ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

www.surgicalneurologyint.com

Surgical Neurology International
Editor-in-Chief: Nancy E. Epstein, MD, NYU Winthrop Hospital, Mineola, NY, USA.
SNI: Randomized Controlled Trials
Editor
Benjamin W. Y. Lo, MD
Montreal Neurological Institute & Hospital, McGill University, Quebec, Canada

SNI
Open Access

Editorial

Short review of randomized controlled trials for Surgical Neurology International: Part II - drain-associated cerebrospinal fluid infections

Benjamin W. Y. Lo[1], Hitoshi Fukuda[2], Satoru Miyawaki[3], Anderson C. O. Tsang[4], Masaomi Koyanagi[5]

[1]McGill University Health Centre, Montreal, Quebec, Canada, [2]Department of Neurosurgery, Kochi University, Kochi, [3]Faculty of Medicine, The University of Tokyo, Tokyo, [5]Amagasaki General Medical Center, Kyoto University, Hyogo, Japan, [4]Department of Surgery, Division of Neurosurgery, Queen Mary Hospital, University of Hong Kong, Hong Kong.

E-mail: *Benjamin W. Y. Lo - lo_benjamin@hotmail.com; Hitoshi Fukuda - fukudaharpseal@gmail.com; Satoru Miyawaki - satorumiyawaki@gmail.com; Anderson C. O. Tsang - acotsang@hku.hk; Masaomi Koyanagi - koyanagm@gmail.com

***Corresponding author:**
Benjamin W. Y. Lo,
Faculty of Medicine, McGill University, 845 Sherbrooke St W, Montreal, Quebec H3A 0G4, Canada.

lo_benjamin@hotmail.com

Received : 13 February 19
Accepted : 15 February 19
Published : 26 March 19

DOI
10.25259/SNI-74-2019

Quick Response Code:

INTRODUCTION

Two methodologically sound randomized controlled trials (RCTs) were published in the third and fourth quarters of 2018 dealing with drain-associated cerebrospinal fluid (CSF) infections. Both RCTs offer significant scientific findings which may be of interest to readers of Surgical Neurology International.

Infectious diseases society of America's 2017 clinical infectious disease guidelines for external ventricular drains

Drain-associated CSF infections have a pooled incidence rate of about 11.4/1000 catheter days.[10] The Infectious Diseases Society of America's 2017 Clinical Infectious Disease Guidelines for external ventricular drains are listed in Table 1.[10]

Infections due to external ventricular drains and lumbar drains

Most infections related to external ventricular or lumbar drains are introduced at the time of drain placement, whereas retrograde infection is another, very secondary mechanism of contamination. Risk factors for ventriculostomy-associated CSF infections include (1) previous craniotomy, (2) systemic infection, (3) skull fracture with CSF leak, (4) intraventricular/subarachnoid hemorrhage, (5) increased duration of drain, and (6) procedural factors (e.g., drain site leaks, lack of tunneling, multiple catheter irrigations, and increased frequency of CSF sampling).[1,5,8]

Use and efficacy of prophylactic antibiotics

Prophylactic antimicrobial agents have not been shown to significantly reduce drain-associated CSF infections in patients without significant risk factors.[10] Prior systematic review demonstrated the effectiveness of silver coated ventricular catheters in preventing ventriculostomy-associated infections.[1,5,8] Even though antimicrobial-impregnated catheters may increase the number of false negative culture results, the following

two 2018 RCTs offer some insight regarding two methods for infection prevention. The first deals with utilizing silver-impregnated lumbar drains to prevent catheter bacterial colonization.[3] The second included chlorhexidine dressings to control scalp bacterial growth around the drain entry and exit points.[9]

The SiLuDrain trial

The SiLuDrain trial is a single-center RCT from Germany comparing infection and complication rates utilizing conventional versus silver-impregnated lumbar drains (both of 1.6-mm outer diameter and 0.8-mm inner diameter).[3] Forty-eight adults (24 per group, randomized in block sizes of 4, with no group crossovers) underwent lumbar drain placement. Reasons for placing drains included posthemorrhagic hydrocephalus, normal pressure hydrocephalus, and CSF fistulas. The following patients were excluded from the study: those with silver allergy, prior lumbar drain placements within 3 months, CSF infections, and leptomeningeal tumor spread. Patients did not receive periprocedural antibiotics.

