Background and importance Monitoring of methotrexate serum levels in osteosarcoma paediatric patients includes estimation of serum levels of methotrexate 24 hours after initiation of the infusion ([MTX_{24h}]), which allows folinic acid rescue to be started at adjusted doses. When pharmacokinetic estimation is not possible, the standard rescue (15 mg/m^2/6 hours) is recommended and subsequently adjusted according to the 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 protocol.
Material and methods A retrospective study of paediatric patients treated with 12 g/m^2 methotrexate monitored by the pharmacy department from January 2014 to June 2020 was conducted. Estimated [MTX_{24h}] was determined with a Bayesian model with PKS software.
Variables collected were 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 the Cohen kappa coefficient.
Results 23 patients, 56.5% (13) men, median age 14 (4–17) years, received 152 cycles of methotrexate. The median number of cycles per patients was 8 (2–8). Median estimated [MTX_{24h}] was 7 (2–80) and real [MTX_{24h}] was 8 (1–85). The Pearson's correlation coefficient and intraclass correlation coefficient for real and estimated [MTX_{24h}] were r=0.949 and CCI=0.974, respectively, indicating a high linear correlation and concordance between the two.

In 71.8% (94) of the cycles, the estimated folinic rescue matched with the dose which the patient should receive according to real [MTX_{24h}]. Assuming the dosing of folinic acid at 24 hours by protocol (15 mg/m^2/6 hours) in all cases, only 35.1% (46) of patients would have received the correct dose. The Cohen kappa between the two methods was 0.189, indicating only slight agreement between both methods in favour of estimating [MTX_{24h}].
Conclusion and relevance Estimated and real [MTX_{24h}] showed high correlation and concordance, and in most cases the folinic acid rescue dose was correctly administered based on 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 systematic administration of 15 mg/m^2/6 hours.

REFERENCES AND/OR ACKNOWLEDGEMENTS

Conflict of interest No conflict of interest

4CPS-281 HIGH DOSE METHOTREXATE IN PAEDIATRIC OSTEOSARCOMA PATIENTS: EFFECTIVENESS AND SAFETY

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Background and importance Osteosarcoma is the most frequent bone tumour, and is more prevalent in paediatric patients. Treatment of osteosarcoma in paediatric patients includes administration of methotrexate at high doses, which allows the drug to penetrate the bone tissue in adequate concentrations. Serum peak methotrexate levels between 1000 and 1500 µM have been correlated with efficacy.
Aim and objectives The objective of this study was to evaluate the effectiveness and safety of methotrexate 12 g/m^2 as treatment for osteosarcoma in paediatric patients.
Material and methods This was an observational retrospective study including paediatric osteosarcoma patients treated with 12 g/m^2 methotrexate infusion from January 2014 to June 2020. Data were extracted from the patients' clinical history. Peak methotrexate serum levels were extracted immediately after the 4 hour infusion. Variables collected were: age, sex, number of cycles received, peak methotrexate serum levels and adverse events associated with the methotrexate infusion during hospitalisation.
Results 25 patients, 56% (14) males, median age 14 (4–17) years, received 159 cycles of methotrexate. The median number of cycles per patient was 8 (2–8). Median peak methotrexate serum levels were 1280 (280–2980) µM; 74.84% of peak serum levels were >1000 µM.
Conclusion and relevance When comparing our results with published studies, we found that the patients included in our study achieved effective concentrations of methotrexate at a higher percentage (75% vs 63%)[1] with severe adverse events being less frequent (9% vs 39%).[2] According to these results, methotrexate infusion was effective and safe in the studied population.

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Conflict of interest No conflict of interest

Abstract 4CPS-281 Table 1 Adverse events associated with methotrexate per cycle

	Adverse event					
Grade	Nausea	Mucositis	Diarrhoea	Cutaneous	Respiratory	Other
I	19	3	5	1	1	4
II	68	0	2	1	0	3
III	10	0	0	0	0	1
IV	0	0	0	0	0	0

96% (24) of patients presented with at least one adverse event during methotrexate infusions. Few adverse events apart from nausea were described. Only 9.33% (11) of adverse events were classified as severe.