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REVIEW

Pharmacokinetics of antivirals in neonate

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KEYWORDS
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Acyclovir;
Ganciclovir;
Pleconaril

Abstract

Backgrounds: About 1000 neonates with HIV infection are born every day worldwide. The antiviral therapy for newborn infants is a real necessity. Pharmacokinetics is an important contribution to therapy and no review has been published on the pharmacokinetics of antivirals in neonates up to now.
Aims: This article provides a review on the pharmacokinetics of antivirals in the neonate. The pharmacokinetic parameters in the neonate are compared with those of the adult, and when possible, the pharmacokinetic parameters were compared in neonates of different ages.
Results: Zidovudine is the antiviral with the largest amount of information on its pharmacokinetics. The clearance (Cl; l/h/kg) of zidovudine is 0.15 (premature), 0.34 (1 day), 0.69 (7 days), 0.65 (≤14 days), 1.14 (>14 days) and 1.56 (adult). $t_{1/2}$ (h) of zidovudine is 7.2 (premature), 4.2 (1 day), 4.0 (7 days), 3.1 (≤14 days), 1.9 (>14 days) and 1.1 (adult). Zidovudine is mainly eliminated by conjugation with glucuronic acid and glucuronosyl transferase develops postnatally. Cl of lamivudine is 0.19 (1 day), 0.32 (7 days) and 0.30 (adult) and the Cl (l/h/m^2) of didanosine is 65 (1 day) and 271 (7 days). A greater volume of distribution (Vd) has been observed in the neonate compared with the adult for nelfinavir, nevirapine and pleconaril.
Conclusions: The pharmacokinetic parameters of antivirals differ in the neonate and in the adult. The Cl is reduced and $t_{1/2}$ is increased in the neonate compared with the adult for zidovudine, lamivudine and ganciclovir. t_{max} is generally greater in the neonate than in the adult due to reduced absorption rate in the neonate. The Vd of nelfinavir, nevirapine and pleconaril is greater in the newborn than in the adult. The neonate is a developing organism and the pharmacokinetic parameters of antivirals vary during the first weeks of life.

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Contents

1. Introduction

The number of woman of child-bearing age living with HIV infection worldwide was estimated about 20 million and 2.5 million children, most of whom acquired HIV infection from vertical transmission, are living worldwide [1]. This perinatal transmission of HIV occurs as a result of transplacental dissemination of the virus and intrapartum exposure to infected blood and the genital tract [2—4]. It has been demonstrated that the prenatal and postnatal treatment with zidovudine reduces considerably the risk of transmission of HIV [5]. The formation of zidovudine-resistant HIV strains requires the use of different antivirals and it is therefore important to know the pharmacokinetics of various antivirals in the neonate. This review includes also results on acyclovir, ganciclovir and pleconaril that are antivirals used against herpes simplex virus, cytomegalovirus and nonpolio enteroviruses, respectively. The placental transfer of antivirals has been reviewed on an earlier occasion [6] and the pharmacokinetics of antivirals in newborn infant is now reviewed.

The physician has to deal with a plethora of antivirals due to the introduction of many antivirals in these last two decades. These compounds differ considerably in their molecular structure such as, for example, the nucleoside reverse transcriptase inhibitors and the protease inhibitors. The pharmacokinetics of the antivirals is also drug dependent. Although standard therapy regimens exist for the prophylaxis of the newborns against maternal—infant HIV transmission and treatment for infected infants, the pharmacokinetics of antivirals is little studied in neonates and has not been reviewed up to now.

The neonate is a developing organism and some vital functions, such as the rate of drug metabolism and renal elimination, improve during the first weeks of life. These functions are involved in the elimination of drugs and the Cl of zidovudine increases during postnatal development [7]. When it has been possible, we have compared the kinetic parameters obtained with an antiviral in neonates of different ages.

It is useful to compare the pharmacokinetic parameters obtained in the neonate with those obtained in the adult to know what parameter differs in the two groups and to optimise the antiviral therapy for the neonate. The aim of this article is to review the pharmacokinetics of 9 antivirals in the neonate and to compare the pharmacokinetic parameters obtained in the neonate with those obtained in the adult.

2. Results

2.1. Nucleoside reverse transcriptase inhibitors

2.1.1. Zidovudine

The pharmacokinetic parameters of zidovudine are summarised in Table 1. The Cl of zidovudine increases with age, the lowest value is observed