Poster

[P26-8] P26-8: Oncologic drugs (4): Pharmacokinetics, TDM practice

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Tue. Sep 26, 2017 12:30 PM - 1:30 PM Annex Hall (1F)

(Tue. Sep 26, 2017 12:30 PM - 1:30 PM Annex Hall)

[P26-8-2] Pharmacokinetics of cyclophosphamide and its metabolites in pediatric hematopoietic stem cell transplant recipients: a comparative study of two conditioning regimens and one posttransplantation regimen

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Keywords: cyclophosphamide, hematopoietic stem cell transplantation, pharmacokinetics, pediatric

Background

High-dose cyclophosphamide (HDCY) is a mainstay in most conditioning regimens for hematopoietic stem cell transplantation (HSCT). The administration of posttransplantation HDCY (PTCY) has been attracting attention as a novel strategy for preventing graft-versus-host disease. To better understand the differences among three notable HDCY regimens, we investigated the PK of CY and its active metabolite 4-hydroxycyclophosphamide (HCY) and inactive metabolite o-carboxyethylphosphoramide mustard (CEPM) among the HDCY regimens in pediatric HSCT recipients.

Methods

Eighteen consecutive children (median 10.5 years, male/female: 14/4) who were all receiving a HDCY (100 mg/kg) before or after undergoing allogeneic HSCT were enrolled in this study. The patients' underlying diseases were acute leukemia (n = 12), and others (n = 6). The PK of the CY, HCY and CEPM were evaluated in each patient by collecting serial blood samples and then analyzing those samples using liquid chromatography coupled with electrospray tandem mass spectrometry. The AUC from zero to infinity ($AUC_{0-\infty}$) was calculated using a one-compartment model.

Results

The dosage regimens of CY were as follows: 60 mg/kg ×2 days (CY60×2) (n = 11), 50 mg/kg ×4 days (CY50×4) (n = 4) as conditioning for HSCT, and 50 mg/kg ×2 days (PTCY50×2) (n = 3) after HSCT. The average $AUC_{0-\infty}$ of CY was 3449 ±1147 (CY60×2), 5359 ±852 (CY50×4), 4157 ±1142 (PTCY50×2). The average $AUC_{0-\infty}$ of HCY was 59 ±32 (CY60×2), 116 ±54 (CY50×4), 44 ±17 (PTCY50×2). The average $AUC_{0-\infty}$ of CEPM was 308 ±200 (CY60×2), 463 ±126 (CY50×4), 243 ±52 (PTCY50×2). The all $AUC_{0-\infty}$ of CY, HCY, and CEPM for CY50×4 regimen were significantly higher than those for CY60×2 regimen. In a comparison of $AUC_{0-\infty}$ of CY, HCY and CEPM between CY60×2 and PTCY50×2 regimens, no statistically significant difference was observed.

Conclusions

We have reported comparative PK of CY and its metabolites in three kinds of HDCY regimens for the first time. The both $AUC_{0-\infty}$ of CY and its metabolites for CY50×4 regimen were significantly higher than those for

CY60×2 regimen.