The University of Nottingham

Biomaterials Related Infection Group

Infections in external ventricular drainage: Causes, diagnosis, treatment and prevention

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Incidence of infection in EVD

Around 10%

Holloway et al	1996	10.4%
Berger et al	2000	3.9%
Wong et al	2002	7.8%
Zabramski et al	2003	9.4%
Schade et al	2006	9.6%
Moon et al	2007	8.6%
Nottingham	2003-6	7-9%
	2006-10	2-3%

Incidence of infection in EVD

Sometimes higher than 10%

Leverstein v-Hall et al	2004	17%
Korinek et al	2005	12%
Hayhurst et al	2007	27%
Dasic et al	2009	27%
Keong et al	2010	21%

What are the reasons for this? Possibly different diagnostic criteria or different patient demography etc

Causative bacteria

- Mainly staphylococci
- Mainly CoNS (S epidermidis)
- Some S aureus, occasionally MRSA

- Gram negatives eg E coli, Klebsiella, Pseudomonas

- Acinetobacter baumannii (MDR)
  20-27% mortality (Krol et al J Hosp Infect 2009)

- Occasionally Candida

75% of infections are due to Gram positive bacteria

Diagnosis of EVD- associated ventriculitis

- Patients often already ill: impaired consciousness, fever, etc
- CSF picture unclear: blood, white blood cells, glucose, protein etc all unreliable in bleeds or trauma
- CSF culture: contaminants?

Mayhall et al NEJM 310: 553-9, 1984

- CSF +ve culture
- Fever >38°C: ≥48hr before or after CSF + culture, persisting ≥3 days
- CSF WBC ≥11/mm^3, 50% polymorphs ≥48hr before or after CSF + culture, persisting ≥3 days
- Peripheral blood WBC up ≥48hr before or after CSF + culture, persisting ≥3 days

Mayhall et al 1984

- CSF +ve culture
- Fever >38°C: ≥48hr before or after CSF + culture, persisting ≥3 days
- CSF WBC ≥11/mm^3, 50% polymorphs ≥48hr before or after CSF + culture, persisting ≥3 days p= 0.0001

  But 4 of 19 infections had normal WBC!

- Peripheral blood WBC up ≥48hr before or after CSF + culture, persisting ≥3 days

Changes over 24-48hrs might be more indicative than snapshot data

Does it matter if the catheter is colonised but the CSF is sterile with no white blood cells?

Significance of drain colonisation

Pfisterer et al J. Neurol. Neurosurg. Psychiatr 74;929-932 2003:

- Increasing CSF WBC led to “suspicion of bacteriological drainage contamination” or “incipient catheter contamination”
- They considered these to be infection and treated them as such
- Drains were sampled daily

Daily CSF sampling: does it lead to earlier diagnosis of infection?

Hader & Steinbok Neurosurg:46 (5):1149-1155,2000:

- Routine daily CSF sampling did not help in early diagnosis: recommend only if symptoms or suspicion of infection

- Risk of introducing infection
- More “contaminants” isolated

How to distinguish contaminants?

- Lozier: Single CSF positive culture / gram stain, no other changes = contaminant

- Hader & Steinbok 2000:

  Culture +ve, Gram film –ve = contaminant

  Culture +ve on two days, same organism, Gram film +ve = infection

Diagnosis of CSF infection in EVD

Clinical signs / symptoms?

Laboratory measurements?

Pfisterer et al J. Neurol. Neurosurg. Psychiatr 74;929-932 2003:

- **Infection rate 16.2%**
- **Blood WBC, CSF glucose or protein, serum CRP, other inflammatory markers not reliable.**
- **Only Cell Index correlated with positive cultures**

Pfausler cell index

- Cell index: $\frac{\text{WBC (CSF)}}{\text{WBC (Blood)}} / \frac{\text{RBC (CSF)}}{\text{RBC (Blood)}}$

