

# HIGH DOSE METHOTREXATE IN PEDIATRIC OSTEOSARCOMA PATIENTS: EFFECTIVENESS AND SAFETY.

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## Background and importance

Osteosarcoma is the most frequent bone tumor, being more prevalent in pediatric patients. Treatment of osteosarcoma in pediatrics includes the administration of methotrexate at high doses, which allows the drug to penetrate the bone tissue in adequate concentrations, serum peak methotrexate levels between 1000-1500 mcM have been correlated with efficacy.

## Aim and objectives

To evaluate the effectiveness, based on the peak concentration, and the safety, based on the adverse effects of the administration of Methotrexate 12g/m<sup>2</sup> as treatment of osteosarcoma in pediatrics. To compare the results from 10 different anticholinergic scales.

## Results:

96% (24) of patients presented 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.

## Material and methods

Observational retrospective study including pediatric osteosarcoma patients treated with 12g/m<sup>2</sup> methotrexate infusion from January 2014 to June 2020. Data was extracted from patients clinical history. Peak methotrexate serum levels were extracted immediately after the 4-hour infusion.

**Table 1. Patient's characteristics and MTX administration data.**

|                                    |                     |
|------------------------------------|---------------------|
| Patients                           | 25                  |
| Sex                                |                     |
| Male                               | 14 (56%)            |
| Female                             | 11 (44%)            |
| Age                                |                     |
| Median age (range)                 | 14 (4-17)           |
| MTX administration                 |                     |
| MTX cycles                         | 159                 |
| Median MTX cycle (range)           | 8 (2-8)             |
| MTX serum levels                   |                     |
| Mean Peak serum level (range)      | 1280 (280-2980) mcM |
| MTX peak serum level over 1000 mcM | 119 (75%)           |

MTX: methotrexate.

**Table 2. Adverse events associated with methotrexate per cycle.**

| Grade* | Adverse events |           |          |           |             |       |
|--------|----------------|-----------|----------|-----------|-------------|-------|
|        | Nausea         | Mucositis | Diarrhea | 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     |

\*Adverse events graded according to CTCAE guidelines.

## Conclusion and Relevance

According to peak serum level, methotrexate reached effective concentrations on ¾ of cycles. Few severe adverse events were described with nausea being the most frequent. Methotrexate infusion was effective and safe on the studied population.

