Labetalol Analysis with the TOXI-LAB® A Drug-Detection System

To the Editor:

A false-positive result is due to either a limitation of the method or operator error. The recent report of an interference in the TOXI-LAB screening procedure, when used for the analysis of labetalol, is an example of operator error and is avoidable by use of procedures recommended by the manufacturer.

In a recent article (Clin Chem 1985;31:1250), false-positive indices were reported for amphetamines and possibly trimethoprim by the TOXI-LAB A System. TOXI-LAB is a commercially packaged, modified thin-layer chromatography system (1). Reference material, standards, training, and customer consultation provided by the manufacturer help ensure the most effective utilization of the system (1, 2).

The system provides for drug detection characteristics to be observed through four different detection stages. After presumptive identification, unknowns are run alongside standards and their $R_f$ values and color characteristics are compared. Identification is made after detection characteristics are demonstrated to be the same between unknown and standard in all four detection stages (2).

Even though the authors of the aforementioned article observed that detection characteristics were dissimilar in many respects, they reported the presence of amphetamine, methamphetamine, and trimethoprim. Using the TOXI-LAB procedure, we investigated the possibility of both false-positive findings and confusion among these four analytes.

Patients' urine specimens containing labetalol and metabolite were solicited from clinical laboratories. A specimen was also obtained that contained amphetamine and methamphetamine. These specimens were analyzed with the System, with appropriate reference standards. The results (Figure 1) demonstrate typical $R_f$ values obtained for standards and patients' specimens containing (a) amphetamine and methamphetamine and (b) labetalol. The $R_f$ values and colors are dissimilar for amphetamine, methamphetamine, and labetalol. By following the manufacturer's recommended procedures for comparing and interpreting detection characteristics, it was obvious that there was no match between labetalol and any of the other three analytes through the four stages. The color characteristics for labetalol, amphetamine, and methamphetamine are similar in Stage I but $R_f$ values are dissimilar. In addition, Stage III fluorescences for labetalol, trimethoprim, and the amphetamines are dissimilar.

Although this comparative analysis demonstrates some similarity in color detection characteristics between the four analytes at Stage I, positive identification of substances depends upon certain factors: (a) unknowns must be analyzed alongside known standards, and (b) the unknown substance must display characteristics consistent with that standard (color and $R_f$) throughout all four stages.

Because drug-screen test results directly influence patient care, the laboratory has a great responsibility to establish and maintain proficiency in their analytical methods. By the use of proper technique and recommended procedures, the possibility of misinterpretations would be lessened, and the quality of analyses greatly improved.

References


3. TOXI-LAB Drug Compendium. Ibid.

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Concentration of Myelin Basic Protein in Cerebrospinal Fluid in Prognosis of Multiple Sclerosis

To the Editor:

Myelin basic protein (MBP), which constitutes 30% of the total protein in the myelin sheath of the central nervous system, is one of the best-characterized specific antigens. Acute experimental allergic encephalomyelitis, a model for human demyelinating disease, has been experimentally induced by this protein. MBP is exclusively located in the oligodendrocyte-myelin complex and its determination in cerebrospinal fluid (CSF) by radioimmunoassay (RIA) is considered a marker for active demyelination (1).

The concentration of MBP in CSF is increased in multiple sclerosis (MS) during exacerbations of the disease, but usually declines to within the normal range during remissions. Concentrations of MBP in CSF may also be increased in non-MS neurological diseases (2-8).

We measured MBP in CSF from 23 patients with definite MS and five with probable MS, as classified by criteria of Rose et al. (9).

Routine diagnostic investigations of the patients included clinical evalua-
tion, CSF analysis, neurophysiological studies, cranial computer tomography, and nuclear magnetic resonance imaging. Lumbar puncture was performed during acute relapses as a routine clinical diagnostic procedure, never only for the purpose of measuring MBP. We determined MBP with use of materials from Diagnostic System Laboratories, Inc., Webster, TX, with a double-antibody method. The lower sensitivity limit was 0.5 $\mu$g/L. The mean concentration of MBP in CSF from 33 control subjects with no neurological disease was 2.4 (SD 0.8) $\mu$g/L, range 1.0 to 4.3 $\mu$g/L.

The values of MBP in CSF were increased in 26 of the 28 MS patients. These concentrations correlated significantly ($r = 0.383; p < 0.05; y = 16.4x + 10.9$) with the Kurtzke disability status scale (10), but not with the duration of the illness ($r = 0.073$), the severity score of neurological symptoms and signs in the relapse ($r = 0.100$), the duration of the relapse ($r = 0.050$), or the number of previous relapses ($r = 0.161$).

Assays of MBP in CSF have been found to be useful although not specific tests for the diagnosis of MS. There are no previous reports about the prognostic value of these determinations. The clinical course of MS patients is heterogeneous, and there are no criteria that can predict the development of neurological sequelae, which makes difficult the indication of aggressive treatment. Our findings suggest that those patients with greater demyelination and consequently higher concentrations of MBP in CSF develop a higher incidence of neurological dysfunctions. This correlation, however, does not exist for the dysfunctions that occur in the immediate post-relapse period.

Determinations of MBP in CSF of patients with MS relapses can be useful in defining a prognostic index of the disease. The patient with poor prognosis could, therefore, be identified and treated accordingly. Further studies about determinations of MBP in patients with MS are needed to confirm these results.

References

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Increased Urinary Excretion of Retinol-Binding Protein during Normal Pregnancies

To the Editor:

Recently, normal reference standards for retinol-binding protein (RBP) in serum and urine, as measured by radioimmunoassay, were reported by Beetham et al. (1). We have also developed a sensitive and precise RIA for RBP in urine and have established normal values that are similar to theirs for non-pregnant individuals (2). However, we would like to report increased urinary excretion of RBP during uncomplicated pregnancy.

Renal function, including the excretion of proteins, changes during pregnancy (3). Measurement of the increased excretion of proteins with a relative molecular mass below 30 000 such as RBP, is considered to reflect decreased tubular reabsorption if the concentrations in plasma remain essentially unaltered (4). We have therefore established normal excretion patterns for RBP during uncomplicated pregnancy and compared them with RBP excretion in "normal" non-pregnant individuals.

We collected 24-h urine specimens from 37 healthy pregnant women in the first, second, and third trimesters (up to 14, 28, and 40 weeks of gestation, respectively), and from 11 non-pregnant healthy women, matched for age. None of these persons had ingested any drug known to influence kidney function for at least 10 days before the specimen was collected. Samples were immediately frozen and stored at $-20 \, ^\circ C$ until assay. Results were expressed both as RBP excretion rates and as RBP/creatinine ratios.

RBP excretion rates for the 24-h specimens from the 11 non-pregnant women had a median value of 50 ng/min, and 95% confidence limits of 32 to 75 ng/min, and were not significantly different from rates for a larger sample of overnight-urine collections (n = 61; median 53.6 ng/min; 95% confidence limits: 11 to 189 ng/min; p > 0.05) (2).

In contrast, the RBP excretion rate was increased during normal pregnancy (Figure 1). The observed increases were not enough to be significantly different from the non-pregnant controls during the first or second trimester of pregnancy, but were pronounced

Fig. 1. Retinol-binding protein excretion rates as determined with 24-h urine specimens from normal non-pregnant (N) and pregnant women (1st: first trimester; 2nd: second trimester; 3rd: third trimester).