

Methadone even at therapeutic levels can kill

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Methadone is a possible cause of sudden cardiac death even when it isn't overdosed but is taken at therapeutic levels primarily for relief of chronic pain or drug addiction withdrawal, a new study by Oregon Health & Science University researchers suggests.

The study's findings, described in the January 2008 issue of *The American Journal of Medicine*, are based on an evaluation of all sudden cardiac deaths in the greater Portland, Ore., metropolitan area between 2002 and 2006 where detailed autopsies were performed.

The analysis was based on a comparison of two case groups. One group consisted of 22 sudden cardiac deaths in which toxicology screens turned up 1 milligram or less of methadone — defined as a therapeutic level. These cases were compared with a second group of 106 cases where no evidence of methadone was found. Seventeen of the first case group of 22 — or 77 percent — had no significant cardiac abnormalities, while five had evidence of significant coronary artery disease. By contrast, 60 percent of the case group where no methadone was present had identifiable evidence of cardiac disease or structural abnormalities, all of which are established potential causes of sudden cardiac death.

“The unexpectedly high proportion of otherwise unexplained sudden deaths in the therapeutic methadone group points to a significant contribution of this drug toward the occurrence of sudden cardiac death among these patients,” said Sumeet Chugh, M.D., lead investigator, director of OHSU's Cardiac Arrhythmia Center, and associate professor of cardiovascular medicine in the OHSU School of Medicine.

The findings lend support to a growing body of individual case reports linking methadone to a rare ventricular arrhythmia, known as torsade de pointes, which can degenerate into ventricular fibrillation leading to sudden death in the absence of medical intervention.

The study's authors conceded that they could not rule out the possibility that some of the deaths in the first case group actually were due to suppression of breathing, especially during sleep. Previous studies have found that stable patients in a methadone prevention program had more sleep architecture abnormalities and a higher prevalence of sleep apnea.

More than half – or 14 – of the 22 in the first case group were using the drug for pain control, three for drug addiction, three for recreational use and four for an undetermined reason. The mean age of the group was 37 and 68 percent were males. The mean age of the non methadone group was 42 and 69 percent were males.

The therapeutic use of methadone, a synthetic opiate, is increasing steadily not only for drug addiction but also among cancer patients for managing chronic pain largely because it is less costly than the alternatives and also because it is fast-acting and its effect is long-lasting. The OHSU study's authors proposed that a large prospective evaluation of methadone therapy be undertaken since a sizeable and growing number of people benefit from therapeutic use of the drug. They also suggested that additional safeguards prior to therapy might be necessary, such as an electrocardiogram and an assessment of the potential risk for respiratory suppression both awake and asleep.

The OHSU research was based on the work of the landmark Oregon Sudden Unexpected Death Study (Ore-SUDS), which Chugh initiated five years ago. It is the latest among a series of studies done by Chugh and his team. The Ore-SUDS study is a community-based effort that includes a partnership with the emergency medical response system, the

state medical examiner network and 16 area hospitals, enabling a systematic study of all sudden cardiac arrests that occur in the Portland metropolitan area. A separate collaborative effort also is under way with the Donald W. Reynolds Cardiovascular Clinical Research Center at Johns Hopkins University Reynolds Cardiovascular Center (Eduardo Marban, M.D., Ph.D., director) is focusing on the link between cardiac arrest and the human genome.

Source: Oregon Health & Science University

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