Oral

[O27-4] O27-4: Oncology (2)

Chairs: Takayasu Kurata, Japan / Etienne Chatelut, France
Wed. Sep 27, 2017 2:30 PM - 3:30 PM Room C1 (1F)

(Wed. Sep 27, 2017 2:30 PM - 3:30 PM Room C1)

[O27-4-1] Therapeutic drug monitoring (TDM) approaches for the treatment of neonates and children with cancer: a UK experience

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Keywords: Cancer, Children, Oncology, TDM, Neonates

Background

The Newcastle Cancer Centre Pharmacology Group (NCCPG) have conducted studies designed to determine key factors which influence the efficacy of anticancer drugs over many years, focusing on how this information can be used to optimise the treatment of childhood cancer[1,2]. Defining chemotherapy dosing regimens for neonates with cancer is particularly challenging and commonly not standardized based on any scientific rationale. The NCCPG provide a national therapeutic drug monitoring (TDM) service to guide treatment in such challenging patient populations. As an example of this approach to treatment, we report on the use of carboplatin TDM in preterm and full-term neonates, anephric patients and children receiving high dose chemotherapy.

Methods

Carboplatin TDM was performed to achieve target drug exposures (AUC values) in 9 preterm and full-term neonates diagnosed with retinoblastoma, 4 patients with bilateral nephrectomy diagnosed with Wilms' tumour and 12 patients receiving high dose chemotherapy for the treatment of rhabdomyosarcoma at centres across the UK. Carboplatin was administered over 3-5 days of treatment with TDM utilized to target cumulative AUC values of 5-20mg/ml.min depending on treatment protocol. This involved the collection of blood samples on day 1 of carboplatin treatment and overnight courier to Newcastle for real-time sample analysis. Carboplatin levels were determined by atomic absorption spectrometry as previously described[3] and dose modifications on days 2-5 of treatment carried out as required.

Results

AUC values achieved following TDM were within 15% of target values in >95% of cases, with dose modifications up to 220% required to achieve target AUC values, compared to protocol-based dosing schedules. Carboplatin clearance determined across consecutive chemotherapy courses in two neonates increased from 3.4-7.1ml/min and 7.2-16.5ml/min (>2-fold increases over several weeks of treatment), reflecting early renal function maturation. Carboplatin was well tolerated, with TDM approaches limiting the likelihood of patients experiencing serious adverse effects commonly associated with treatment.

Conclusions

The study highlights the benefits of utilising TDM to achieve cumulative target carboplatin AUC values in challenging patient groups including neonates, particularly in view of marked increases in drug clearance observed during the first weeks of life. TDM approaches should be more widely utilised in oncology, to guide dosing in patients where unpredictable pharmacokinetic profiles may be anticipated.

References

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