

## **Attachment B**

### **COMMENTARY ON THE PITFALLS OF OPIOIDS FOR CHRONIC NON-MALIGNANT PAIN OF CENTRAL ORIGIN**

Stephen G. Gelfand, M.D.

There is a serious medical and social problem today under intense media, law enforcement, and regulatory scrutiny concerning the misuse and abuse of OxyContin for chronic non-malignant pain. This situation has made the drug difficult to obtain for many patients with malignant and other types of intractable chronic pain, and has recently influenced the FDA to issue a black box warning in order to lessen the chance of inappropriate prescribing of this Schedule II narcotic. In addition to recent D.E.A. autopsy findings of nearly 300 OxyContin overdose deaths nationally since January 2000, there is a large volume of patients with chronic non-malignant pain who have become dependent or addicted as a result of legitimate prescriptions written for OxyContin [as well as other opioids]. In a recent case, the D.E.A. suspended physician narcotic licenses and closed a South Carolina pain clinic for the excessive prescribing of OxyContin, although the physicians involved believed they were following current established standards [New York Times, Dec. 10, 2001].

How did this situation occur? In the first place, on closer inspection, certain statements in the narcotic guidelines established by the Federation of State of Medical Boards [1] have received insufficient or cursory attention. These include the recommendations pertaining to the importance of psychological and substance abuse evaluations, the necessity for other treatments depending upon the etiology of the pain and extent of psychosocial impairment, and the requirement for consultation with or referral to an expert for comorbid psychiatric disorders. These are common omissions, particularly in rural environments, where the OxyContin problem first originated, and in which psychosocial factors receive less attention, resulting in fewer numbers of and referrals to mental health providers. Even before OxyContin, however, another opioid, hydrocodone, was one of the most widely abused drugs, particularly in rural areas of the South[2].

Clearly, the large volume of prescriptions and chronic use of OxyContin have increased the supply, availability, and opportunities for every type of abuse, while also filtering into our schools. Contributing to this situation has been an attempt to expand the indications for opioid therapy to the entire spectrum of chronic pain, regardless of cause. As a result of an organized educational and marketing campaign by the manufacturer of OxyContin and a number of pain societies, the message has spread that there is too much undertreatment of pain in general, and that opioids are safe in most instances and should be prescribed more often for chronic pain of all types [3,4]. There would be general agreement with this appeal if restricted to patients with cancer or other forms of intractable peripheral pathology, but it is also intended and has been used for many patients with non-malignant, non-structural chronic pain.

Since chronic widespread pain and psychological distress in the general population are closely associated [5], the indications for opioids have thus been expanded to this large population of patients with chronic pain of central affective origin, including those within the wide spectrum of fibromyalgia, one of the most common rheumatic disorders. Thus, the indications for opioid therapy has been extended to this large, heterogeneous group closely associated with a wide range of psychological distress, including the affective spectrum disorders [6]. It is these vulnerable patients who are at risk for the dangers of opioid therapy, especially in rural regions where

insufficient attention is given to pain-generating and amplifying psychosocial factors, in lieu of a more patient-popular drug-oriented approach.

The current "pain revolution" has also widened the use of opioid drugs for chronic pain by focusing on quantitative criteria such as degrees of pain [a largely subjective parameter], rather than on etiology. However, the degree of pain often correlates poorly with objective findings, and quantitative factors have different levels of significance for the types of chronic pain common to different specialties, i.e. oncology as opposed to rheumatology. This approach does not account for the essential distinctions in the biological and psychological origins of chronic pain subgroups, which are important to understand in making informed therapeutic decisions. Furthermore, the appeal to broaden the indications for opioids has also trivialized possible long-term adverse consequences, particularly of OxyContin [3,4]. Consequently, as cited above, a number of pain clinics have formed for the major reason of prescribing analgesics, especially opioids, while at the same time frequently downplaying or disregarding non-pharmacological approaches including psychological testing and management necessary for a large number of the chronic pain population. Thus, the combined effect of expanding the indications for opioid use, and insufficient attention to guideline recommendations, has facilitated the current environment of OxyContin abuse which has grown into a major medical, social, and law enforcement problem in many rural areas, as well as in an increasing number of metropolitan regions throughout the country. The extent of this situation, which often involves law-abiding citizens, was recently reported in special television broadcasts on both CBS News' 48 HOURS entitled "Addicted", anchored by Dan Rather, and MTV's: "True Life: I'm Hooked on OxyContin". Susan Zirinsky, executive producer of "Addicted" which aired on Dec. 12, 2001, states that "the growing addiction to prescription painkillers is a story that is touching every age group, and its effects are often devastating". In the last several years, OxyContin abuse and addiction have quickly spread and have reached epidemic proportions.