Pfausler et al, Acta Neurochir 146, 477-81, 2004

Pfausler cell index

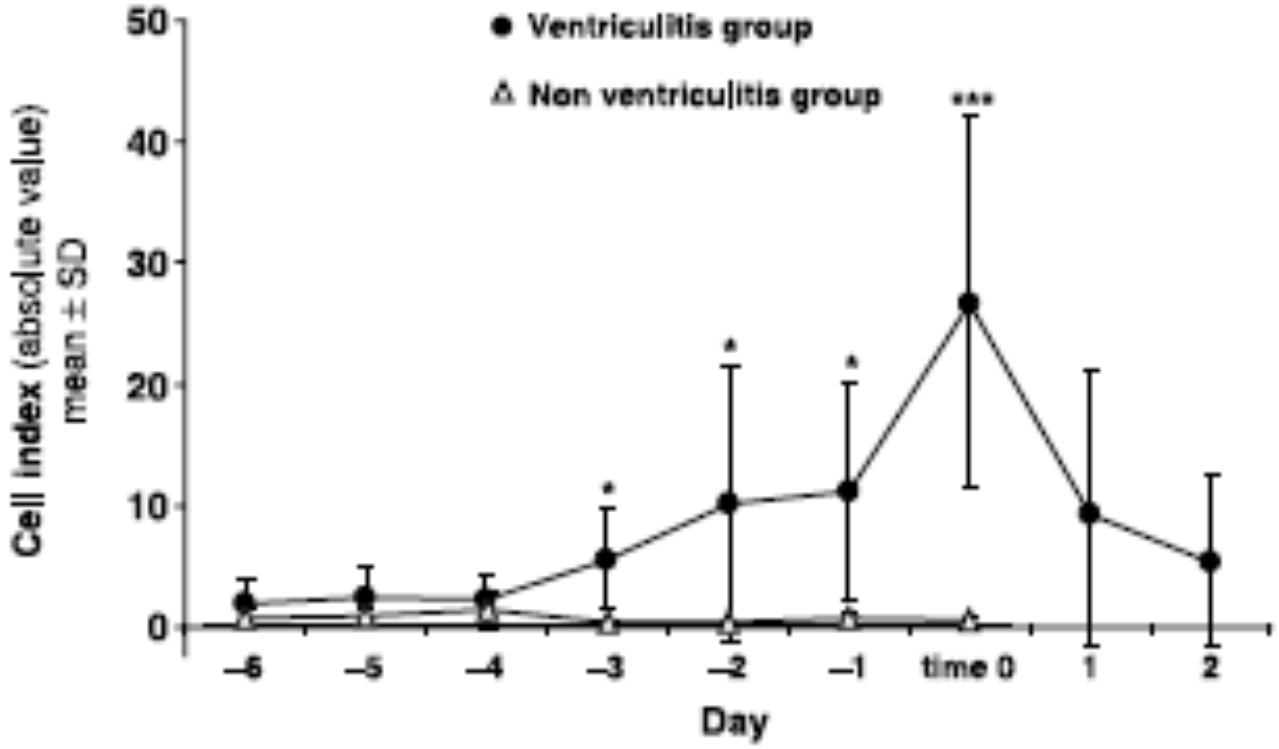


Fig. 1. Time course of mean CI (±SD) of 7 patients with EVD associated ventriculitis (filled circles) compared to mean CI (±SD) of 6 patients without EVD associated ventriculitis (triangulars)

Round up and recommended way forward

Symptoms:

- change in mental status
- New fever

- CSF +ve gram stain plus culture +ve
- Repeat culture if +ve with -ve Gram film or if change in symptoms or WBC etc

Recommendations for discussion

- If clinical suspicion of infection or new fever, etc: CSF sample
- Ask for Gram film stat and semi-quantitative culture
- If decision is catheter colonisation, remove and treat (1 dose)
- If decision is ventriculitis, remove and treat
- If decision is sample contamination, observe carefully! (sample contaminated might mean CSF contaminated!)

Sources of infection in EVD

- Risk at insertion
- Continued risk during use

Contamination of lumen from:

- Disconnections
- CSF sampling
- Patient's skin, staff fingers, environment

Contamination of skin track from patient's skin

- Schade et al 2005:

If EVD is in for >15 days, the risk of infection is seven times greater than if <15 days

Strategies for prevention

Changes in surgical practice:

“bundling”

Putting into practice “common sense” measures, none of which alone necessarily has RCT evidence

Importance of protocols

Korinek et al Acta Neurochir 147:39–46,**2005:**

- **"…the only statistically significant risk factors for infection were CSF leak, and protocol violation.**
- **Patients with a protocol violation score of 0 or 1 (no violations) had no infections P<0.0001**

Prophylactic antibiotics for EVD

Three options:

