

MEASUREMENT OF METHOTREXATE IN CEREBROSPINAL FLUID BY FLUORESCENCE POLARISATION IMMUNOASSAY IN PATIENT WITH MEDULLOBLASTOMA

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BACKGROUND.

Medulloblastoma is one of the most frequent malignant brain tumors in infancy. Conventional treatment is based on combined radiotherapy and chemotherapy after surgical resection of the tumor. Methotrexate is administered in intravenous (i.v.) infusion at high doses combined with intrathecal injection at low doses. The use of fluorescence polarisation immunoassay (FPIA) to monitor blood methotrexate levels is widely validated, but there have been few studies on its application to analyze cerebrospinal fluid (CSF) concentrations of this drug.

OBJECTIVE

Analyze cerebrospinal fluid (CSF) concentrations of methotrexate by fluorescence polarisation immunoassay (FPIA) in patient with medulloblastoma.

MATERIALS AND METHODS.

A 22 month-old female diagnosed with medulloblastoma underwent intensive chemotherapy. The regimen was three two-month courses of chemotherapy with methotrexate and other anti cancer agents. The patient has received one complete course to date.

Table 1: Chemotherapy regimen administered

	DAY 1	DAY 2	DAY 3	DAY 4
WEEK 1	MTX 2mg IT CYC IV	MTX 2mg IT CYC IV	MTX 2mg IT CYC IV	MTX 2mg IT
WEEK 3	MTX 2mg IT MTX 2.7 g INF VIN IV	MTX 2mg IT		
WEEK 5	MTX 2mg IT MTX 2.7 g IV VIN IV	MTX 2mg IT		
WEEK 7	MTX 2mg IT CAR IV ETO IV	MTX 2mg IT CAR IV ETO IV	MTX 2mg IT CAR IV ETO IV	MTX 2mg IT

IT: Intraventricularly Ommaya IV: Intravenous INF: 24-h Intravenous infusion

CYC: Cyclophosphamide VIN: Vincristine CAR: Carboplatin ETO: Etoposide

Methotrexate CSF samples were drawn before the first intraventricular injection and a 24-h after each intraventricular administration.

CSF methotrexate levels were determined by FPIA using an Abbot TDX analyzer.

RESULTS

Table 2: Analysis of methotrexate in cerebrospinal fluid by FPIA

Measure concentration (M)	DAY 1	DAY 2	DAY 3	DAY 4
WEEK 1	14.26 x 10 ⁻⁶	218 x 10 ⁻⁶	0.75 x 10 ⁻⁶	0.33 x 10 ⁻⁶
WEEK 3	0.05 x 10 ⁻⁶	2.96 x 10 ⁻⁶		
WEEK 5	0.02 x 10 ⁻⁶	2.16 x 10 ⁻⁶		
WEEK 7	0 x 10 ⁻⁶	1.46 x 10 ⁻⁶	0.94 x 10 ⁻⁶	1.07 x 10 ⁻⁶

The mean value was 1.38x10⁻⁶ M.

Values on day 1 of each cycle were obtained prior to the intraventricular injection; therefore, day 1 values were not considered in the calculation of the mean CSF concentration. Values on days 1 and 2 of week 1 were excluded from our analysis because the corresponding samples were contaminated.

CONCLUSION

FPIA proved to be a reliable method to measure CSF fluid methotrexate concentrations, within published ranges, although further studies are required to verify these findings.