Table 1. Observed vs. Calculated Vitamin A Valuesa

<table>
<thead>
<tr>
<th>Drug</th>
<th>No.</th>
<th>Observed av.</th>
<th>Calculated av.</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No drug</td>
<td>129</td>
<td>38.7</td>
<td>39.1</td>
<td>0.51</td>
<td>N.S.</td>
</tr>
<tr>
<td>Diphenylhydantoin</td>
<td>195</td>
<td>41.5</td>
<td>39.1</td>
<td>3.24</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Isosorbide dinitrate</td>
<td>4</td>
<td>62.4</td>
<td>42.5</td>
<td>3.78</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>259</td>
<td>40.7</td>
<td>38.8</td>
<td>2.84</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Thioridazine</td>
<td>267</td>
<td>44.1</td>
<td>40.5</td>
<td>5.37</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

a “Drug” is the medication received regardless of dose, schedule or other medication; “number” is the number of individuals receiving this medication; “observed” and “calculated” averages are explained in the text; t is the Student’s t-value for matched pairs; P is the probability. “N.S.” is not significant.

Effects of Medication on Plasma Vitamin A Concentrations

To the Editor:

In the recent tabulation of effects of drugs on clinical laboratory tests by Young et al. (1), two drugs are shown to increase serum vitamin A concentrations and two to decrease them.

In 1974 we surveyed 1018 mentally retarded individuals for plasma vitamin A concentrations, by the method of Thompson et al. (2). As a part of this survey, we recorded the medication each patient was receiving at the time the blood was drawn. Because most of the patients were on long-term medication, it was impossible to establish premedication vitamin A values. Curtis and Swicord (3) have demonstrated that vitamin A concentrations in serum are a function of sex and age and that this relationship can be expressed mathematically to yield a calculated vitamin A value. We used their formula to calculate what the normal drug-free vitamin A value would be for each individual.

We divided the population by drug (regardless of amount, schedule, or any other medication) and compared the observed and calculated values for vitamin A for each individual by use of the paired t-test (4). As a control on our approach, we also compared those within the population who were drug free, using the same procedure. The observed and calculated values for the no-drug population of 129 were not significantly different and the average values differed by about 1% (Table 1).

As shown in Table 1, diphenylhydantoin, isosorbide dinitrate, phenobarbital, and thioridazine cause a highly significant increase in values for plasma vitamin A. (Thirty-six other medications had no apparent influence on vitamin A values).

This increase could either be the result of a measurement artifact caused by the presence of the medication or an in vivo increase in the homeostatic control level. We added 1 mg/100 ml of each of the drugs to drug-free plasma and again checked the apparent vitamin A. Only thioridazine caused an increased value. The apparent increased vitamin A concentrations in individuals taking the other drugs is probably a change in the homeostatic level.

Obviously this was purely a retrospective study. However, these data indicate that more investigations in the area of drug/vitamin A interaction are needed and indicate that four additional drugs influence actual or apparent plasma vitamin A values.

References


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Enzymatic Determination of Cholesterol in High-Density Lipoprotein Fractions Prepared by Polyanion Precipitation

To the Editor:

The Note of Steele et al. (1) was of great interest to me because we have had the same problem for almost a year. When we started to assay the HDL-cholesterol of the local population by the enzymatic technique we quickly realized that the heparin–manganese procedure produced too high and irreproducible results. We are running our cholesterol and triglyceride determinations on a two-channel AutoAnalyzer (Technicon), using the enzyme solutions from Boehringer (Mannheim). Because control experiments demonstrated that heparin by itself had no influence on the assay, we circumvented the problem with Mn2+ salts, not by adding chelating agents (EDTA) to the solutions, but rather by searching for a substitute bivalent cation. After trial and error it was found that the method described below gave reliable and reproducible results: 1 ml of serum (not plasma) was mixed with 50 μl of 2 mol/liter MgCl2 and 50 μl of a 20 g/liter solution of dextran sulfate 500 (Pharmacia), allowed to stand for 5 min, and centrifuged. By immunoochemical techniques we ascertained that this method precipitated quantitatively all the VLDL plus LDL up to a serum concentration of at least 20 g/liter. The excess of MgCl2 had no influence on the enzymatic cholesterol assay and neither had the dextran sulfate. We isolated some HDL (cf. 1.065–1.121) by preparative ultracentrifugation (2) and assayed them with the AutoAnalyzer at various concentrations in the presence and absence of the precipitating agents. Absolutely no difference was found for results for cholesterol and triglycerides. The coefficient of variation of our enzymatic assay (day-to-day) is less than 3% for cholesterol, less than 4% for triglycerides. In addition it is possible to solubilize the precipitated VLDL + LDL in 0.1 mol/liter sodium citrate and assay them directly on the machine as a separate control. In all cases the sum of VLDL + LDL and HDL cholesterol was 97–103% of the value for the parent serum.

We therefore propose as an alternative to the procedure described by Steel et al. (1) to change the precipitating agents and use the enzyme solutions in the conventional way. An additional advantage of this procedure might be that no background staining at all is produced by dextran sulfate–MgCl2; an apparent cholesterol of 10 ± 6 mg/liter in the HDL-reagent blank is reported from the heparin–Mn2+ procedure (1).

References


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