

Pseudocholinesterase Levels and Rates of Chloroprocaine Hydrolysis in Patients Receiving Adequate Doses of Phospholine Iodide

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Anesthesiologists have been concerned for some time about administering succinylcholine and ester-type local anesthetics to patients who are receiving phospholine iodide for treatment of glaucoma. This caution stems mainly from studies showing that phospholine iodide can severely depress pseudocholinesterase levels,^{1,2} and from case reports^{3,4} describing prolonged apnea in patients receiving phospholine iodide therapy. However, one recent report⁵ describing uneventful chloroprocaine analgesia in such a patient raises questions about the causal relationship between phospholine iodide therapy and succinylcholine-induced apnea. The present study was undertaken in an effort to explain this apparent discrepancy.

MATERIALS AND METHODS

Pseudocholinesterase levels were determined at 25 C according to a previously described modification⁶ of the method of Ellman *et al.*,⁷ in which 2 mM butyrylthiocholine was used as substrate. Activity is expressed as micromoles of butyrylthiocholine hydrolyzed per min. Chloroprocaine hydrolysis was measured spectrophotometrically as described by Lalka *et al.*,⁸ but at 25 C and using 0.033 M morpholinopropane sulfonic acid (MOPS), pH 7.6, as buffer. Activity is expressed as picomoles of chloroprocaine hydrolyzed per minute.

Serum samples were obtained from randomly selected healthy subjects or from glaucoma patients seen in the glaucoma clinic at Elmhurst Hospital. All treated patients were judged to have intraocular pressures controlled as well as possible, and all had experienced marked decreases in intraocular pres-

TABLE 1. Rates of Butyrylthiocholine and Chloroprocaine Hydrolysis in Patients Receiving Phospholine Iodide Therapy

	Butyrylthiocholine (U/ml)	Chloroprocaine (U/ml)	Chloroprocaine/Butyrylthiocholine
Patient 1	2.75	80.9	29.4
Patient 2	2.21	45.4	20.5
Patient 3	1.55	28.7	18.5
Patient 4	1.25	—	—
Patient 5	2.53	75.0	29.6
Patient 6	0.68	13.1	19.3
Patient 7	1.48	22.0	14.9
Patient 8	0.98	18.8	19.2
Treated mean	1.68 (±0.74)	40.6 (±27.5)	21.6 (±5.65)
Untreated mean	3.56 (±1.00)	63.3 (±23.3)	18.2 (±5.23)
Significance of differences between means	$P < 0.01$	$0.01 > P > 0.05$	$0.3 > P > 0.2$

ures. The Student *t* test was used to determine the significance of differences between normal and treatment groups.

RESULTS

Pseudocholinesterase activity, as measured by the rate of butyrylthiocholine hydrolysis, in the group of randomly selected patients not receiving phospholine iodide was 3.56 (±1.00 SD) units/ml serum. This value is appropriate for the temperature and substrate employed.⁹ In the same group, the rate of chloroprocaine hydrolysis was found to be 63.3 (±23.3) units/ml serum. Hydrolysis rates of butyrylthiocholine and chloroprocaine were 1.68 (±0.74) units/ml and 40.6 (±27.5) units/ml, respectively, in the group treated with phospholine iodide. As expected, the difference between enzymatic activities in the control and treated groups was significant when measured with either of the substrates. On the other hand, the ratios of activities measured using the two substrates in the control and treated groups were the same. This indicates that both activities were inhibited to the same extent by phospholine iodide.

Of 334 patients being treated in the glaucoma clinic, eight were receiving phospholine iodide.

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Among these patients, four had normal (16–20 torr) intraocular pressures in both eyes, one had normal pressure in one eye, but not in the other, and three had elevated pressures in both eyes. Thus, even though they were being treated adequately in the opinion of the ophthalmologists, half of the patients still had some elevation of intraocular pressures.

DISCUSSION

We determined the rates of butyrylthiocholine and chloroprocaine hydrolysis in a group of patients currently receiving phospholine iodide in a typical hospital clinic setting. Although the pseudocholinesterase activity measured with either of the substrates was significantly lower than normal, the mean was reduced only 35–52 per cent and was not lower than 20 per cent of normal in any case. Thus, while some patients may have enzyme levels reduced to 3–5 per cent of normal,^{3,4} this does not appear to be true of the typical patient in our series.

Is it surprising that Brodsky *et al.*⁵ found a normal response to chloroprocaine? On one hand, it is well known that the duration of local anesthesia is not determined by the rate of metabolism, but by the rate at which the drug is transported away from the injection site by the circulation. On the other hand, it is likely that pseudocholinesterase levels must be reduced to about 10–15 per cent of normal in order for the dose of 1,200 mg in 2.7 hours to have elicited a toxic systemic reaction.¹⁰ Taking these considerations into account, it is not at all surprising that this patient, whose pseudocholinesterase level was 43 per cent of the normal mean, should have had an uneventful course of anesthesia.

In the light of our findings, it would appear that the majority of patients receiving phospholine iodide would metabolize ester-type anesthetics normally. Since patients who have noticeable side effects from phospholine iodide are particularly likely to have reduced cholinesterase levels,¹¹ those who are most at risk can probably be identified by history. In fact,

Gesztes' patient³ had abdominal pain resulting from the parasympathetic overactivity that accompanies systemic acetylcholinesterase inhibition. Of course, it would still be prudent to determine pseudocholinesterase levels, but use of the ester class of anesthetics should certainly not be discounted automatically. Today, phospholine iodide is not used often because of its ability to cause cataracts. Therefore, it can probably be predicted that with the advent of newer anti-glaucoma medications, these patients will present even less of a problem to anesthesiologists.

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