K47 Stability of Methadone in Frozen Postmortem Whole Blood for Five Years After Fatal Methadone Intoxication for Complex Regional Pain Syndrome

J. Scott Denton, MD, Nancy B. Wu Chen, PhD, and Edmund R. Donoghue, MD, Cook County Medical Examiners Office, 2121 West Harrison Street, Chicago, IL 60612*

After attending this presentation, attendees will understand that methadone is stable in frozen -20°C whole blood, and sudden death can occur after initiating methadone therapy for chronic pain syndromes.

Recognition that methadone use is increasing in clinical chronic pain syndromes, sudden death can occur from such use, and that medicolegal re-testing of frozen autopsy whole blood is valid if court ordered.

Methadone is a synthetic opioid narcotic commonly used for the treatment of heroin addiction. It was developed in the 1940s in Germany as a substitute for morphine, but its unpredictable and variable biologic behavior and half-life between patients soon rendered it unsuitable for clinical use. Today methadone is increasingly used in the treatment of chronic pain due to its longer action than other opiates, and also possibly due to the recent adverse publicity of long-acting oxycodone preparations. We present a case of fatal methadone intoxication occurring in a 39-year-old white man who suffered a work-related injury to his right ankle with development of Complex Regional Pain Syndrome (CRPS) that required toxicology re-testing for methadone five years later. Six days prior to death, the deceased had a spinal stimulator for pain control removed, and 10 mg twice daily oral methadone was added to his medication regimen. His stable chronic medications were trazodone, gabapentin, fluoxetine, baclofen, and dicloxacillin for which he was compliant. Six days after initiating methadone therapy, his wife noted he was lethargic and somnolent sitting on the couch watching television. Before she went to bed she noticed him apparently sleeping in the same position with unusual snoring respirations. The next morning she found him dead in the same position on the couch with abundant white edema foam on his face. Postmortem examination showed a well-developed and well-nourished 208 pound, 5-foot nine-inch white male with facial edema foam, and a markedly edematous, hyperpigmented and scaled right foot and ankle of CRPS. Internal examination showed cardiomegally without dilatation (534 gm), recannalized atherosclerotic thrombotic occlusion of the left anterior descending coronary artery, anterior left ventricular wall interstitial myocardial fibrosis with few scattered lymphocytes of a healing infarct, marked pulmonary edema and congestion with airway foam. The stomach contained brown food without pill material.Toxicology testing in whole blood showed methadone in the blood and liver of 0.46 ug/ml and 1.42 ug/gm, fluoxetine 0.70 ug/ml and 10.8 ug/gm, norfluoxetine 0.69 ug/ml and 10.4 ug/gm, trazodone in blood of 0.95 ug/ml, and gabapentin in blood 6.5 ug/ml. Methadone concentration in the blood was within fatal range of 0.4-1.8 ug/ml, although levels in high-dose methadone maintenance therapy in opiate tolerant patients can overlap. Gabapentin was three times normal levels for his dose. Medication bottles were inventoried and pill counts documented with appropriate pill numbers. The cause of death was certified as methadone intoxication due to CRPS due to an industrial accident. Healing myocardial infarct due to coronary atherosclerosis was considered a significant contributing factor in his death. His pain control regimen may have prevented symptoms of his healing infarct. The manner was certified accidental. His wife filed lawsuits after workmen compensation death claims were rejected. Autopsy whole blood was saved frozen at -20° Celsius in our toxicology lab in sodium fluoride for an extended time. Numerous outside physician consultant opinions regarding cause of death were generated for all parties in the lawsuits. After five years of frozen storage the blood was re-tested through court order by an independent laboratory for methadone and metabolite EDDP. Blood methadone concentration was stable at 0.41 ug/ml and metabolite EDDP 0.064ug/ml. Lawsuits were settled after this second testing apparently confirmed that methadone can rise to known fatal levels in low dose therapy for chronic pain in a non-opiate tolerant person. Possible mechanisms for this remarkable elevation are either genetic deficiency of the enzyme that metabolizes methadone in the liver, or a competitive drug interaction, or a combination of both. These factors are important as methadone is increasingly being used as a longacting alternative to sustained-release opiates for chronic pain treatment. A rediscovery of methadone's unpredictable biologic behavior may be repeating fifty years later. If lawsuits do arise from methadone intoxication, as have occurred in other drugs used to treat chronic pain, it is important to know that methadone is stable in frozen postmortem blood for at least five years if confirmation re-testing is ordered.

Methadone, Complex Regional Pain Syndrome, Frozen Whole Blood

 ** Presenting Author*