Intrathecal and Intraventricular antibiotics administration

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Outlines

- Physiology and anatomy involve CSF production
- General concept of IT and IVT injection
- Colistin IT and IVT
  - PK/PD parameter predicted efficacy
  - PK colistin IVT
  - Dosage and administration colistin IT and IVT
  - Evidence base

Physiology and anatomy involve CSF production

- Volume of CSF in adults approximate 150 ml; ventricle 25 ml and subarachnoid space 125 ml
- CSF clearance rate; 20-25 ml/hr.
- pH CSF = 7.31-7.37
- osmolarity = 281-306 mosm/kg
Pharmacist should know ......

- Position of administration
  - Intrathecal
  - Intraventricular
- Properties of drugs
- PK/PD of antibiotics

Properties of Drugs

- IV drugs and free preservative
- Dissolved in vehicle and stable in body temperature
- Volume: 5-10 ml
- pH and osmolarity not more than 10% of physiological range

Position of IT

http://biology-forums.com/index.php?action=gallery;sa=view;id=9729

Position of IVT

J. Devul Pham Pharm. 2009; 15: 45-52.
Colistin intrathecal and intraventricular administrations

- The incidence of ventriculitis in neurosurgical patients is up to 27% and it is associated with high morbidity and mortality rates
- Colistin possesses a poor ability to penetrate the CSF
- Colistin concentrations in the CSF did not exceed 0.5 mcg/mL
- MIC breakpoint
  - *P. aeruginosa*: susceptible = < 2 mcg/mL
  - *A. baumanii*: susceptible = < 2 mcg/mL

PK/PD parameter

Target in clinical practice

- Because of colistin-associated with concentration-dependent killing, a target Cmax/MIC ratio between 8 and 10 has been found to be optimum, so this ratio may be considered desirable for colistin
- AUC/MIC ratio of total and unbound colistin is the index that best predicts the antibacterial activity against *P. aeruginosa*, superior to Cmax/MIC

Colistin IVT; Pk data

![Colistin IVT Pk data](image)

2.61 mg CMS = colistin base 1 mg
10.44 mg CMS = colistin base 4 mg

4 mg: 9-22 mg/ml cover MIC 1-3
4 mg: 180-261 mg/ml cover MIC 3-4

Colistin IT and IVT; Dosage

- Manufacturer:
  - 10 mg q 12 hr. or 20 mg q 24 hr.

Duration: no data
Interval: no data

Practice Guidelines for the Management of Bacterial Meningitis

Table 7. Recommended dosages of antimicrobial agents administered by the intraventricular route (A-III).

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>Daily intrathecal dose, mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin</td>
<td>5-200</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>1-100</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>5-20</td>
</tr>
<tr>
<td>Amikacin</td>
<td>5-60</td>
</tr>
<tr>
<td>Polymyxin B</td>
<td>10-50</td>
</tr>
<tr>
<td>Colistin</td>
<td>10</td>
</tr>
<tr>
<td>Quinupristin/dalfopristin</td>
<td>2-5</td>
</tr>
<tr>
<td>Ticarcillin</td>
<td>5-50</td>
</tr>
</tbody>
</table>
Successful clinical and bacteriological outcome was achieved in 89% (72/81) of A. baumannii ventriculitis/meningitis cases.

The median time required for sterilisation of the CSF was 4 days (range 1–28 days).

71/81 were adults (range 15–78 years), 10/81 were children and neonates (range 2 months to 9 years).

IVT and IT routes was 52 and 22, respectively.

30 cases were defined as MDR strains and 51 as XDR.

Information on the MIC was report only in 25 cases, with a distribution of, ≤ 0.2 mg/ml.

Monotherapy with local colistin was given in 11 cases, whereas combination of IV and IT/IT colistin administration was reported in 37 cases.

Dosage: adults: 1.6 - 40 mg/day (median dose 10 mg/day) administered once or twice daily.

-children: 0.16 mg/kg/day - 10 mg/day

The median duration of treatment was 18.5 days (2-56 days).

ADR: seizure 4%, Topical reaction (chemical ventriculitis or chemical meningitis) 11%.

“Thank you”

The end....