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Methadone Isomers and QTc Interval

*QTc appears shorter with (*R*)-methadone.*

Methadone, which can be associated with QTc prolongation, torsades, and sudden death, commonly is prescribed as a mixture of (*S*)-methadone and (*R*)-methadone. The (*R*) isomer has substantially stronger activity on the µ-opioid receptor and has much greater analgesic potency; the (*S*) form interacts with channels responsible for QTc prolongation. In this prospective study, 39 opioid-dependent patients in Germany and Switzerland were treated sequentially with (*R,S*)-methadone and (*R*)-methadone; each treatment lasted 14 days. Because (*R*)-methadone has greater potency, it was administered at half-dose.

When (*R,S*)-methadone was replaced by (*R*)-methadone, QTc intervals decreased by a mean of –3.9 milliseconds weekly. When (*R*)-methadone was replaced by (*R,S*)-methadone, the QTc intervals rose by 4.7 milliseconds weekly.

Comment: In this small short trial, the more common (*R,S*) isomer of methadone was associated with a longer QTc interval than was the (*R*) isomer. If these results can be duplicated in a longer larger trial with a wider set of clinical endpoints, (*R*)-methadone, which currently is available only in Germany, could prove to be an important treatment option for opioid-dependent patients. However, the clinical importance of the QT prolongation, and its relation to deaths that have occurred in patients taking methadone, is somewhat controversial (JW Gen Med May 7 2009 and JW Gen Med Jan 27 2009).

— ***Jamaluddin Moloo, MD, MPH***

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Ansermot N et al. Substitution of *(R,S)*-methadone by *(R)*-methadone: Impact on QTc interval. *Arch Intern Med* 2010 Mar 22; 170:529.

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