Short Reports

Effect of Exchange Transfusions on Plasma Digoxin Levels

Digitalizing newborn babies before exchange transfusion has been advocated as a prophylactic measure against heart failure and used to be the policy in the neonatal unit of Hammersmith Hospital (Tizard, 1963). However in subsequent years this policy has not always been carried out because it was felt that some glycoside might be removed in the exchange, thus introducing an unknown factor into the control of dosage. A sensitive specific assay for plasma digoxin concentration has made it possible to assess the effect of exchange transfusions on the plasma level of the drug, and to measure the amount removed.

Patients and Methods

Two newborn babies, in whom severe rhesus isoimmunization had been diagnosed antenatally, were admitted to the neonatal unit within an hour of delivery. Exchange transfusions were carried out using heparinized blood collected from donors less than 6 hours previously. The exchange was performed in 20 ml aliquots and all the removed blood was collected and pooled for analysis. Approximately 90 minutes before each initial exchange 0.025 to 0.03 mg/kg digoxin was administered in-

FIG. 1.—Plasma digoxin level, dosage, volume of blood exchanged, and amount of digoxin removed in relation to time in Case 1.

FIG. 2.—Plasma digoxin level, dosage, volume of blood exchanged, and amount of digoxin removed in relation to time in Case 2.

tramascularly. Subsequent digoxin dosage was variable, as indicated in Fig. 1 and 2, but was given in dosages considered sufficient to maintain digitalization.

Plasma digoxin concentrations were measured by radioimmunoassay, as previously described (Chamberlain *et al.*, 1970), from samples taken before and after the exchanges and from an aliquot of the pooled exchanged blood. High bilirubin levels caused heavy quenching of the radioisotope in the assay procedure resulting in falsely high plasma digoxin levels. The plasma was therefore filtered by centrifugation through Amicon Centriflo Membrane Cone before assay. This procedure separated the bilirubin from the assayable digoxin.

Results

Case 1 was given 75, 75, 32, and 20 μ g digoxin before 4 of his 5 exchanges during which 4.5, 3.9, 4.5, and 4.1 μ g of digoxin were removed. However, the plasma levels after each exchange were similar to the pre-exchange levels of 12, 12, 11, 12 ng/ml. Case 2 was given 75 and 36 μ g digoxin before two of the three exchanges during which 4.8, 4.0, and 0.29 μ g digoxin were removed. Plasma levels after the exchange transfusions of 11, 9, and 2.1 ng/ml were similar to the pre-exchange levels of 9, 11, 2.4 ng/ml. The experimental procedure and results are depicted graphically in the Figures.

Discussion

Radioimmunoassay has provided a safe, quick, sensitive clinical estimate of plasma digoxin levels in adults (Smith, Butler, and Haber, 1969; Chamberlain *et al.*, 1970) and in children (Coltart, Cree, and Howard, 1972). Therapeutic plasma levels are between 1 and 2 ng/ml. However, these levels are estimated at least 6 hours after administration of the drug when full equilibration has taken place between tissue stores and plasma. The pharmacodynamics of digoxin in children have been previously described by Hernandez and his colleagues (1969) using tritiated digoxin. The high plasma levels obtained in this study are due, at least in part, to the fact that the samples were taken before full equilibration had taken place.

Though between 220 and 440 ml of blood were exchanged, when digoxin concentrations were between 1.3 ng/ml and 12 ng/ml, the digoxin levels were maintained, presumably by re-equilibration of the plasma with the large tissue stores of the drug. A similar situation has been found in adult patients undergoing cardiopulmonary bypass (Coltart *et al.*, 1971), in which procedure the plasma is heavily diluted by the volume of blood priming the bypass machine. However, though no digoxin is administered on the day after surgery, these patients have a digoxin concentration identical with the preoperative figure. Thus in both exchange transfusion and cardiopulmonary bypass, the large tissue stores of digoxin not only limit any tendency for an acute fall in plasma concentration, but also allow a restoration of plasma level as re-equilibration occurs.

Electrocardiographic changes during digoxin therapy in neonates in heart failure have been described (Levine and Blumenthal, 1962). Significant cardiographic changes including arrhythmias have been noted during exchange transfusions (Van Praagh, 1961). Monitoring was used during all exchanges in this study and no significant changes were seen.

Summary

A sensitive method for assaying plasma digoxin has made it possible to assess the effect of exchange transfusion on plasma digoxin levels and to quantitate the amount removed during an exchange. Plasma digoxin levels before and after exchange were similar. It therefore seems unnecessary to revise dosage schedules when digoxin therapy is to be used during an exchange transfusion.

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Automated Method for Exchange Transfusion

Despite prophylactic measures against isoimmunization, haemolytic disease of the newborn remains a common problem, and many exchange transfusions still have to be undertaken in special baby units. A number have to be done also for hyperbilirubinaemia. Orthodox procedures continue to be laborious, time consuming, and occasionally hazardous.

The method of Ata and Holman (1966) has the great asset of providing continuous flow in by the umbilical vein at a rate to match that dripping out from one umbilical artery. This completely obviates the relatively large blood volume changes necessarily produced by other methods, which is probably one of the most dangerous factors in exchange transfusions, and is one reason for them having to be so time consuming. Everyone experienced in this work knows the discomfort and