

Title: **EXTRACTION OF NARCOTICS BY HEMODIALYSIS**

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Purpose:

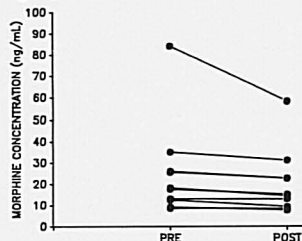
Although the limited data published suggests that narcotics are poorly dialyzed, no careful study of their extraction during hemodialysis has been done. Data reported for one subject on hemodialysis suggested that less than one percent of the daily dose of methadone is removed by dialysis (1). Similar studies have not been performed with meperidine or morphine. The purpose of this study was to determine the extraction of morphine, meperidine and methadone during hemodialysis.

Methods:

This study was approved by the Institutional Review Board. After obtaining informed consent, thirty three experiments (11/drug) were carried out in eighteen inpatients over the age of 18 who had chronic renal failure and had undergone hemodialysis for at least three months and required narcotic analgesics for a long term pain problem. The only hemodialysis membrane used in this study was the TAF-12M dialyzer manufactured by Teromo. Each subject received one of three narcotics during dialysis: morphine, methadone or meperidine. No other narcotic medications were used immediately preceding or during the study period. Dosages (mg) for IV morphine (N=11), meperidine (N=11), and methadone (N=11) were 2-8; 10-25; 2.5-15 respectively and were titrated based on each patient's specific analgesic requirements. For each dialysis experiment, two simultaneously drawn blood samples consisting of 4 mls of blood from upstream and downstream relative to the hemodialysis membrane were collected between 15 and 30 minutes after the narcotic dose. The patient's age, weight, drug dose, temperature, hematocrit, dialysis rate, dialysis type, and elapsed time from dosage to blood sample were recorded. Plasma, obtained by centrifugation, was frozen until assayed. Meperidine, normeperidine and methadone concentrations were measured using gas chromatography as previously reported (2). Following an extraction to separate the morphine metabolites, unchanged morphine concentrations were measured using radioimmunoassay with a commercial kit (Roche Abuscreen^R). Intrapatient comparisons between the pre- and post-dialysis drug concentrations were made using a Wilcoxon rank sum test. A p value of less than 0.05 was required to reject the null hypothesis.

Results:

There were no significant intrapatient differences between pre- and post-dialysis concentrations of either methadone or meperidine. The median percent extractions for meperidine and methadone were 8 and 9 respectively. No detectable concentration of normeperidine was present in any of the meperidine samples. On the other hand, post-dialysis morphine concentrations were significantly lower than the corresponding pre- concentrations ($p < 0.01$). The median percentage of morphine extracted was 15. (See Figure)



Conclusions:

Because methadone and meperidine are lipophilic and highly bound to plasma proteins, it is not surprising that an insignificant amount was removed by hemodialysis. Morphine is only 35% bound to plasma protein. In patients with uremia the binding of morphine is decreased thus further increasing the free fraction. So, a significant amount of MSO_4 could be filtered out during hemodialysis. While there is a statistically significant amount of MSO_4 extracted during hemodialysis, the amount is small and is unlikely there is a clinical significance. Withdrawal occurring from hemodialysis should not be a concern, nor should dosing changes be necessary.

References:

1. Kreek MJ, Schechter AJ, Gutjahr CL, Hecht M: Methadone use in patients with chronic renal disease. *Drug Alcohol Depend* 1980;5:197-205.
2. Coyle DE, Denson DD: Simultaneous measurement of bupivacaine, etidocaine, lidocaine, meperidine and methadone. *Ther Drug Monitoring* 1986;8:98-101.