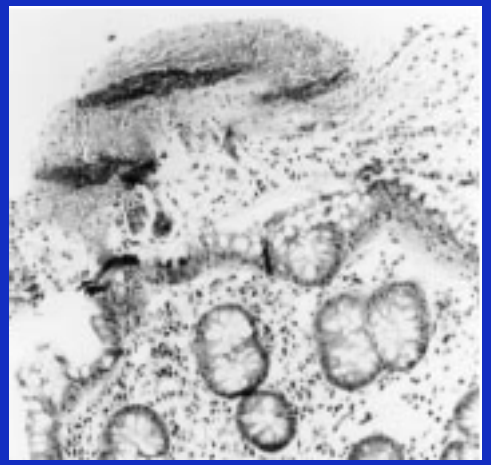
- None
- At insertion only
- Throughout use of EVD
- And a fourth: antibiotics for infections elsewhere

Prophylactic antibiotics for EVD

Risks of prophylactic antibiotics

- Drug reactions: eg nausea, anaphylaxis
- Promotion of antibiotic resistance eg MRSA
- Selection of intrinsically resistant organisms eg Pseudomonas, Candida

- Increased risk of *C difficile* infection



Prophylactic antibiotics

Alleyne et al Neurosurg 47,1124–1129, 2000:

Results

Two Groups:

- **Group A, antibiotics at insertion and during EVD**
- **Group B, antibiotics only at insertion**
- **No difference in infection rate**
- **Found more Gram negative infections in Group A**
- **All Acinetobacter and Pseudomonas were in Group A**
- **In Group B, savings were $80k each year**

Prophylactic antibiotics

Korinek et al 2005:

Reduced antibiotic use (80% to 65%) and reduced infection rate 10% to 4.6% p=0.05

Non-use of antibiotic prophylaxis, even at insertion only, was not a risk factor for infection

But 50% more resistant bacteria in antibiotics group

- No clear evidence of efficacy for antibiotics
- Current infection rates in USA (8.8%) are *with* antibiotics (Lozier et al 2000)

Antimicrobial EVD catheters

Conflict of interest: Author is named inventor of Bactiseal and receives speaker fees from Codman

Antimicrobial EVD catheter (Bactiseal)

- Impregnated (NOT COATED) with rifampicin and clindamycin
- ~50 days antibacterial protection against colonization

  (Bayston, Ashraf and Bhundia J Antimicrob Chemother 53, 778-782, 2004)

- This should be adequate duration cover for all EVDs

Limitations of Bactiseal

- Does not protect against Gram negative bacteria (usually ≤ 25%)

Alternatives to Bactiseal for EVD

- **Hydrogel – coated catheter (can be soaked in antibiotic solution:** Kaufmann et al Can J Neurol Sci 2004; 31: 506-510**)**
- **Silver processed catheter**

Silver catheter clinical study

Fichtner et al J Neurosurg 112:840–846,2010

- **Retrospective review, 164 patients**

- **Control Arm (90): infn rate 4.7%**
- **Silver EVD Arm (74): infn rate 2.7%**

- **Not stat significant p= 0.55**

Silver EVD clinical study

Keong et al *J Neurol Neurosurg Psychiatr* 2010;81:1064-1067

- **Double blind RCT, 278 patients**
- **Control Arm: infn rate 21.4%**
- **Silver EVD Arm: infn rate 12.3% P=0.045**

- **Significant reduction in EVD infection but rate remains high.**

Bactiseal EVD Clinical trials?

- **Muttaiyah et al** J Clin Neurosci 17 296–298,2010**:**

EVD infection reduced 15% to 5% (p=0.06) (60 vs 60; historical controls)

Bactiseal vs prophylactic antibiotics

Wong et al J Neurol Neurosurg Psychiatr 2010;**81:1064-1067**

- **184 patients:**
  Bactiseal + antibiotics at insertion only
  Plain catheters + longterm antibiotics

- **Bactiseal 1% infection**
- **Plain + AB 3% infection (p=0.282)**

Bactiseal vs prophylactic antibiotics

Wong et al 2010: Adverse effects

***Clostridium difficile* infection:**

- **Bactiseal: 0**
- **Plain catheters + longterm antibiotics 3**
  (1 case colectomy)

Therefore, more systemic antibiotics leads to more resistance and more adverse events

Korinek showed that using no antibiotics at all was not a risk factor for infection….

Conclusions

- Diagnosis of EVD ventriculitis is made difficult by underlying pathology
- Infection rates vary considerably
- Rates can be reduced by protocol adoption
- Antimicrobial EVD catheters reduce infection rate and adverse events
- Prolonged antibiotic prophylaxis is of no benefit and leads to complications