

PKP-012. METHOTREXATE LEVELS IN CEREBROSPINAL FLUID IN CHILDREN TREATED WITH HIGH-DOSE METHOTREXATE

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Background

The use of intrathecal (IT) methotrexate (MTX) in combination with systemic high-dose MTX (HDMTX) is an established procedure for central nervous system prophylaxis in patients with acute lymphoblastic leukemia (ALL), but the evidence for the necessity of this combination is not conclusive.

An MTX concentration of $1\mu\text{M}$ is assumed to be the lowest concentration for an antileukemic effect.

Purpose

To evaluate the rate of sufficient cerebrospinal fluid (CSF) MTX concentrations ($1\mu\text{M}$) in pediatric patients with ALL who received HDMTX to value the suitability use of IT MTX, and to correlate MTX plasma and CSF concentrations.

Material and methods

Retrospective observational study, between April 2015 and September 2016. We included children up to 18 years old with ALL who received $5000\text{mg}/\text{m}^2$ over 24h in accordance with LAL-SEHOP-PETHEMA-2013 protocols .

CSF samples were obtained 18 hours (16-20 hours) after starting the HDMTX infusion and immediately before the IT administration of MTX. Plasma samples were obtained at 2, 12, 23, 36, 42 and 60 hours after the start of infusion.

CFS samples and plasma MTX at 12h were correlated by *Spearman's correlation*

MTX was measured by architect chemiluminescence immunoassay.¹

Results

We included 12 children from 2 to 16 years old (7 ± 3.6) who received 36 cycles of MTX. Patients received $5000\text{mg}/\text{m}^2$ over 24h, an only child who received $3000\text{mg}/\text{m}^2$ was finally included.

MTX plasma at 12 hours and CSF concentrations were highly variable, ranging from 48.8 to $179.0\mu\text{M}$ (median, $72.2\mu\text{M}$) and from 0.85 to $2.9\mu\text{M}$ (median, $1.4\mu\text{M}$), respectively.

An MTX concentration above $1\mu\text{M}$ was found in 33 of 36 of CSF samples (91.7%). Patient who received $3000\text{mg}/\text{m}^2$ (2 cycles) showed a lower CSF MTX concentration (0.83 and $1.08\mu\text{M}$), corresponding to a lower plasma MTX concentration (54.37 and $60.88\mu\text{M}$)

The correlation between plasma levels at 12 hours and CSF MTX concentrations was moderate-high (Spearman rank order correlation, $r = 0.71$; $P < 0.01$).

Conclusion

A potentially antileukemic MTX concentration of $1\mu\text{M}$ is obtained in CSF during the majority of MTX infusions ($5000\text{mg}/\text{m}^2$ over 24h).