

BENEFITS OF PHARMACOKINETIC ESTIMATION OF METHOTREXATE LEVELS ON PEDIATRIC OSTEOSARCOMA

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Background and importance

Monitoring of methotrexate serum levels in osteosarcoma pediatric patients includes the estimation of methotrexate serum levels 24h after the initiation of the infusion ([MTX_{24h}]) which allows folinic acid rescue to be started at adjusted doses. When pharmacokinetic estimation is not possible, it is recommended to administer the standard rescue (15mg/m²/6h) and subsequently adjust it according to real [MTX_{24h}].

Aim and objectives

To evaluate the correlation and concordance of the estimated and real [MTX_{24h}] and the benefits of the estimation in comparison with the dosage by

Material and methods

Retrospective study of pediatric patients treated with 12g/m² methotrexate monitored by the pharmacy department from January 2014 to June 2020. Estimated [MTX_{24h}] was determined with a Bayesian model with PKS software.

Variables collected: Age, sex, number of cycles received, estimated and real [MTX_{24h}] and folinic rescue dose.

Pearson and intraclass correlation coefficients between real and estimated [MTX_{24h}] were calculated. The agreement between the dosage of folinic acid by protocol and by estimating [MTX_{24h}] was assessed with Cohen Kappa coefficient.

Results:

23 patients were treated during the studied period.

Sex	
Male	13 (56.5%)
Female	11 (43.5%)
Age	
Median age (range)	14 (4-17)
MTX administration	
MTX cycles	152
MTX cycles with [MTX _{24h}]	131
Median MTX cycle (range)	8 (2-8)

MTX pharmacokinetic data		Pearson's correlation coefficient.	Intraclass correlation coefficient.
Median estimated [MTX _{24h}]	7 (2-80)	0.949	0.974
Real [MTX _{24h}]	8 (1-85)	High linear correlation	High concordance.

Folinic acid rescue		Cohen Kappa Test
Estimated rescue was adequate (Cycles)	94 (71.8%)	K=0.189 A slight agreement between both methods in favor of estimating [MTX _{24h}] was found.
Hypothetical dose by protocol was adequate (Cycles)	46 (35.1%)	

MTX: methotrexate; [MTX_{24h}]: Methotrexate concentration after 24 hours of infusion initiation

Conclusion and Relevance

Estimated and real [MTX_{24h}] showed high correlation and concordance, in most cases the folinic acid rescue dose was correctly administered thanks to the estimated [MTX_{24h}]. These results seem to indicate that the estimation of [MTX_{24h}] and posterior estimation of folinic acid rescue are superior to the systematic administration of 15 mg/m²/6h.

