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EFFECT OF EXCHANGE TRANSFUSION ON ELIMINATION OF ANTIBIOTICS IN PREMATURE INFANTS*

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SUMMARY: Özkan H, Çevik N. (Department of Pediatrics, Dokuz Eylül University Faculty of Medicine, İzmir, Turkey). Effect of exchange transfusion on elimination of antibiotics in premature infants. Turk J Pediatr 1994; 36: 7-10.

Although the use of exchange transfusion has become routine in intensive care nurseries, little information is available on drug loss resulting from exchange transfusion. The aim of this study was to review the effect of exchange transfusion on the elimination of some antibiotics in premature infants according to the recent pharmacokinetic data. A pharmacokinetic equation was used to estimate drug loss from the body by exchange transfusion. Our data suggest that exchange transfusion can significantly decrease the serum concentrations of antibiotics with smaller volumes of distribution, but the drug loss of antibiotics with larger volumes of distribution can be acceptable. *Key words: exchange transfusion, antibiotics, premature infants.*

Exchange transfusion is commonly used in neonatal intensive care units in the management of certain newborn disorders such as hyperbilirubinemia, neonatal sepsis and disseminated intravascular coagulation[1]. Ill neonates undergoing exchange transfusion frequently receive concomitant antibiotic therapy. Because drugs are removed by exchange transfusion, the need to replace removed antibiotics or alter the dosage regimen is generally questioned. There are very few reports about the effect of exchange transfusion on serum antibiotic concentrations[2-6]. Although a pharmacokinetic equation for predicting drug loss has been described and hypothetical drug loss by exchange transfusion has been calculated[7], there is no information in the literature about recently used antibiotics in regard to exchange transfusion.

The aim of this study was to determine the effect of exchange transfusion on elimination of some antibiotics in premature infants according to recent pharmacokinetic data.

Material and Methods

In the present report, a one-compartment pharmacokinetic model with first-order elimination was used to calculate the hypothetical drug loss by two-volume

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exchange transfusion. The relationships of volume of distribution, elimination rate constant, and time after dosing on the fraction of the dose eliminated in the blood exchange were developed on the basis of a one-compartment body model. Drug loss from the body by two-volume exchange transfusion was calculated using a pharmacokinetic equation:

$$1 - e^{V / Vd}$$

Where V: plasma volume exchanged (determined from post-transfusion hematocrit) (liters) and Vd: apparent volume of drug distribution (liters).

In this model, the mean gestational age of the study group was 31.34 ± 4.45 weeks, mean birthweight was 1717.2 ± 875.1 grams, and mean postnatal age was 4.19 ± 4.20 days. All patients underwent two-volume exchange transfusion at a dose of 200 ml / kg for hyperbilirubinemia. At the time of exchange, the patients were receiving concomitant antibiotic therapy. Post-transfusion hematocrit of these premature infants was 0.416 ± 0.050. All data were derived from a recent report[8] and used for V in the equation.

For Vd, mean volumes of distribution of antibiotics according to recent reports in the literature were used (Table I). The reported values of Vd in these studies were derived from pharmacokinetic studies performed in newborn infants with normal rates of drug metabolism and elimination.

The hypothetical drug loss by two-volume exchange transfusion was calculated using the above-mentioned pharmacokinetic equation.

Table I: Mean Volumes of Distribution and Hypothetical Drug Loss by Two Volume Exchange Transfusion in Preterm Babies

Drug	Vd (L / kg)	Percent Loss
Amikacin[9]	0.57	18.5
Aztreonam[10]	0.29	33.5
Cefotaxime[11,12]	0.45*	23.0
Gentamicin[13-16]	0.54*	19.4
Netilmicin[17]	1.19	9.3
Ticarcilline/[18]	0.34	29.0
Clavulanate	0.41	25.0
Vancomycin[19-21]	0.55*	19.1

* An average value according to the reported mean Vd (L / kg) values in these studies.

Results

Drug loss for each antibiotic by exchange transfusion in preterm infants was calculated (Table I). As can be seen in the table, drug loss by exchange transfusion for most of the antibiotics evaluated was negligible. However, considerable loss of aztreonam and ticarcilline was calculated.

Discussion

As can be seen in Table I, considerable loss of aztreonam and ticarcilline was calculated. The reported percentages of gentamicin lost by exchange transfusion are similar to the percentage estimated in this calculation[5,6]. Hypothetical drug loss by exchange transfusion for amikacin, gentamicin and vancomycin in the study was found to be greater than that predicted by Lackner[7]. The difference can be explained by the higher blood and plasma volumes[22] and lower post-transfusion hematocrit values of premature infants[8]. The hematocrit value of 0.54 used by Lackner[7] is a remarkably high post-transfusion hematocrit value for preterm infants in comparison to the value mentioned above[8]. As expected from the equation, both of these factors increase drug loss by exchange transfusion. No information is available in the literature on measured or calculated drug losses of aztreonam, cefotaxime, netilmicin and ticarcilline / clavulanate resulting from exchange transfusion. Our data suggest that unless exchange transfusions are repeated and performed during the distribution phase rather than elimination phase, the drug loss of antibiotics with larger volumes of distribution can be acceptable. On the other hand, exchange transfusions can significantly decrease the serum concentrations of antibiotics with smaller volumes of distribution, and an alteration in dose may be necessary in critically ill premature neonates.

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