Plasma cholinesterase levels during cardiopulmonary bypass

A report on 10 cases

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Summary

Plasma cholinesterase levels of 10 male patients were determined before, during and after cardiopulmonary bypass surgery. These levels dropped significantly below the pre-anaesthetic values after commencing anaesthesia. In 6 patients levels returned to pre-anaesthetic values before or on the 2nd postoperative day. This could not be explained in terms of enzymic biosynthesis alone, and it is suggested that postoperative fluid readjustments may play an important role in certain cases.

A significant decrease in plasma cholinesterase levels in patients who underwent elective caesarean section under general anaesthesia was reported in 1978. Serum cholinesterase activity is inhibited by several drugs, such as ecdothiopate-iodide eye-drops, anti-cancer agents, muscle relaxants and anaesthetic agents such as ketamine. Of the volatile anaesthetic agents it has been suggested that methoxyflurane may result in decreased plasma cholinesterase levels. Kaniaris et al. measured serum cholinesterase levels in 30 female patients anaesthetised with enflurane for excision of lumps in the breast. They found a temporary decrease of serum cholinesterase levels after enflurane anaesthesia which could not be considered clinically significant (i.e. the enzyme levels remained within normal limits). The exact mechanism of this decrease was unclear, but it could not be attributed to fluoride release from the enflurane, since a similar agent, methoxyflurane, does not depress cholinesterase concentration, although its fluoride production potential is much greater.

At present two types of physiologically active cholinesterases, acetylcholinesterase and serum pseudocholinesterase, are recognised. Historically, pseudocholinesterase has been used to assess nutritional status. Milhorat first reported that pseudocholinesterase activity in a female with anorexia nervosa varied.

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with her well-being and body weight. While acetylcholinesterase is present at myoneural junctions and is responsible for the hydrolysis of acetylcholine, the latter is found in serum. Serum cholinesterase is found in many tissues, but especially in hepatic, nervous, cardiac, intestinal and cutaneous tissue. However, in human blood these enzymes are localised in different compartments. Acetylcholinesterase is found in the red cells and serum cholinesterase in the plasma. Serum cholinesterase is synthesised mainly in the liver and has a lifespan of 28 days; in various hepatic diseases its synthesis is reduced markedly. Serum cholinesterase levels are therefore widely employed as an important index to evaluate hepatic function in the clinical field. Although no clearly defined physiological functions can be attributed to the pseudocholinesterase present in serum, it is an important enzyme for the inactivation of drugs such as succinylcholine and ester-type local anaesthetics such as procaine and 2-chloroprocaine.

Jackson et al. found that plasma cholinesterase levels dropped after cardiopulmonary bypass to approximately one-third of the pre-operative values. It was proposed that this was due to haemodilution during the procedure. We investigated the effects of extracorporeal circulation on plasma cholinesterase activity in 10 patients.

Patients and methods

Ten male patients, ranging in age from 16 to 70 years, were the subjects of the study. All had been admitted for coronary artery bypass surgery, and all received standard premedication consisting of an opiate and a phenothiazine 1 hour pre-operatively. General anaesthesia was induced with etomidate 0.15 mg/kg, fentanyl 0.010 mg/kg, and diazepam 0.2 mg/kg intravenously. The trachea was intubated after intravenous injection of pancuronium bromide 0.1 mg/kg. Anaesthesia was maintained with 50% nitrous oxide in oxygen supplemented with additional doses of fentanyl. Respiration was controlled throughout the surgical procedure by intravenous injection of pancuronium bromide. Blood gases, pulse rate, blood pressure, central venous pressure, cerebral perfusion pressure and urine output were carefully monitored during the operation. The pump was primed with 2.2 litres of a balanced electrolyte solution (Plasmalyte B). No blood was added to the pump. All the patients received 400 ml fresh-frozen plasma 15 minutes after coming off the bypass.

Blood samples for determination of plasma cholinesterase activity were obtained just before and 20 minutes after the start of anaesthesia, just before the start of the bypass, 15, 30 and 60 minutes after the start of the bypass, 15 minutes after coming off the bypass (before and after fresh-frozen plasma was given), 60 minutes after the end of bypass and on days 1, 2 and 7 postoperatively (Table I). The patients were ventilated for 6-12 hours postoperatively. Plasma cholinesterase levels were determined according to the butyrylthiocholine colorimetric method using Monotest Cholinesterase kits (Boehringer Mannheim). Cholinesterase variants were screened for by determining both dibucaine and fluoride numbers of pre-anaesthetic plasma samples for each patient.

