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# Summary

**Hannes Wahlroos**

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Editorial

## The pharmaceutical field and e-future

One of the pharmaceutical fields greatest challenges in the next few years will be to create suitable, safe, and well-functioning systems for electronic communication, dissemination of information, and commerce. The system would cover electronic prescribing and dispensing, e-commerce of medicines, marketing and dissemination of drug information in the Internet, and access to electronic services in pharmaceutical matters for consumers and businesses alike. The development of information technology and international examples are stimulating this process.

Interested individuals and IT-companies have taken the initiative in developing systems associated with electronic prescribing and dispensing in Finland. As a bystander, it seems to me that the basic framework and conditions applicable to health and medical services, within which e-prescriptions should function, have been forgotten. The system must at least take into account data protection, the rights of patients, pharmacovigilance, rational prescribing and the drug reimbursement system. Furthermore, due to the nature of the business, national coverage for the systems would be preferable. It is excellent that the Ministry of Social Affairs and Health has paid attention to these matters in connection with the Satakunta Macro Pilot Study of Processing Medicine Information. Accepting practical realities is also useful. The sad truth is that the majority of doctors working at Municipal Health Centres do not have access to appropriate workstations.

E-commerce refers usually to commercial transactions via the Internet. The concept could be broadened to cover other modes of distance trading, such as orders transmitted and processed via television and telephone. Pressures to develop the e-commerce of medicines further seem to emanate from the USA and the illicit traders in pharmaceuticals in the Internet, whose trading and merchandise give rise to warnings in international forums from time to time.

The instructions issued by the World Health Organisation (WHO) last year make up the most definitive and cautionary set of advice issued so far on how to approach trading in medicines in the Internet. From a

Finnish point of view, it would be preferable that a controlled system that takes into account the above mentioned aspects would be implemented. The possible need for legislative reforms or amendments should be assessed. It would seem natural that the actors in the pharmaceutical field were in charge of this developmental work. The European Commission has only recently appointed working groups to assess the potential need for EU legislation or directives for the e-commerce of medicines. One of the two working groups should take a stand on the promotion of prescription medicines in the Internet especially aimed at consumers, which is allowed in the USA.

The image of consumers and patients as passive recipients of regulated information is now history. This applies also to medicines. Today's consumer is sophisticated, aware of his rights, and willing to find information on his own medication or to discover potential drug therapies for himself. This situation has created tremendous marketing potential, especially for the pharmaceutical industry, not to mention the so-called portal companies. As a medium, the Internet is virtually impossible to control completely. It is therefore necessary to find ways to ensure that impartial, validated information on medicines, free from commercial interests, is available. The demand such information is constantly growing even among health care professionals. EMEA (The European Agency for the Evaluation of Medicinal Products) and the authorities in many EU member states already publish summaries of product characteristics, consisting of accepted and official drug characteristics, and information packages describing correct drug usage. The Finnish National Agency for Medicines will also support this development.

According to reports in the press, it is typical that enterprises relying on teenage coders and network experts are in the vanguard of developments among IT-companies. It is therefore important that actors aware of their responsibilities and competent supervisory authorities lead the e-projects of the pharmaceutical and medical fields.

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# Summary

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## Fibromyalgia

*The main characteristics of fibromyalgia (FM) are pain in the musculo-skeletal system, night sleep without resulting relaxation, and inexplicable exhaustion immediately upon awakening. The patients also suffer from psychosomatic, psychiatric, neurological and other symptoms difficult to categorise. Despite this, there are no objective findings in these patients.*

The pathogenesis and pathophysiology of the syndrome are poorly known. The clinical diagnosis is based on the history and the tenderness found in anatomically predictable areas, which seem to reflect the general distress and misery of the individual. Due to the multitude of symptoms of FM, it is usual for the patient to be labelled with several diagnoses that do not reflect the symptoms complained of by the patient or the clinical findings, but which reflect the specialisation of the doctor.

