. Exercise therapy for nonspecific low back pain. Ann Intern Med 2005;142:765-75.

58. Liddle S, Baxter G, Gracey J. Exercise and chronic low back pain. What works? Pain 2004;107:176-90.
59. Mannion A, Muntener M, Taimela S, Dvorak J. Comparison of three active therapies for chronic low back pain. Results of a randomized clinical trial with one-year follow-up. Rheumatology 2001;40:772-8.
60. Chatzitheodorou D, Kabitsis C, Malliou P, Mougios V. A pilot study of the effects of high-intensity aerobic exercise versus passive interventions on pain, disability, psychological strain and serum-cortisol concentrations in people with chronic low back pain. Phys Ther 2007;87:304-12.
61. Iversen MD, Fossel AH, Katz JN. Enhancing function in older adults with chronic low back pain. A pilot study of endurance training. Arch Phys Med Rehabil 2003;84:1324-31.
62. Rydeard R, Leger A, Smith D. Pilates-based therapeutic exercise. Effect on subjects with nonspecific chronic low back pain and functional disability. A randomized controlled trial. J Orthop Sports Phys Ther 2006;36:472-84.
63. Malmivaara A, Häkkinen U, Aro T. The treatment of acute low back pain. Bed rest, exercises, or ordinary activity? N Engl J Med 1995;332:351-5.
64. Bennett R, Clark S, Goldenberg L, Nelson D, Bonafede R, Porter J, et al. Aerobic fitness in patients with fibrositis. Arthritis Rheum 1989;32:454-60.
65. Valkeinen H, Häkkinen A, Hannonen P, Häkkinen K, Alen M. Acute heavy-resistance exercise-induced pain and neuromuscular fatigue in elderly women with fibromyalgia and in healthy controls. Effects of strength training. Arthritis Rheum 2006;54:1334-9.
66. Buckelew S, Conway R, Parker J, Deuser W, Read J, Witty T, et al. Biofeedback /relaxation training and exercise interventions for fibromyalgia. A prospective trial. Arthritis Care Res 1995;11:196-209. 67. Richards SCM, Scott DL. Prescribed exercise in people with fibromyalgia. Parallel group randomised controlled trial. Br Med J 2002;325:185-7.
68. Cedraschi C, Desmeules J, Rapiti E. Fibromyalgia. A randomised, controlled trial of a treatment programme based on self-management. Ann Rheum Dis 2004;63:290-6.
69. Gowans S, deHueck A, Voss S, Richardson M. A randomised controlled trial of exercise and education for individuals with fibromyalgia. Arthritis Care Res 1999;12:120-8.
70. Mannerkorpi K, Nyberg B, Ahlmén M, Ekdahl C. Pool exercise combined with an education program for patients with fibromyalgia syndrome. J Rheumatol 2000; 27:2473-81.
71. Gusi N, Tomas-Carus P, Häkkinen A, Häkkinen K, Ortega-Alonso A. Exercise in waist-high warm water decreases pain and improves health-related quality of life and strength in the lower extremities in women with fibromyalgia. Arthritis Rheum 2006;55:66-73.
72. Schachter C, Busch A, Peloso P, Sheppard M. The effects of short versus long bouts of aerobic exercise in sedentary women with fibromyalgia. A randomized controlled trial. Phys Ther 2003;83:340-58.
73. Gustafsson M, Ekholm J, Broman L. Effects of a multiprofessional rehabilitation programme for patients with fibromyalgia syndrome. J Rehabil Med 2002;34:119-27.