Results

According to the dibucaine and fluoride numbers determined, no abnormal cholinesterase variants were found among the patients included in this study. From the results obtained (Table I) all patients had plasma cholinesterase levels within the normal range of 3.5-8.5 U/ml before induction of anaesthesia. Approximately 20 minutes after commencing anaesthesia all levels dropped by 1.8-24% below the pre-anaesthetic values. This decrease could possibly be attributed to the combined effects of haemodilution caused by the administration of intravenous fluids, induction agents and pancuronium. The latter has been shown to decrease cholinesterase levels by 9-10% below control values. Of further interest, however, is the consistent reduction of plasma cholinesterase activity in 10 patients.

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<th>Table I: Plasma Cholinesterase Levels in 10 Patients Undergoing Cardiopulmonary Bypass Surgery</th>
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FPF = fresh-frozen plasma.
terase levels by 35–60% from the pre-anaesthetic values after 15, 30 and 60 minutes of cardiopulmonary bypass.

This concurs with the degree of reduction found in the previous study. However, in contrast to the case report, 4 patients in the present study had plasma cholinesterase levels on the 1st postoperative day higher than or at least similar to the pre-anaesthetic values, while the enzyme in another 2 patients reached these levels on day 2. This is not consistent with the normally slow hepatic biosynthesis of cholinesterase and the low biosynthetic activity of the liver after hypothermia. Infusion of 200 ml fresh plasma, which contains normal amounts of plasma cholinesterase, 15 minutes after coming off the bypass did not increase the cholinesterase levels significantly.

Discussion

Maier and Fischer reported that low plasma cholinesterase levels in patients with heart failure were raised markedly by digitalis administration. Heinecker and Mayer reported reduced plasma cholinesterase levels after myocardial infarction. The lowest levels were found during the 7 days after the attack. Although there was no patient with severe heart failure in our study, slightly low plasma cholinesterase levels before anaesthesia were probably due to the pre-existing cardiac disease. A decrease in plasma cholinesterase levels was reported after glucocorticoid administration. We administered betamethasone 30 mg/kg to each patient before induction of anaesthesia - this might be another factor contributing to the fall in plasma cholinesterase levels.

It seems that the deployment of haemodilution cardiopulmonary bypass techniques may lower the blood concentration of both exogenously administered drugs and endogenous substances that are usually necessary for a favourable outcome. We do not believe that the absorptive qualities of the bypass tubing and filters affect cholinesterase activity. Persistent low plasma cholinesterase levels during the first 7 postoperative days may be consistent with the normally slow hepatic biosynthesis of cholinesterase and the low biosynthetic activity of the liver after hypothermia. It is to be expected that cardiopulmonary bypass priming techniques that employ packed red blood cells and/or albumin solutions would produce similar reductions of plasma cholinesterase levels. We consider that the extracorporeal circulation itself might be the most significant contributor to reduction in plasma cholinesterase levels. A predictable lowering of plasma cholinesterase could possibly be routinely anticipated as a result of haemodilutional cardiopulmonary bypass.

One does not expect obvious clinical sequelae to low cholinesterase levels unless a drug is given which is primarily biodegraded by cholinesterase. The duration of action of suxamethonium, a short-acting muscle relaxant, is inversely proportional to the level of the genotypically normal plasma cholinesterase. Clinically prolonged suxamethonium-induced neuromuscular block is usually not encountered until the plasma cholinesterase activity is less than 25% of the lowest aspect of the normal range. If suxamethonium is to be used in a patient who has been subject to haemodilutional cardiopulmonary bypass, then the plasma cholinesterase level should be a general guideline to the dose of suxamethonium that may be used without resulting in a prolonged neuromuscular block.

Conclusion

In our study, plasma cholinesterase levels were appreciably reduced by anaesthesia and surgery, with pronounced further decreases during extracorporeal circulation, even considering the effect of haemodilution due to priming of the pump. Although the reduction in plasma cholinesterase levels during cardiopulmonary bypass surgery may well be at least partially attributable to haemodilution, the postoperative restoration of the levels is probably far more complex than the biosynthesis of new enzyme alone. Other factors such as postoperative physiological readjustment of fluid volumes may very well be more important in this respect in certain patients.

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