Serum Alkaline Phosphatase of Intestinal Origin: Detection by Acrylamide Gel Electrophoresis and L-p-Bromotetramisole Inhibition Compared

To the Editor:
The intestinally derived isoenzyme of alkaline phosphatase (ALP; EC 3.1.3.1) in serum is easily differentiated from other isoenzymes by electrophoresis on either starch, acrylamide, agar or agarose gels, or cellulose acetate membranes. In general, these techniques are not quantitative, but differential-inhibition techniques allow one to estimate the activity of the intestinal isoenzyme. L-Phenylalanine preferentially inhibits intestinal (1) and placental (2) ALP; L-p-bromotetramisole inhibits the enzymes from bone and liver, but has little effect on the intestinal or placental enzymes (3). The intestinal and placental isoenzymes can easily be differentiated, the latter being stable to heating at 65 °C for 60 min (4).

The amount of intestinal isoenzyme present customarily is expressed as a percentage of the total serum ALP activity, and for serum samples with above-normal ALP activity there appears to be a good correlation between detection of the intestinal enzyme after electrophoresis and the percentage of serum ALP activity inhibited with L-p-bromotetramisole (3).

We have been interested in measuring the activity of the intestinally derived enzyme in patients whose total serum ALP activity is within the normal reference interval, because we believe changes in the proportion of intestinal enzyme may be important even in the absence of a significantly increased total ALP activity in serum.

We examined the ALP isoenzyme pattern of 500 serum samples with normal ALP activity (<90 U/L) by acrylamide gel electrophoresis (5) and measured the L-p-bromotetramisole inhibition of activity on p-nitrophenyl phosphate at pH 10 (2) to assess the intestinal enzyme. The results (Figure 1) show that those 98 samples in which the intestinal isoenzyme could be detected by electrophoresis had intestinal isoenzyme activities ranging from 3 to 30 U/L. In the case of those samples without detectable intestinal enzyme after electrophoresis, the upper limit of the reference range (95% confidence) was 13 U/L. This suggests that for serum samples with normal total ALP activity, inhibition-technique values for intestinal alkaline phosphatase of 14 U/L and greater are an index of the proportion of the intestinal enzyme.

Intestinal isoenzyme activity is related to blood groups, those persons of blood groups O or B and positive secretors having higher values than those of blood group A or nonsecretors (6). It is also influenced by dietary factors, being increased after a fatty meal (7). Increase in intestinally derived enzyme without increased values for total serum ALP activity are common in patients with chronic renal failure (5) and in insulin-dependent diabetics (Skillen, Harrison, and Worth, ms. in preparation).

References

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