Psychopharmaceuticals in the Treatment of Pain

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[Summary]

Praktický lékař [General Practitioner] 84, 2004, suppl. 1, pp. 40–44

Pain is an unpleasant sensory and emotional experience associated with acute or potential tissue damage or described in terms of such damage.
Pain is always subjective…

From the definition of pain by the World Health Organization (WHO)

The treatment of pain is perhaps the most fundamental function of medicine and one that remains an undeniable necessity even now, when all medicine has a rational and scientific basis. In spite of the extensive body of serious work on analgesic methods, there still exists an alarming amount of evidence suggesting that a high percentage of patients suffering from pain do not receive adequate treatment. Amongst other things, the level of treatment quality can be measured by the consumption of opioids per inhabitant: this indicator places the Czech Republic in thirteenth place **below the average consumption of all** European countries.
The rational use of psychopharmaceuticals as adjuvants in the treatment of pain first emerged in analgesia as a "scale" (given in table 1) for the treatment of pain in cancer patients. As well as treating symptoms, adjuvant therapy comprises treatment with classical psychopharmaceuticals, primarily antidepressants.

TABLE 1 WHO recommendations for the treatment of cancer pain

1. STANDARD ANALGESIA + adjuvant therapy	→ easing of pain → *pain does not diminish* →
2. STANDARD ANALGESIA + weak opioids + adjuvant therapy	→ easing of pain → *pain does not diminish* →
3. STANDARD ANALGESIA + strong opioids + adjuvant therapy	→ *pain goes away*
Preference should be given to peroral, rectal or transdermal application over parenteral application	

TABLE 2: The biopsychological profile of the patient in pain

Nociception – neurochemical level
Perception – neuropsychological level
Experience – complex intrapsychic level
Pain behaviour – social level
Existential sense – spiritual level

TABLE 3: The Coping Strategy Questionnaire
Swartzman L.C. et al.: The factor of the Coping Strategies Questionnaire. Pain, 1994, 57, p311–316 (Czech translation by R. Honzák)

Categories: 1. Distraction, 2. Challenge, 3. Reformulation, 4. Catastrophization; 5. Faith and Hope	
Please mark which of the activities below you do when you are in pain. At the end of the line, indicate whether and how much they help you. Thank you for your cooperation. We would like to reassure you that all data you provide will be regarded as confidential.	
1	I think of things that I enjoy doing I think of people with whom I enjoy doing things I go over pleasant past experiences in my thoughts I do something I enjoy, like watching TV or listening to music I go out and do something I enjoy, like going to the cinema or shopping. I try to be with other people I read I take a shower or a bath
2	I continue as though nothing was going on I don't pay any attention to it I tell myself that I simply won't allow the pain to prevent me from doing what I'm doing Even though the pain bothers me, I carry on with what I'm doing I don't think about the pain I ignore it I think of the pain as a challenge that I simply can't let bother me No matter how bad it gets, I know I'll cope
3	I imagine that the pain is somewhere outside my body I pretend that it isn't a part of me I try to distance myself from the pain as much as possible, to the extent that it's as if it were in someone else's body I try not to think of it as something in my body, but as something quite separate from me I don't think of it as pain, but as a dull or hot sensation I focus on other sensations, e.g. numbness
4	I feel as if I can't stand it any more I feel I can't go on any longer like this I am always worrying about whether it will ever end I feel my life is worthless It's horrible and I can feel how it's holding me back It's terrible and I know that it's never going to be any better
5	I pray to God that it won't last long I pray that my pain will go away I know that someone will come at some point who will help me and make my pain vanish in an instant I count on my faith in God Any other activities that help me: …….. ……..

In the diagnosis and treatment of pain, it is essential to completely disregard the model set out by the French philosopher René Descartes (who amongst other things claimed that animals cannot feel pain because they lack the spiritual principle and said "if they cry out when you beat them, it is no different to beating a piano and its producing a sound"

On the basis of current knowledge, we can divide the experience of pain into several categories (see table 2) to form a working model. These are **nociception** – the processing of the painful stimulus at a neurochemical and neurophysiological level; the **perception** of pain and the involvement of the emotional components by the limbic system; and finally the full and complex **experience**, which, in addition to the above elements of the nervous system, also involves the cortex region of the brain. The experience of pain results in **pain behaviour**, which has the aetiological goal of alerting those around to the fact that the individual is suffering, and thereby gaining help. Finally we must not forget the existential and spiritual level, which is affected by the higher (moral and ethical) feelings and the value scheme of the individual (the same pain may be dealt with very differently by the sportsman whose only interest is in getting through a match and the individual who knows that his pain is caused by a terminal illness).