Pain is a complex sensation modulated by central brain pathways, including the nerve centers and networks responsible for emotions. The types of chronic pain for which opioids were originally intended are caused by pathological processes in tissues or organs from diseases such as cancer or intractable nerve or joint damage. In these conditions, the drugs combine with opioid receptors on nerve cell bodies in the brain and spinal cord which connect to and attenuate the electrical activity of these afferent nerve pathways stimulated by peripheral tissue lesions. However, in other common types of chronic pain, similar structural abnormalities in peripheral tissues are not present; instead pain is produced and intensified by central brain mechanisms, including emotions, which are stimulated by a spectrum of chronic psychological distress, and results in disordered central pain regulation and amplification [7]. This latter type of chronic pain includes the fibromyalgia syndrome, in which symptoms have neurophysiological correlates originating from persistent central nervous system activation from a large range and degree of stressful psychosocial life events [8]. The outcome is a persistent chronic stress response characterized by dysfunctional neuroendocrine reactivity to psychological, as well as to physical and physiological stressors [9,10,11]. Since opioids may have mood-elevating or altering effects, particularly in individuals with chronic pain and psychic distress [conscious or subconscious], these drugs may facilitate psychological dependence by their action on central affective nerve networks, as opposed to the peripheral afferent nerve pathways of tissue damage or destruction. In essence, it appears that opioids work on different nerve pathways in fibromyalgia than they do in cancer, intractable nerve damage, or end-stage arthritis. This central action may also occur in vulnerable patients with non-structural low back pain and tension headache.

The localization of opiates in the pleasure centers of the human brain and the recent demonstration of mu opioid receptors in the amygdala of nonhuman primates [12], a brain region

essential for emotional content and behavior, is further evidence of the intimate relationship between emotional states and pain processing. In my view, the treatment of pain of central origin should focus on attenuating the causative and perpetuating psychobiological factors, rather than masking them with exogenous opioids. These drugs carry the risk of long-term dependency or addiction by their direct effects on the emotional component of pain while depleting the brain's natural endogenous opioids.

Even in conditions of chronic pain associated with peripheral pathology such as the synovial inflammation or cartilage destruction of arthritis, central pain-modulating mechanisms may play an important role, a fact which has definite therapeutic implications. For instance, the recognition and management of underlying psychological disorders in patients with rheumatic diseases can significantly improve pain levels and function [13]. Self-management programs including education, exercise, and behavioral-cognitive therapies have likewise resulted in positive benefits beyond that of drug therapy alone [14,15]. Furthermore, dependence upon painkillers including opioids, may directly inhibit the learning of the construct of self-efficacy, which affirms the belief that people themselves, with their own resources, can significantly reduce pain and other symptoms [16]. Unfortunately for too many today, "taking a pill is easier than building the necessary will", a socio-cultural reality contributing to our national problem of prescription drug abuse, including that of OxyContin.

Self-efficacy and dependence upon drugs for pain are opposite therapeutic objectives. Although certain medications such as low dose tricyclic antidepressants for improved sleep, and SSRIs for depression and /or persistent pain are beneficial in selected patients, conventional drug management by itself has not been shown to improve outcomes in fibromyalgia [17,18]. The same conclusions also apply to chronic low back pain not caused by specific structural lesions. Both conditions frequently have multiple psychosocial and cognitive variables unique to each individual which need to be recognized and treated as part of a multidisciplinary treatment program including self-management techniques. Disregarding these factors, which are essential in the origin and amplification of symptoms, predisposes to polypharmacy, drug dependence, and a dysfunctional state in which each symptom is medicalized.

One of the most common reasons for patient visits today is the large range and severity spectrum of multiple unexplained symptoms, including pain, which are associated with stressful life events, psychological distress, depression, and anxiety disorders [19]. Fibromyalgia syndrome should be viewed and managed in this broader context, rather than as a discrete disease requiring medications [including opioids] as principle therapy. Recognition that a number of these patients would rather have a "physical disease" than confront the effects of stressful past or present life circumstances may be helpful in their overall evaluation process. Furthermore, this comprehensive approach considers the chronic muscle pain of fibromyalgia syndrome to be just one of many symptoms that can be generated by chronic tension and stress originating from biopsychosocial factors, rather than as a distinct disease in the traditional biomedical sense [8].

The lessons of OxyContin could serve to strengthen the importance of good clinical judgement and the need to evaluate each patient in context. This includes determining whether chronic pain originates from peripheral or central mechanisms, and adhering to the narcotic guideline recommendations for adequate psychosocial evaluations prior to prescribing opioids. Pain should not be treated in isolation without understanding its roots, just as fever mandates a search for causes. Undertreatment should refer not only to drug therapy, but also to the absence of important non-drug interventions. The appropriate management of chronic pain is multimodal including non-pharmacological therapies, especially for pain of central origin. Diagnosis and care should

be individualized and involve other disciplines as indicated, including clinical psychology, psychiatry, stress management, health education, and physical and/or occupational therapy.

As a result of the OxyContin problem, certain pain societies are now calling for a more balanced approach to the diagnosis and management of chronic pain [20]. Hopefully, the aftermath of OxyContin will show that a "one drug fits all" orientation to chronic pain is a risky practice with many pitfalls. In the public interest, more attention must be paid to proper patient selection rather than to marketing ploys intended to increase company drug sale figures.

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Stephen G. Gelfand, M.D.  
Intracoastal Arthritis & Rheumatology, PC  
3516 Caduceus Drive  
Myrtle Beach, SC  
843-293-1022; fax: 843-293-0096