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Neuropathic abuses

KOMMENTARARTIKKEL

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The medicalisation of everyday maladies is not a new phenomenon, but is increasingly being pushed by the pharmaceutical industry. The hunt for new «diagnoses» is good business, and now our bad backs have also become the subject of the industry's unsought attention: they have become neuropathic. Help is not far off, however, if we are to believe the manufacturer of Lyrica.

There appears to be a growing tendency to equip patients who have indeterminate pain conditions with specific diagnostic labels. One possible interpretation of the phenomenon may be that there are forces at work at both individual and societal level to make more «acceptable» diagnoses, and that attempts are being made to squeeze the jumble of vague pain conditions that doctors often face into specific diagnostic categories – almost like an exercise in diagnostic laundering. The hunt for «new diseases» is also driven by the pharmaceutical industry (1).

Not all diagnoses have an equally high status. The heyday of both fibromyalgia and whiplash injuries seems to be waning, while chronic fatigue syndrome and post-traumatic stress syndrome are diagnoses that appear to be on the rise. Diagnostic labels may confer a certain legitimacy. For example, disability pensions are granted just as frequently for a whiplash diagnosis without neck pain as for neck pain without a whiplash diagnosis (2).

Another diagnosis that is currently in vogue is neuralgia. A little paresthesia here and slightly reduced sensibility there and the diagnosis of neuropathy is good to go. The culmination of this trend so far is perhaps represented by a full-

page Pfizer advertisement in the Norwegian medical periodical *Dagens Medisin*. The message broadcast here is that 37 % of patients with chronic back pain have a neuropathic pain component. An article published in 2006 is the sole reference cited (3). The same advertisement stresses that Lyrica (pregabalin) has central and peripheral neuropathic pain as one of three indications. A point is also made of the fact that individual reimbursement can be applied for under the Norwegian blue prescription scheme, and that the application form is ready and waiting in WinMed.

A «useful» study

The study referred to in the advertisement is German, and was written by two neurologists, an anaesthesiologist (all with financial support from Pfizer) and a Pfizer employee. There are two parts to the study. In the first part, the authors aimed to investigate the validity of a newly developed questionnaire for identifying neuropathic pain. The gold standard was a clinical and paraclinical survey by two «experienced pain specialists» (unspecified), who independently surveyed 392 pain patients. In the light of the predominant symptoms and the findings of the survey, the patients were grouped as having mainly neuropathic or mainly nociceptive pain mechanisms. Patients with back pain accounted for 23 % of those in the category «neuropathic pain» (radiculopathies appear not to be included), while in the category «nociceptive pain», low back pain accounted for 61 %.

The patients then completed the PainDETECT questionnaire, developed by the authors as a screening instrument to detect neuropathic pain. The form lists seven «typical» characteristics of this type of disorder. The authors found a high correlation between the results of the clinical examination and scores on completed questionnaires. With a threshold score of 19 points or more, both specificity and sensitivity were found to be an impressive 84 %.

In the next stage, a total of 7 772 patients who had had low back pain for more than three months were recruited. They completed the questionnaire without an accompanying clinical examination. According to the study, 37 % of them had a neuropathic pain component (score ≥ 19 on the PainDETECT questionnaire). There was substantial comorbidity in this group, with a much higher prevalence of psychopathological disorders and physical disability.

Can a neuropathic diagnosis be made by means of screening?

The authors conclude that the PainDETECT questionnaire is a reliable, simple and validated screening instrument for detecting neuropathic components of chronic pain conditions, including back pain. They are also of the view that the instrument is adequate for making such a diagnosis. In an article published in 2009, however, the first author points out that screening tests cannot replace a

clinical examination, and that they are not intended to be used for diagnostic purposes (4). In the same article, he stresses the importance of identifying sensibility changes (including allodynia or hypoesthesia) in the painful regions.

The authors draw wide-reaching conclusions from these two part studies, and make no reservations regarding the proportion of neuropathic back pain. On the basis of data on 52 selected back patients, they go so far as to say that 14.5 % of German women and 11.4 % of German men suffer from predominantly neuropathic low back pain. It may be mentioned by way of comparison that the incidence of neuropathic pain with a specific aetiology (including post-herpetic neuralgia) is estimated at 0.081 per 100 person years (5).

What is meant by «gold standard»?

The article states that the two «pain specialists» who assessed the back patients separately disagreed on the diagnosis in only 2 % of the cases, and that the survey represented the gold standard against which the completed questionnaire was assessed. However, it is not stated which criteria were used to distinguish between nociceptive and neuropathic pain, only that the specialists used their «experience», supplemented by «other relevant tests». The concept of a gold standard presupposes that the reference test is valid, unambiguous and does not overlap with the test variable. In such cases, it is meaningful to calculate the sensitivity, specificity and positive predictive value of clinical tests. In the study in question these conditions do not appear to have been met, and the conclusions regarding the reliability of the test are therefore somewhat tautological.