The experience of pain may be caused at any level of the system as a whole, i.e. not just from tissue damage with nociceptive consequences (stimulation of free nerve endings by substances causing perception of pain), but also by malfunctioning of the structures that carry the signals, the negative "tuning" of the emotional structures, and the sensation of pain evaluated by the cognitive centres as such, even though it arises from the psychosocial sphere (e.g. loneliness). The

integrating substance that connects all these levels appears to be **substance P**, a decapeptide that is found from the periphery to the central cortex in connection with pain, without regard to whether the pain is of physical or psychological origin.

TABLE 4: An overview of psychopharmaceuticals with an analgesic effect, and other adjuvants

Name	Indications	Daily dosage	Notes
ANTICONVULSANTS			
Phenytoin	Neuropathic pain, acute lancing pains (tic douloureux, trigeminal neuralgia)	100–300 mg	Begin treatment with a low dose; increase as required
Carbamazepine	Acute neuralgic pain, lancing pains, tic douloureux, neuralgia	100–800 mg	Especially suitable for paroxysmal pain
Valproic acid	Neuropathic (postherpetic) lancing pains	200–1000 mg	Damaged liver parenchyma is a contraindication
Clonazepam	Neuropathic lancing pains	1.05–5.0 mg	Also suitable for emotional lability and manifestations of anxiety
Gabapentin	Primarily neuropathic and tension pain	100–900 mg	As a GABA receptor agonist, this also has a calming effect
ANTIDEPRESSANTS			
TCA (tricyclic antidepressants: imipramine, desimipramine, amitriptyline, nortriptyline, dosulepin)	Neuropathic pain (diabetes), postherpetic neuralgia, adjuvant treatment for cancer pain	25–50 mg; if depression is present, the full antidepressant dose is indicated	In complex treatment, their otherwise undesirable effects (anticholinergic = spasmolytic effect, sedative effect) may be exploited. Tricyclic antidepressants have been tested in many studies and can be considered as a drug of first choice
Maprotiline	As for TCA	25–125 mg p.o., 25–75 mg i.v.	Significantly lower anticholinergic effects in comparison with the previous group. Application by infusion is possible (25–50 mg); this bypasses the hepatic barrier and thereby achieves more rapid effects
Fluoxetine (SSRI)	All types of pain; to be tried where previous antidepressants have failed, especially where there is major anxiety	20–60 mg	Owing to its long half-life, a maintenance dose may be administered every other day or twice a week
Fluvoxamine (SSRI)	As for fluoxetine	50–200 mg	Interacts with immunosuppressants
Paroxetine (SSRI)	As for fluoxetine	10–60 mg	Indicated in cases where compulsive elements are present
Citalopram (SSRI)	As for fluoxetine	10–60 mg	Very well tolerated
Venlafaxine	SNRI (dual – acts on both noradrenaline and serotonin); analgesic effects similar to TCA	17.5–75 mg	Contradictory results on interactions with tramadol – better not to combine
ANTIHISTAMINES			
Hydroxyzine	Somatic and visceral pain	25 mg, to 100 mg	Potentiates analgesic effect, has anxiolytic, sedative and antiemetic effects
NEUROLEPTICS			
Levopromazine	Somatic and visceral pain. Suitable for patients who have developed tolerance to analgesics	10–50 mg	Also has anxiolytic, sedative and antiemetic effects
Prochlorperazine	Potentiation of analgesic effects, suitable for pruritus	10–30 mg	Also has anxiolytic and antiemetic effects
Fluphenazine	Somatic and visceral pain	1–8 mg	No significant pain-inhibitory effects; acts as an antiemetic and anxiolytic
Pimozide	Resistant trigeminal neuralgia	2–8 mg	May cause extrapyramidal side-effects
Haloperidol	As for levopromazine	2–6 mg	As for levopromazine

Psychopharmaceuticals may be of help in all the levels mentioned. Owing to their myorelaxant effect, **anxiolytics** help to limit the initiation of the vicious circle that arises from exaggerated protective responses (such as spasms, whose original aim is immobilization of the affected area, but which may eventually become the cause of further nociceptive stimuli) and also assist in pain modulation. **Anticonvulsants** limit pathological nerve activity arising from disturbance to the structure (e.g. in neuralgia or neuropathy); **neuroleptics** with their central inhibitory effect potentiate the effect of anodynes. Antidepressants have a special place among psychopharmaceuticals: they modulate the experience of pain through their effect on the limbic system, and they also have their own independent analgesic effect, probably as a result of their strengthening of the gating system. This is particularly the case with tricyclics (amitriptyline, melipramine [imipramine], nortrilen [nortriptyline] and prothiaden [dothiepin], and it is also possible to make use of their otherwise undesirable side-effects (anticholinergic and sedative).

