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Study Links the Risk of Hypogonadism in Men to Long Acting Opioids in Patients Using Daily Opioid Therapy for Chronic Noncancer Pain

February 24, 2012, Palm Springs, CA—Results were presented today from the first study to show that the daily use of long-acting opioids increases the risk of hypogonadism (low testosterone) in men when compared to those taking short-acting opioids. These results were reported today at a poster session at the American Academy of Pain Medicine's 28th Annual Meeting.

Although this was a small retrospective study, Dr. Rubinstein believes this higher rate of hypogonadism shows that there may be some safety considerations that we were not aware of 10 years ago. "There has been a movement over the last 10 to 15 years to convert patients to long-acting opioids from short-acting opioids with the idea that they were more effective and less risky, comments Dr. Rubinstein. "This is the first study that calls into question whether or not there is a safety difference between long-acting and short-acting opioids."

Andrea Rubinstein, MD, of the Department of Anesthesiology and Chronic Pain, Kaiser Permanente Santa Rosa Medical Center, in Santa Rosa, California, in collaboration with the Division of Research, presented the results. Since the 1970s hypogonadism in men has been linked to men using daily opioid therapy, but to date, no one has evaluated whether the risk of hypogonadism was linked to specific opioids, the duration of action of the opioid, or total daily opioid use. A small retrospective cohort study of 81 men, between the ages of 18 and 80 was conducted with men that were referred by primary care to the tertiary pain clinic. These men were on a stable dose of daily opioids for at least 90 days, and none had a previous diagnosis of hypogonadism. The study excluded patients with any known endocrine disease other than stable, treated hypothyroidism, or those with a prior diagnosis of cancer or HIV. Kaiser Foundation Research Institutional Review Board approved the study with waiver of consent.

The morning testosterone levels were taken from each man referred to the clinic that was currently on daily opioid therapy for chronic noncancer pain. The study found that 57 percent of men were hypogonadal overall, but that 74 percent (34/46) of men on long-acting opioids were hypogonadal. Of the men on short-acting opioids, 34 percent (12/35) were hypogonadal, which was statistically significant at $p < 0.001$. The study defined hypogonadism as a total AM testosterone < 250 ng/dl.

Using a multivariate analysis correcting for dose, the study found that patients on a long-acting opioid formulation had a 4.78 greater odds of becoming hypogonadal, than did patients on an equivalent dose of a short-acting opioid formulation (95% confidence interval 1.51-15.07, $p = 0.008$). The study also found that dose was not significantly associated with hypogonadism in the multivariate model.

Although the study was not large enough to examine the differences between specific drugs, a subsequently awarded grant is currently underway to study men across the Kaiser Northern California System on opioids who had their testosterone levels checked. Dr. Rubinstein hopes to see a prospective study examining this question in the future.

[View Poster 229](#) - *Hypogonadism in Men Using Daily Opioid Therapy for Chronic Noncancer Pain is Associated with Duration of Action of Opioid*

About AAPM

The American Academy of Pain Medicine is the premiere association for 2,400 pain physicians and their treatment teams. Now in its 28th year of service, the Academy's mission is to optimize the health of patients in pain and eliminate it as a major public health problem by advancing the practice in the specialty of pain medicine. More information is available at www.painmed.org.

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