According to one British study, over 40% of the adult population is reported to suffer from chronic pain, and according to another one, over 10% suffer from pervasive pain. FM can be diagnosed in 2–3% of the population. The majority of the patients are women, and, since only few patients are cured, the frequency of the syndrome increases with age.

Electrical activity of the brain during sleep, neuro-endocrinological disturbances and circulatory and metabolic disturbances of the muscular system, deformities of connective tissue, the individual's lack of ability to cope with conflicts and primary psychiatric problems have, for example, been offered as pathogenetic mechanisms of fibromyalgia. The debate continues.

### Treatment of fibromyalgia

Close co-operation between doctor and patient is the main precondition for planning individual treatment and monitoring of follow-up. Occasionally the patient has acquired a good

deal of information and requests an appointment with a specialist. Only an unbiased attitude, careful listening to the patient and a thorough clinical examination, together with a comprehensive account of the complex character of the sensation of pain, may enable the doctor to avoid acquiescing to the referral in that situation.

The aim should be a prompt diagnosis without unnecessary exclusion studies that only lead to a merry-go-round of investigations. However, consideration should be given to the causes of exhaustion which need to be treated more specifically (anemia, hypothyroidism, hyperparathyroidism and estrogen deficiency) or chronic pain (arthritis, polymyalgia). It is often useful to listen to the patient's own theories and review them properly in the light of medical evidence. It is also important that the doctor emphasises the functional character of the symptoms and thereby their benign character. A severely depressed patient should be referred for psychiatric treatment.

There is no treatment which provides a cure and consequently the aim of treatment should be to reduce symptoms and improve the patient's ability to function and quality of life. In the treatment of a fibromyalgic patient, all modes of treatment based on medical evidence should be put into practice immediately. However, a large number of patients will be disappointed with the help that medical science can give and will also turn to alternative therapies; popular forms include, for example, the use

of various diets, supplementary trace elements, and also massage involving the musculo-skeletal system, particularly lymph therapy.

A social history is important because it will explain any conflicts there are in the family circle or work environment, the patient's way of life, sleep hygiene and hobbies. It is recommended that the resources of the occupational health services be used to survey the patient's occupational ergonomics and working conditions.

### Treatment without drugs

The physical condition of FM patients is usually poorer than that of healthy volunteers, and it has been possible to reduce patients' symptoms and improve their performance by physical training and muscle-building exercises. The patients are also given information about fibromyalgia and its treatment, taught pain treatment, creation of a positive outlook, relaxation, meditation, yoga, stretching exercises, etc. Individual reports of relief of symptoms have also been received with electrical acupuncture, feedback exercises, hypnotherapy and homoeopathy.

### Treatment of fibromyalgia with drugs - antidepressants used as analgesics

Tricyclic antidepressants in small doses (particularly amitriptyline, 10–50 mg/day) are used in the treatment of FM. The preparations in this group of medical substances are most effec-

tive in improving sleep quality, and reducing pain and exhaustion; but their effect on sensitivity is minor. Even though these drugs provide some mild relief to the majority of patients who tolerate them, they are really helpful only in about one in three patients. A positive response is generally found after 1–2 weeks of treatment.

To reduce adverse reactions (such as dry mouth and sedation), the administration should be started with as low a dose as possible. The drug can be taken periodically. A less anticholinergic tricyclic antidepressant is more appropriate than amitriptyline in some patients.

Cyclobenzaprine, which has a structural resemblance to amitriptyline, is mainly considered a muscle relaxant but it also has a proven beneficial effect on the symptoms of FM.

There are recent reports of beneficial effects of venlafaxine, a serotonin and noradrenaline re-uptake inhibitor, on FM patients. At this stage, however, it is reasonable to wait until research results of controlled studies are made available.