TABLE 4: An overview of psychopharmaceuticals with an analgesic effect, and other adjuvants

Name	Indications	Daily dosage	Notes
ANXIOLYTICS			
Diazepam	Acute pain in which it is appropriate to quell anxiety. Chronic pain of a spastic type (e.g. chronic tension headache, disturbance of the function of the temporomandibular joint accompanied by pain, tic douloureux)	10–30 mg i.v. bolus 10 mg	Suitable for sleep disturbances. Not recommended for long-term use owing to the potential for development of tolerance and habituation. When stopping immediately after long-term use, watch out for the rebound effect and abstinence syndrome. Long-term use of high doses may cause unwanted sedation, sometimes with depressive characteristics
Other benzodiazepine anxiolytics	Analogous indications	4 mg up to several tens of mg according to the character of the preparation	Similar to diazepam, predominantly with a lesser myorelaxant effect
Buspirone	In cases where long-term anxiolytic treatment is indicated	5–25 mg	Non-benzodiazepine anxiolytic that probably acts on the NA and 5-HT systems. Low sedative effect.
ANTIHYPERTENSIVES acting on alpha-2 and alpha-1 receptors			
Conidine	Migraine. Operative (wound) pain – increases the analgesic effect of morphine by means of releasing endogenous opioids in intrathecal application	4.50 μg up to a dose of several tenths of a mg	Must not be stopped suddenly after long-term use. Transdermal application ensures constant concentration and leads to better results and better patient cooperation
Guanethidine	Rheumatoid arthritis	4–50 mg	To begin with, administer only at night owing to the significant orthostatic effects.
Prazosin	Raynaud's syndrome	0.5 mg up to a dose in the order of milligrams	Risk of orthostatic effects at the start of medication
MYORELAXANTS			
Baclofen	Central pain especially after spinal cord damage and secondary muscle spasm	5 mg up to a dose in the order of tens of mg	Side-effects include fatigue, drowsiness and potentially confusion when plasma concentrations are high. Must not be stopped suddenly.
STEROID HORMONES			
Prednisone	Physical and neuropathic pain, inflammatory pain, dystrophia. Anti-inflammatory, anti-emetic and analgesic effects. Effective in intracranial hypertension and sympathetic pain	5 mg up to tens of mg	If used in the longer term, gradual decrease in the dose is necessary when stopping medication. Watch out for interactions. May cause psychological disturbance
Dexamethasone	As for prednisone	0.5 mg up to a dose in the order of milligrams	As for prednisone

In the evaluation of pain and in judging the most appropriate method of treatment, it is important to consider whether the pain is acute or chronic, and also whether it is caused by tumour or some other factor. An arbitrary method of classification according to time considers acute pain to be that which has lasted for less than three months. During that period, appropriate "coping" strategies – such as shutting one's mind to the pain, regarding it as a challenge, reformulating it into other sensations (e.g. a sensation of heat), and hope and faith – may predominate. Between the third and sixth month, the pain becomes "sub-chronic" and patients are more affected by feelings of increasing powerlessness, loss of hope and depression. After the sixth month, most patients are so worn out that a depressive view of their state prevails, and the dominant strategy is that of "catastrophization" (see table 3).

When catastrophization occurs, in 85% of cases it is linked with clinically significant pathological depression (depressive disorder) and the dose of antidepressant must correspond to the therapeutic dose for the psychiatric indications.

Acute pain has generally been eased by standard analgesics, even though in this area too it is possible to make use of the therapeutic effects of psychopharmaceuticals (their spasmolytic and central inhibitory effects and their influence on emotional state and thereby also on the modulation of pain).

However, the action of psychopharmaceuticals plays a more significant role in the treatment of chronic pain. In its evaluation, it is necessary to take a whole range of circumstances into account, in particular the character of the pain, the length of its duration, the patient's personality and social background, psychiatric comorbidity, the possibility of drug interactions and not least the relationship between patient and doctor.

Cooperation with a centre for pain treatment or systematic cooperation with a psychiatrist is extremely desirable.

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