74. McGain G, Bell D, Mai F, Halliday P. A controlled study of the effects of a supervised cardiovascular fitness program on the manifestations of primary fibromyalgia. Arthritis Rheum 1988;31:1135-41.
75. Wigers S, Stiles T, Vogel P. Effects of aerobic exercise versus stress management treatment in fibromyalgia. Scand J Rheumatol 1996;25:77-86.
76. van Santen M, Bolwijn P, Verstappen F. A randomized clinical trial comparing fitness and biofeedback training versus basic treatment in patients with fibromyalgia. J Rheumatol 2002;29:575-81.
77. Häkkinen A, Häkkinen K, Hannonen P, Alen M. Strength training induced adaptations in neuromuscular function of premenopausal women with fibromyalgia. A comparison with healthy women. Ann Rheum Dis 2001;60:21-6.
78. Jones K, Burckhardt C, Clark S, Bennet R, Potempa K. A randomized controlled trial of muscle strengthening versus flexibility training in fibromyalgia. J Rheumatol 2002;29:1041-8.
79. Chiu TT, Lam TH, Hedley AJ. A randomised controlled trial on the efficacy of exercise for patients with chronic neck pain. Spine 2005;30:1-7.
80. Ylinen JJ, Takala EP, Nykänen MJ, Kautianien HJ, Häkkinen AH, Airaksinen OV. Effects of twelve-month strength training subsequent to twelve-month stretching exercise in treatment of chronic neck pain. J Strength Con Res 2006;20:304-8.
81. Falla D, Jull G, Hodges P, Vicenzino B. An endurance-strength training regime is effective in reducing myoelectric manifestations of cervical flexor muscle fatigue in females with chronic neck pain. Clin Neurophysiol 2006;117:828-37.
82. Stewart MJ, Maher CG, Refshauge KM, Herbert RD, Bogduk N, Nicholas M. Randomized controlled trial of exercise for chronic whiplash-associated disorders. Pain 2007;128:59-68.
83. Schrader H, Stovner LJ, Obelieniene D, Surkiene D, Mickeviciene D, Bovim G, et al. Examination of the diagnostic validity of headache attributed to whiplash injury. A controlled, prospective study. Eur J Neurol 2006;13:1226-32.
84. Israel RG, Sutton M, O'Brien KF. Effects of aerobic training on primary dysmenorrhea symptomatology in college females. J Am Coll Health 1985;33:241-4.
85. Golomb LM, Solidum AA, Warren MP. Primary dysmenorrhea and physical activity. Med Sci Sports Exerc 1998;30:906-9.
86. Giubilei G, Mondaini N, Minervini A, Saieva C, Lapini A, Serni S, et al. Physical activity of men with chronic prostatitis/chronic pelvic pain syndrome not satisfied with conventional treatments. Could it represent a valid option? The physical activity and male pelvic pain trial. A double-blind, randomized study. J Urol 2007;177:159-65.
87. Häkkinen A. Effectiveness and safety of strength training in rheumatoid artritis. Curr Opin Rheumatol 2004;16:132-7.
88. Stenström C, Minor M. Evidence for the benefit of aerobic and strengthening exercise in rheumatoid artritis. Artritis Rheum 2003;49:428-34.
89. Hiatt WR, Regensteiner JG, Hargarten ME, Wolfel EE, Brass EP. Benefit of exercise conditioning for patients with peripheral vascular disease. Circulation 1990;81:602-9.

90. Gardner AW, Poehlman ET. Exercise rehabilitation programs for the treatment of claudication pain. A meta-analysis. JAMA 1995;274:975-80.
91. Tsai JC, Chan P, Wang CH, Jeng C, Hsieh MH, Kao PF, et al. The effects of exercise training on walking function and perception of health status in elderly patients with peripheral arterial occlusive disease. J Intern Med 2002;252:448-55.
92. Thompson PD. Exercise for patients with coronary artery and/or coronary heart disease. In: Thompson PD, Ed. Exercise and Sports Cardiology. New York: McGraw-Hill; 2001. p. 354-70.
93. Todd IC, Ballantyne D. Antianginal efficacy of exercise training. A comparison with beta blockade. Br Heart J 1990;64:14-9.
94. Ades PA, Savage PD, Brawner CA, Lyon CE, Ehrman JK, Bunn JY, et al. Aerobic capacity in patients entering cardiac rehabilitation. Circulation 2006;113:2706-12.
95. Hage C, Mattsson E, Ståhle A. Long-term effects of exercise training on physical activity level and quality of life in elderly coronary patients. A three- to six-year follow-up. Physiother Res Int 2003;8:13-22.