CYTARABINE
Version 1

SECTION ONE

Alternative names:

- Cytosine Arabinoside
- Ara -C
- Arabinosylcytosine
- Cytosar TM

Mechanism of action

- Pyrimidine nucleoside analogue which inhibits the synthesis of DNA.
- Cell cycle phase specific for S phase.

Considerations prior to administration

- Cytarabine is contra-indicated in patients with known hypersensitivity to the drug.
- Severe and fatal CNS, GI and pulmonary toxicities have occurred with cytarabine.
- Full blood count
- Prophylactic steroid eye drops (eg prednisolone) must be given with higher doses of cytarabine (>1g/m^2) to prevent conjunctivitis
- Corticosteroids can be used to treat/prevent 'cytarabine reaction'
- Use with caution and at reduced dose in patients with poor liver function

Adverse events [1,2]

Common

- Bone marrow suppression
- Nausea and Vomiting
- Diarrhoea
- Mild oral ulceration
- Conjunctivitis with high doses

Occasional

- 'Cytarabine' reaction including 'Flu'-like symptoms, fever, myalgia, bone pain, chest pain, rash, conjuctivitis and malaise 6-12 hours after administration
- CNS and cerebellar toxicity at higher doses

Rare

- Hepatotoxicity
- Pancreatitis
- Meningismus, parasthesias and paraplegias and seizures
- Severe and sometimes fatal CNS, GI and pulmonary toxicity with higher doses

SECTION TWO

Recommended routes

Cytarabine can be given by intravenous (bolus or intermittent or continuous infusion), subcutaneous (injection and infusion) and intrathecal injection[2,3,4]

Presentation

Ampoules: cytarabine isotonic solution 20mg/ml (2ml and 5ml size) Alexan™
cytarabine hypertonic solution 100mg/ml (1ml and 10ml size) Alexan™

Vials: cytarabine powder 100mg,500mg and 1000mg with diluent

CAUTION

The high strength injection solution should not be given intrathecally due to the hypertonicity of the solution.

Administration[2,3]

Bolus Administration:
SC and IV bolus injections are used in maintainence therapy.

IV infusion:

- High Dose Schedules may be administered by intermittent or continuous infusion in 0.9% Sodium Chloride or 5% Glucose.
- To reduce toxicity infusions should be not less than one hour
- Continuous infusions of cytarabine have ranged from 8-12 hours to 120-168 hours.

Interactions

- Absorption of oral digoxin may be substantially reduced in patients receiving cytarabine.
- Cytarabine may antagonise the activity of gentamicin against K pneumonia and of flucytosine against fungi
- G-CSF may increase the cytotoxic activity of cytarabine
- Fludarabine enhances the production of ara CTP (the active metabolite of cytarabine) and thereby enhances it's cytotoxicity

Overdose

Cessation of therapy followed by supportive care for bone marrow depression.[2]

SECTION THREE

Dilution specification and stability[3]

- Dry powder vials should be reconstituted with Water for injection.
- Cytarabine may then be further diluted (if necessary) with Sodium Chloride 0.9% or Dextrose 5%
- In 0.9% sodium chloride, no decomposition occurred after 24 hours, but a 3% loss at room temperature and a 6% loss at 30^0C was observed over 7 days
- Cytarabine at a concentration 20mg/ml in 0.9% sodium chloride is stable for 14 days at 4^0C
- Photo-degradation of cytarabine does not appear to be significant

Pharmacokinetics[2]

- Cytarabine is deaminated to arabinofuranosyl uracil in liver and kidneys**.** It is a prodrug, which is activated to cytarabine 5'-triphosphate (araCTP) within cells[6].
- Cytosine is metabolised rapidly, primarily by the liver and perhaps by the kidney
- After a 3hour infusion, elimination is biphasic with an initial $t_{1/2}$ of 10mins and reported terminal half-lives of 2.4 to 4.8 hours[6,11]. AraCTP has a longer half-life of 3.3 to 6.9 hours[6].
- Shorter half-lives (less than 2 hours) may be observed with bolus administration[8].
- 5.8% of the dose is excreted unchanged in the urine within 12-24 hours[7].
- 90% of the dose is excreted as the deaminated product[7].
- Widely distributed into tissues, across the blood brain barrier and placenta. Concentrations of cytarabine in the CSF are similar to those in plasma, with possible accumulation of araU in CSF on repeated dosing[10].

Pharmacodynamics

The activity of cytarabine is thought to be related to concentrations of the active metabolite araCTP in leukaemic cells[9]. However, this has not been substantiated in clinical studies[5]. Saturation of araCTP formation may occur at high doses[10].
Children appear to tolerate higher doses of Cytarabine than adults.[2]

References

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