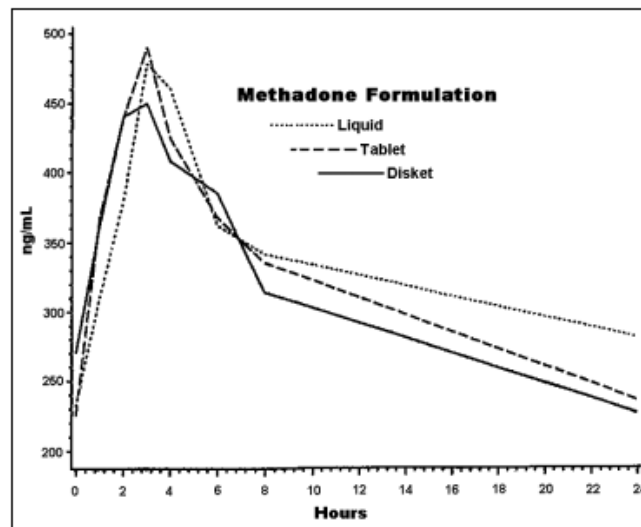


Does Methadone Formulation Make a Difference?

AT Forum Historical Note; February 2003 — Which is better: methadone as a liquid, tablet, or disket? Practitioners and patients in the methadone maintenance field often have debated that question and opinions have varied. However, clinical research reported in 1999 supports the notion that there really is no significant difference.

Investigators at Albert Einstein College of Medicine, Bronx, NY, enrolled 18 patients in an experiment whereby each received either methadone liquid, tablets, or diskets for a period of 3 weeks and was then switched to one of the other formulations. Each patient ended up receiving each of the 3 methadone formulations for 3 weeks in random order. Patients and investigators were blinded; that is, methadone was dissolved in liquid in every case so they did not know if the original formulation was liquid or solid (tablet or disket). Serial blood samples were taken to measure serum methadone levels and assessments of subjective withdrawal symptoms were used to rate the effectiveness of each methadone preparation.



The *median* methadone dose was 70 mg/day (range 30-100 mg/d). As the **graph** shows, there were no statistically significant differences in median methadone blood levels among the 3 formulations during a 24-hour dosing period, although methadone liquid appeared to persist at a higher therapeutic level throughout the day. Furthermore, patient-reported subjective opioid withdrawal symptoms did not differ by methadone formulation. The authors concluded that patient intolerance to changes in methadone formulation, which are sometimes observed clinically, appear to have no basis in the pharmacologic action of methadone itself, whether in liquid or solid forms. Therefore, any difficulties attributed solely to a particular methadone formulation may be due more to psychosocial factors.

See: Gourevitch MN, Hartel D, Tenore P, Freeman K, Marion I, Hecht J, Lowinson J. Three oral formulations of methadone. A clinical and pharmacodynamic comparison. *J Substance Abuse Treatment*. 1999;17(3):237-241.

[It should be noted that all patients in this study were abstinent from illicit or prescribed drugs and free of illnesses that might affect methadone metabolism. No patients received more than 100 mg/d of methadone, although serum trough levels (low-point values) were within a moderate therapeutic range (150-400 ng/mL) for all of them. However, serum levels were only modestly correlated with individual methadone doses and there were many differences across patients.]

Further studies enrolling more patients and in typical clinical settings, including patients requiring greater than 100 mg/d of methadone, would be a helpful expansion of this research. Finally, it should be noted that methadone formulations outside the United States are sometimes quite different, with some liquid preparations containing alcohol along with different sweetening agents and/or preservatives. Therefore, studies from other countries of patients' tolerance of methadone formulations may not be directly comparable with those in the U.S. -Ed.]