The Role of Naltrexone in the Treatment of Opioid Dependence

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1. TREATMENT FOR OPIOID DEPENDENCE

For many years clinicians considered the treatment of opioid dependence with pessimism. But, over the last 15 years, even as the problem of addiction has grown, we have come to know more about the physiological and psychological bases of drug dependence; and we have developed a number of new pharmacologic and psychosocial modalities of treatment. These have met with varying degrees of success and have given physicians and patients alike varying degrees of hope or encouragement.

The use of methadone in a clinical setting has been successful in many cases, but methadone itself has certain liabilities and does not suit all patients (see Chapter 8). Naltrexone, an opioid antagonist approved by the Food and Drug Administration in late 1984, is a different pharmacological approach. As long as it is taken by the patient on a regular basis, it will prevent readdiction to opioids. It is thus a viable and often rewarding alternative to methadone or to approaches that depend on total abstinence. For the physician, nurse, or other professional person who is dependent on opioids and would not be permitted to work while on a methadone maintenance program, naltrexone has been and can be remarkably effective. In short, naltrexone accompanied by psychotherapy, job counseling, urine testing, and, when necessary, psychoactive medication can be another very helpful means of treatment. After a brief look at the rationale for antagonist therapy and its relationship to the pharmacology of naltrexone,
we will consider the types of patients for whom naltrexone seems to be most appropriate and perhaps the most effective, some of the studies of its use in a clinical setting, and suggestions as to how treatment may be conducted in a typical protocol, comprising detoxification, induction, and stabilization.

Opioid Antagonists

Opioid antagonists such as naltrexone are substances that bind to opioid receptors but do not produce opioid effects (Martin et al., 1973). By acting in this way they block or compete with both exogenous opioids and endorphins. When an antagonist is present in sufficient quantity to occupy all or most opioid receptors, agonist substances such as morphine cannot reach and bind to the receptors. An injection of heroin will have little or no agonist effect, and the pattern of addiction (or readdiction) may be interrupted.

It is generally agreed that naltrexone is pharmacologically effective. When an individual is protected by naltrexone, the effects of opioids are blocked or attenuated in a dose-related fashion (O’Brien et al., 1975). After a 150- or 200-mg dose of naltrexone, significant antagonism of injected opioids can persist for 72 hr. The duration of the pharmacological efficacy of naltrexone exceeds the time one would expect from its plasma level kinetics (Meyer et al., 1984). It is important to note, however, that naltrexone antagonizes competitively; it does not block absolutely. In the controlled conditions of the laboratory, some opioid effects can be perceived by subjects injecting opioids while receiving naltrexone, but the attenuation is such that even fairly large doses of heroin are relatively unrewarding.

Safety of Naltrexone

Toxicity data from animal studies indicate that naltrexone has a wide margin of safety; the LD_{50} in several species is quite high, and studies of long-term administration also indicate lack of toxicity (Rosenkrantz, 1984; Christian, 1984). In animal studies, a full range of testing has found naltrexone to be noncarcinogenic; one model even suggests some antitumor activity. In the more than 2000 opioid abusers who have taken naltrexone over the past 10 years, the drug has shown few clinically evident signs of toxicity. The endocrine changes associated with naltrexone and noted in normals have tended to occur mainly in acute studies. In normal subjects abruptly given full doses of naltrexone, dysphoria has been reported, but postaddicts gradually inducted have few complaints. In chronic dosing, no evidence has appeared so far of any clinically significant long-term endocrine changes, tumorigenic effects, or clinically relevant reproductive effects. Up to 800-mg doses per day have been given under short-term experimental conditions to subjects without apparent toxicity. However, obese