Isoflurophate in Esotropic Children

Effects on the Serum Cholinesterase

Cesar R. Samson, M.D.
John S. Hermann, M.D.
New York, N.Y.

It is well established that topical administration of anticholinesterase compounds may lead to systemic symptoms of muscarinic and nicotinic poisoning in occasional patients. The blood cholinesterase has been extensively studied in adults receiving long-term glaucoma therapy, and de Roeth has stated that practically every patient with local instillation of phospholine iodide showed a considerable decrease in blood cholinesterase. Some of de Roeth’s patients on eprothiophate showed blood levels less than 5 per cent normal. Although systemic symptoms rarely appear in these patients with low cholinesterase values, Ellis has noted that all patients who acquire systemic symptoms also have a lower blood cholinesterase value.

In a study comparing ocular instillation of eprothiophate and isoflurophate on cholinesterase values in rabbits, Wilensky reported a marked inhibition of cholinesterase levels in blood, muscle, and nerve with eprothiophate, but no inhibition of cholinesterase in any tissue with the ocular use of isoflurophate. Ellis stated that no depression of erythrocyte cholinesterase has been found in patients who are on isoflurophate for a prolonged time.

Because of the widespread use of these anticholinesterase compounds in the diagnosis and treatment of esodeviations in a large population of children at the Motor Anomalies Department of the New York Eye & Ear Infirmary, an investigation of plasma cholinesterase values in response to isoflurophate was undertaken. Of considerable importance was the fact that many of these children underwent surgery in which succinyl choline was used soon after isoflurophate therapy, and there were no previous data available on serum cholinesterase levels as specifically applied to this pediatric group. It is known that patients with low blood cholinesterase values are more subject to the toxic effects of succinyl choline and procaine which might occur during general anesthesia. Cardiac arrest has occurred in patients with lowered cholinesterase levels from topical instillation of anticholinesterase compounds.

Study and Methods

From a larger group of esotropic children undergoing intensive orthoptic therapy combined with isoflurophate therapy, nine consecutive patients had blood drawn weekly for serum cholinesterase determinations. Three of these children received a 0.1 per cent isoflurophate solution in both eyes every night, and the other six received the 0.025 per cent isoflurophate ointment in the same manner. All controlled determinations were well above the 40 unit normal. The average age of this group was eight years, and no patient was over eleven years old.

Several blood specimens from this group were discarded because of hemolysis, an indication of an overly long interval between blood collections and laboratory determination of enzymes. All values in Fig. 1 are for freshly collected blood with no hemolysis.

Serum specimens were frozen immediately after they were obtained, and were examined within 72 hours after extraction. Serum cholinesterase was measured by the procedure of Rapaport, Fischl, and Pinto. The principle of the
procedure is based on the following reaction:

Cholinesterase

Acetylcholine → Acetic Acid + Choline
(buffered at pH 7.8) (lowers pH)

When the reaction is conducted in an indicator M-nitrophenol, the acetic acid formed lowers the pH, and the amount of color which disappears is proportional to the amount of cholinesterase added. Results are expressed in Rappaport units; normal values usually range from 40-80 Rap. units/ml of serum.

Results

None of the nine pediatric subjects showed a drop in serum cholinesterase to significantly abnormal levels. Three patients showed borderline readings; the lowest was that of R.V. at the four week level to 38 Rappaport units. In patients R. B. and D. B., a low of 40 Rappaport units was reached. These three patients were then switched to isoflurophate on alternate days, and the cholinesterase levels climbed in all of them. Even after 16 weeks of therapy, no significant depression occurred.

There was no evidence of any significant clinical side effects in these nine subjects. However, all subjects showed characteristic miosis and reduction in the stimulus ACA ratio, an indication that the dosage schedule was being adhered to by the parents.

Conclusions and Summary

In a series of nine patients receiving daily instillation of isoflurophate over intervals reaching 16 weeks, no child suffered a significant reduction below normal levels of serum cholinesterase. Because of the theoretic and clinical implications of lowered cholinesterase levels, especially under the influence of a general anesthetic, it may be advantageous to have available a specific anticholinesterase compound which does not depress serum enzymatic levels.

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References


(Dr. Hermann)
40 Park Avenue
New York, N. Y.

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