### Other medical treatment

Anti-inflammatory analgesics and glucocorticoids have been found to be equal to placebos in controlled studies. A compound of ibuprofen and codeine was not found to be more effective than a placebo in our own study either. According to evidence-based information, anti-inflammatory analgesics should not be used to treat pain caused by fibromyalgia.

In a cross-over controlled study consisting of a small number of patients, intravenous tramadol relieved the pain in FM patients better than did a placebo. According to preliminary reports, patients who were randomly chosen to take tramadol withdrew less often than volunteers taking a placebo, due to the relative ineffectiveness of the drug under study.

In a study from which patients with adverse reactions to tramadol were excluded, the reduction in pain on the active drug was superior to that on the placebo. However, a compound of paracetamol and codeine has been found to have an equivalent effect to tramadol in the

treatment of patients with various types of chronic pain such as fibromyalgia.

Primarily due to the risk of addiction, benzodiazepines should be avoided in the treatment of chronic pain, even though one cross-over study showed that patients on a combination therapy of alprazolam and ibuprofen experienced a significant relief of pain in comparison with patients receiving a double placebo.

Sleep disturbance is one of the predominant symptoms of FM, which is why sleep aids are also used in the attempt to relieve patients' symptoms. Both zopiclon and zolpidem have been found to improve patients' rate of falling asleep, quality of sleep and exhaustion the following day, but they have not been found to have an effect on pain.

Symptoms of some FM patients have been relieved successfully by specific 5-HT<sub>3</sub> receptor blockers (tropisetron, ondansetron). In a five-day study on ondansetron, volunteers were given 1,000 mg of paracetamol daily. Symptoms of the patients in this group of volunteers actually became worse during follow-up.

In a Norwegian study lasting for 8 weeks, a compound of paracetamol, caffeine and carisoprodol was found to reduce the symptoms of FM patients. Due to the significant response in the placebo group, the response of the patients on active therapy was not substantially different statistically from that of the volunteers.

Gammahydroxybutyrate is a natural metabolite of the central nervous system which is believed to act as a neurotransmitter and neuromodulator. Eleven patients in an open study received 4.5 g of gammahydroxybutyrate in the evening over a period of four weeks, which was found to reduce pain and exhaustion at the same time as the patients' nocturnal EEG findings were normalised.

Growth hormone is known to be secreted mainly during deep sleep and its concentration can be monitored by measuring the concentration of serum insulin type growth factor I. Patients with reduced concentrations were randomised to a 9-month growth hormone or placebo therapy. Active treatment relieved the patients' symptoms and improved their

ability to function, but the response disappeared after interruption in the treatment.

### Conclusion

FM is a pain syndrome which is common, obviously multi-etiological, broad-spectrum with regard to its seriousness, inadequately understood with regard to its pathogenesis and which has very important consequences for public health. Furthermore, patients with the severest symptoms frequently rely on the health care services. Increased research evidence indicates that mechanisms of CNS origin lead these patients to interpret as pain some sensations which healthy individuals interpret as normal stimuli.

The treatment of patients with the severest symptoms should be managed on a multidisciplinary basis. I have specifically noticed the particular importance of a personal nurse and a physiotherapist but the help of an occupational therapist, nutritionist and psychologist can also be important. Patients with extremely severe symptoms should receive treatment at centres with special expertise.

Some patients may benefit from regular appointments with their doctor. However, there is no need to re-view all the patient's symptoms again or to repeat the examinations just in case, but the aim with follow-up visits should be to support the patient in his/her effort to follow the prescribed treatment and rehabilitation programme by giving positive feedback.

There is a contradiction between the multitude of symptoms exhibited by the patients and the small number of objective findings. Consequently the patients' symptoms are often belittled and the patients are categorised as either somatisers, or they are assumed to be malingering to get social benefits or to be suffering from a psychological illness. As the neurochemical basis of somatisation is not known, it cannot be treated specifically. In the absence of a highly specific treatment, all the treatment modes where efficacy is supported by medical evidence should be introduced immediately the syndrome is diagnosed.