



## PIC QUESTION OF THE WEEK: 3/12/07

Q: Can you recommend a dose of naltrexone for treating generalized pruritus?

A: Naltrexone is a derivative of oxymorphone with activity similar to naloxone. It is a pure opioid antagonist with highest affinity for the  $\mu$ -opioid receptor. FDA labeled indications include opiate and alcohol dependence. The drug has also been used for managing generalized pruritus secondary to a number of disorders. The typical first-line medications used to treat generalized pruritus are the first-generation H<sub>1</sub> antihistamines such as diphenhydramine and hydroxyzine. Second-generation antihistamines such as fexofenadine, cetirizine, and loratadine have also been used. When these agents are ineffective or poorly tolerated, several other drugs, e.g. cholestyramine, ondansetron, rifampin, and danazol have been helpful in selected patients. Naltrexone has shown promise in alleviating pruritus of various etiologies. The rationale for use of opioid antagonists in the treatment of pruritus is based on the ability of endogenous opioids (e.g.  $\beta$ -endorphin and dynorphin A) to influence this condition. These substances affect opioid receptor activity (e.g.  $\mu$  and  $\kappa$ ) and may serve as the basis for some types of pruritus. It has been suggested that over-activity of the  $\mu$ -receptor plays a role in the development of pruritus. Naltrexone (50 mg daily) has been used in several studies, but its effectiveness has been variable. Two trials of naltrexone treatment in patients with cholestasis concluded that the drug was effective in reducing or improving pruritus. The onset of therapeutic response was usually within 48 hours of initiation of therapy. For most patients, adverse effects were generally mild and appeared to resolve within 2-3 days of continued treatment. Adverse reactions included nausea, vomiting, headache, dizziness, abdominal pain, irritability, and asthenia. However, a study comparing the effects of naltrexone and loratadine in patients with uremic pruritus concluded that naltrexone generally provided little benefit in this type of patient. The authors also found an increased incidence of adverse effects with naltrexone including sleep disturbances, vertigo, and gastrointestinal complications. Because naltrexone is an opioid antagonist, it can also cause withdrawal reactions and should not be initiated unless the patient has been opiate-free for a minimum of 7-10 days. Additional clinical trials are necessary to determine the usefulness of naltrexone in the treatment of pruritus.

### References:

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