Negative Direct Coombs’ Tests in Narcotic Addicts Receiving Maintenance Doses of Methadone

By Geoffrey K. Sherwood, Mary H. McGinniss, Richard N. Katon, Robert L. DuPont, and J. Blair Webster

Direct Coombs’ tests (antiglobulin tests) were performed on blood from all of the methadone maintenance patients were, in fact, taking methadone, as well as other drugs. This result conflicts with a report in which 85% of the methadone maintenance patients had positive direct Coombs’ tests.

In a recent report to the American Society of Hematology, Sivamurthy et al. found that treatment of narcotics addicts with oral methadone maintenance was associated with a high incidence of positive direct Coombs’ tests (direct antiglobulin tests). In that study, direct Coombs’ tests were done on blood samples from 78 narcotics addicts prior to formal methadone therapy. Seven of those individuals had a positive direct Coombs’ test for an incidence of 9%, and the incidence rose to 85% positive direct Coombs’ tests (68 of 80 patients) after methadone maintenance therapy was begun.

We have studied a group of narcotics addicts prior to methadone therapy and a group of patients on long-term oral methadone maintenance. The results of our study, in contrast to those of Sivamurthy et al., do not show an association between methadone maintenance and a positive direct Coombs’ test.

MATERIALS AND METHODS

One hundred and three opiate users seeking attention at the Narcotics Treatment Administration (NTA) of the District of Columbia were included in the pre-methadone treatment group. These patients gave a history of recent drug abuse and either were referred to the NTA or presented voluntarily for treatment.

Sixty-seven patients from the NTA treatment population already on long-term methadone maintenance were included in the methadone maintenance group. These patients had been receiving oral methadone at dosages of 30–140 mg/day, with a median dose of 90 mg/day. The majority of these patients had been on methadone maintenance for...
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1–2 yr, and they all had methadone consistently detected in urine samples in the month prior to Coombs' testing.

Blood samples were drawn in tubes containing citrate as anticoagulant. The red cells from each sample were washed four times in saline and resuspended to a 2% cell suspension in saline. Direct Coombs' tests were performed using four separate commercial antihuman globulin reagents. (Commercial reagents were purchased from: Ortho Diagnostics, Raritan, N.J.; E. R. Squibb and Sons, New Brunswick, N.J.; Spectra Biologicals, Oxnard, Calif.; and Pfizer, New York, N.Y.)

One of these reagents was known to have activity against IgG, IgA, and complement-coated red cells. The remaining three had good activity against IgG-coated red cells, varying activity against complement-coated red cells, and no activity against IgA-coated red cells. The direct Coombs' tests were done by the tube method4 and were read macroscopically and microscopically. Cells coated with IgG anti-D (Rh0) were tested with each batch of Coombs' tests as a positive control for the antihuman globulin reagents.

Urine samples obtained at the time of venipuncture for the premethadone population were analyzed for methadone, morphine, quinine, and other drugs by fluorometric and gas chromatographic techniques. Repeated urine samples, analyzed for drugs by thin-layer chromatography, were available on all methadone maintenance patients. Commercial laboratories performed all urinalyses.

RESULTS

No positive direct Coombs' tests were demonstrated in either group (Table 1). The analysis of urines from the methadone maintenance patients revealed that they were all taking methadone; however, evidence of other drug abuse was occasionally found. Of the premethadone population, 4% were found to have methadone on initial urinalysis.

DISCUSSION

Long-term methadone maintenance is currently the most feasible approach to social and medical rehabilitation of narcotics addicts. Consequently, many patients are taking methadone in relatively high doses and for extended periods of time. The number of patients on long-term methadone maintenance is increasing.

It is important, therefore, to investigate thoroughly reports of untoward effects of the drug. The direct Coombs' test is a measure of inappropriate globulin binding to red cells and in some cases is a sign of abnormal clinical hemolysis. From the present study in which no positive direct Coombs' tests were observed in addicts on methadone maintenance, we found no evidence that oral methadone alters red cells in this fashion.

Table 1. Results of Direct Coombs' Tests and Urine Drug Analyses in Premethadone Treatment and Methadone Maintenance Patients

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>No. of Patients</th>
<th>Positive Direct Coombs Tests</th>
<th>Urine* Methadone</th>
<th>Morphine</th>
<th>Quinine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premethadone treatment</td>
<td>103</td>
<td>0</td>
<td>4 (4%)</td>
<td>25 (25%)</td>
<td>33 (33%)</td>
</tr>
<tr>
<td>Methadone maintenance</td>
<td>67</td>
<td>0</td>
<td>67 (100%)</td>
<td>3 (4%)</td>
<td>4 (6%)</td>
</tr>
</tbody>
</table>

* Results of drug analysis on urine samples collected at the time of venipuncture.
It is conceivable that a drug other than those consumed by the addicts in the District of Columbia is being used by the addict population studied by Sivamurthy et al.¹ and is responsible for the positive direct Coombs' tests observed by them. Narcotics treatment groups in other locales may help resolve this problem.

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REFERENCES

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