Pseudoneurological symptoms associated with non-specific pain conditions

The study does not indicate how many patients experienced pain in regions other than the low back. It is a common clinical experience that patients with regional and extensive pain conditions also describe pseudoneurological symptoms. The pain is often described as burning or stabbing. Pronounced superficial tenderness, diffuse sensibility impairment and uncharacteristic radiation are also common in this group. In a fibromyalgia study, paresthesia was described in 54 %, numbness (anywhere) in 50 % and burning pain in 38 % (6).

There is little doubt that with chronified pain conditions, changes occur in neurohumoral and pain-modulating systems, but does this justify using the term neuropathy? With such a reductionistic pain model, it is easy to overlook the many-faceted psychosocial factors that we now know play a major role in the development of chronic pain-conditioned disability (7, 8). Such a holistic conceptual model receives indirect support from the study's finding of considerable psychiatric comorbidity in the «neuropathy» group. Instead of

discussing the possibility that anxiety and depression could be the primary cause of the group's pain condition, the authors appear to be so blinded by their success in «revealing» neuropathy that they are unable to consider psychosocial problems as anything other than secondary effects of pain.

Is detailed diagnosis of back patients possible?

Back pain syndromes are often the predominant clinical problem at physical medicine clinics. The clinical knowledge base is too limited to allow valid, pathogenetically based diagnoses to be made for the majority of patients with non-specific back pain with no signs of radiculopathy (9). There is a generally low degree of diagnostic consensus, and the diagnosis that is made depends to a large extent on the type of «back specialist» consulted (10). Such diagnostic disagreement contributes to patients' confusion and anxiety about their health and often leads to over-treatment and at worst further chronification (7, 8).

With radiculopathies there is a higher diagnostic precision, and here it is more meaningful to use the term neuropathy. The Freynhagen study leaves doubt as to what type of back problems are being described, but radiculopathies appear to be excluded. We look in vain for the concept «back pain with a neuropathic component» in modern, quality-assured literature on backs. The study's use of the concept is poorly founded as long as the authors make no attempt to describe the underlying neuroanatomical lesion.

Time to tighten up use of the term neuropathy

Drawing generalised conclusions about pathogenesis on the basis of verbal pain descriptors in a questionnaire is a dubious practice, as phenotypic similarities are not synonymous with shared pathophysiological conditions. The verbal pain description of patients with definite neuropathy overlaps with symptoms associated with non-specific pain (11). It is recommended that the term neuropathy be restricted to «pain that arises as a direct consequence of a lesion or disease that affects the somatosensory system» (12). Here, «disease» means identifiable conditions of an inflammatory or autoimmune nature, while «lesion» refers to macro- or microscopically identifiable injury. It is largely a matter of focal or multifocal injuries to the peripheral nervous system, generalised polyneuropathies and damage to the central nervous system.

According to this definition, definitive neuropathic pain requires confirmation of objective neurological disease or injury through supplementary clinical and/or laboratory-based tests, and it is stressed that clinical examination is mandatory for enabling the diagnosis to be made. The Freynhagen study does not describe the clinical or paraclinical criteria used to make the diagnosis «back pain with a neuropathic component», nor does it make any attempt to grade the probability of such mechanisms. Thus the authors contribute to a regrettable misuse of the term «neuropathy».

The authors of the study point out that it is crucial that patients with neuropathic back pain get a diagnosis, because there is «strong evidence» that their pain can be alleviated by medicinal treatment, including anticonvulsants (read pregabalin). Recent placebo-controlled studies provide some support for the efficacy of pregabalin for well-defined neuropathic pain (13), to a lesser extent for radiculopathy (14). However, there are no placebo-controlled trials of pregabalin for chronic back pain. According to ClinicalTrials.gov, Pfizer was planning a trial of pregabalin for back pain (NCT01298466) in 2011. It was intended to focus greater attention on and improve the diagnosing of patients with chronic low back pain with a neurogenic component, and determine the efficacy of and tolerance for pregabalin. The trial was withdrawn in April 2012 without any reason being disclosed.

Conclusion

Pfizer is deceiving Norwegian doctors by claiming that a large proportion of back patients have a neuropathic pain component, and that they will benefit from Lyrica. The claim is based on one single study, planned, conducted and financed by Pfizer. The study draws conclusions for which there is no foundation, and one might suspect that the objective has been first and foremost to prepare the ground for increased sales of Lyrica by expanding the scope of the term neuropathy.

Pfizer Norge's back campaign joins the depressing ranks of examples of the pharmaceutical industry – often with the aid of hired consultants, patient associations and the media – adopting a «crusader role», the object of which is to inform both the general public and health personnel about disorders that are underdiagnosed and undertreated (1). Another serious aspect of this campaign is that, by exploiting the liberal blue prescription rules, Pfizer is attempting to pass the costs of this undocumented treatment on to Norwegian taxpayers. Replacing lost market share by «inventing» a new indication for a potentially habit-forming drug may be good news for the Pfizer group and its shareholders, but it is bad news for the taxpayers and all those who expect a modicum of scientific and ethical integrity from the pharmaceutical industry.

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