Clínica Universidad de Navarra
Servicio de Farmacia

ANTHRACYCLINES DOSAGE IN PAEDIATRIC OBESE PATIENTS

New abstract number: 4CPS-084
ATC code: L01 - Cytostatics

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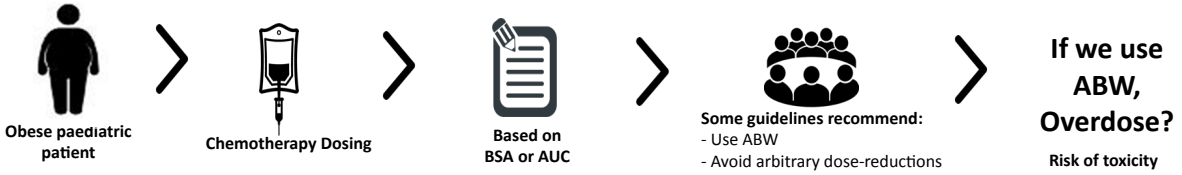
Introduction

In 2016, the World Health Organization estimated that 41 million children aged under 5 years were overweight. Clinicians are increasingly likely to have under their care obese children requiring chemotherapy. Optimal drug dosing for this population is unclear. Anthracyclines are often used in paediatric cancers and given its cardiotoxicity optimize the dose is mandatory.



Objective

To clarify the most adequate anthracycline dose in obese children with the available data of safety, effectiveness, pharmacokinetics and pharmacodynamics.

Methods

A formal literature search was performed for each chemotherapy drug (daunorubicin/doxorubicin/epirubicin/idarubicin) on three databases: Pubmed, Scopus and Web of Science (WoS) in March 2019. The following strategies were used:

- Pubmed → ((obese [Title] OR obesity[Title])) AND drug[Title/Abstract]
- Scopus → (obese or obesity) AND TITLE-ABS-KEY (drug)
- WoS → TITLE: (obese or obesity) AND TOPIC: (drug)

Exclusion criteria:

(A) Not useful or incomplete information for the aim of the study
(B) Insufficient simple size (Total n<10, Subgroup n<5)
(C) Obesity criteria ≠ IMC≥30 kg/m²
(D) Systematic review
(E) Full-Text no available
(F) Only English or Spanish

Inclusion criteria: Use of ABW in obese paediatric patients, PKPD and analysis of toxicity and/or efficacy

Results and Discussion

DAUNORUBICIN 8 articles → All of them are duplicities with the doxorubicin search (See the table below).

10 articles excluded: (A) 8 articles, (D) 1 article, (F) 1 article.

DOXORUBICIN 14 articles

4 articles included	**Pharmacokinetics**	The doxorubicin pharmacokinetics is controversial. One article finds no difference in clearance using adjusted-weight versus actual-weight (Ritzmo, 2007 and Orgel, 2014); the other shows lower clearance in obese paediatric patients than in normal-weight paediatric patients (p<0.05) (Tolbert, 2014). For daunorubicin and doxorubicin, pharmacokinetics in vitro models suggest that the presence of adipocytes markedly reduced the clearance of chemotherapy agents used as induction therapy in ALL (Thompson, 2008).
	Efficacy and toxicity	The efficacy of **doxorubicin** was measured in one article in which the patient achieves complete remission using adjusted doses. No changes in the electrocardiogram were found during the treatment and neither 2-months and 2-years after its end. No other specific toxicity was observed. (Ritzmo,2007)

Doxorubicin CL is similar to reference values for normal weight children

Doxorubicin dose based on BSA calculated by using TBW seems appropriate.

1. Tolbert, 2014. The challenge of obesity in paediatric leukaemia treatment: It is not just size that matters.
2. Ritzmo, 2007. Pharmacokinetics of doxorubicin and etoposide in a morbidly obese pediatric patient.
3. Orgel, 2014. Obesity is associated with residual leukemia following induction therapy for childhood B-precursor acute lymphoblastic leukemia.
4. Thompson, 2008. Impact of body composition on pharmacokinetics of doxorubicin in children.

EPIRUBICIN 1 article → It is a duplicity with the doxorubicin search (See the table above).

IDARUBICIN → **None found**.

Conclusions

It seems that adjusted-doses of anthracyclines in obese pediatric patients can be effective and safety but due to limited data, this recommendation must be taking with caution.