Lumbar drain protocol

All patients had lumbar drains placed for an average of 4 days (range 1–10 days). Daily inspection of puncture sites was accompanied by routine CSF sampling on the day of drain placement and every 2nd day until drains were removed. Here, drain-associated CSF infection was defined as a confirmed cultured organism or clinical sign suggestive of meningitis. Patients in the silver-impregnated lumbar drain group experienced significantly fewer catheter-related complications [Table 2]. Fewer patients (1 in the study group versus 4 in the control group, not statistically significant) experienced drain-associated CSF infections, diagnosed after 7 days of drain placement (range of 6–9 days). For the five patients with CSF infections, 14 CSF samples confirmed the growth of microorganisms (13 CSF cultures grew Staphylococcus species, one Gram-negative *Escherichia coli*, and one candida species). Ten of 14 Gram-positive CSF cultures showed significantly reduced bacterial growth when cultured in the presence of silver-impregnated catheters.

Table 1: Infectious Diseases Society of America's 2017 Clinical Infectious Disease guidelines for external ventricular drains.

Infection – Single or multiple positive CSF cultures with CSF pleocytosis and/or hypoglycorrhachia, or an increasing cell count, and clinical symptoms suspicious for ventriculitis or meningitis
Colonization – Multiple positive CSF cultures or Gram stains, with normal CSF cell count, glucose, and protein concentrations, as well as lack of clinical symptoms suspicious for ventriculitis or meningitis
Contamination – An isolated positive CSF culture or Gram stain, with normal CSF parameters and lack of clinical symptoms suspicious for ventriculitis or meningitis

CSF: Cerebrospinal fluid

The external ventricular drain-associated infection (EVDAI) study

In Roethlisberger *et al.*, single-center controlled RCT investigators studied scalp bacterial growth and silver-impregnated ventriculostomy colonization in patients with and without chlorhexidine wound dressings (chlorhexidine gluconate 2%).[9] Fifty-five adults, 28 in the study group and 27 in the control group, were randomized to undergo emergency ventriculostomy placements from 2013 to 2016. Exclusion criteria included CNS infections, posttraumatic dural breaches, and concomitant antimicrobial therapy. Patients underwent ventriculostomies in the operating theater, utilizing preprocedural cefuroxime and skin preparation of 30 s after hemicranial hair removal. They underwent silver-impregnated external ventricular drain placement utilizing 5 cm of subcutaneous tunneling of the catheter away from drain entry site.

Culture from the scalp

Sampling of scalp at drain exit sites was performed at the time of procedure for a skin area of 12 cm^2, with dressing changes every 5 days. Those with silver-impregnated ventriculostomies placed for an average of 8 days (range 5–12 days), utilizing the chlorhexidine protocol, exhibited significantly less bacterial growth versus those with uncoated dressings [Table 3]. More virulent Gram-positive cocci were detected for those with uncoated dressings. Given the small study cohort sizes, both groups showed nonsignificant differences in bacterial colonization of subcutaneous catheter segments, catheter tips, and ventriculostomy-associated infections.

DISCUSSION

The SiLuDrain trial and EVDAI study offer insight regarding the prevention of drain-associated infections. The SiLuDrain trial demonstrated that silver-impregnated lumbar drains are well tolerated with fewer Gram-positive bacterial infections. Findings from this study are consistent with prior meta-analysis of prospective studies demonstrating the effectiveness of silver-coated ventricular drains in preventing ventriculostomy-associated infections.[2,5-7] Silver-coated catheters contain combinations of metallic silver and insoluble luminal silver salts with demonstrated patient safety profiles and antimicrobial properties.[4,5,10] Silver-coated drains may not be as effective as antibiotic-impregnated drains in preventing Gram-negative bacterial colonization. Dependent on the silver particle size, the positive charge of silver ions may be mitigated by negative charges of bacterial cell wall proteins as the duration of drain placement increases.[1]

Most drain-associated infections are caused by bacteria introduced at the time of drain insertion and subsequent catheter colonization, possibly as a result of scalp bacterial growth. The EVDAI study demonstrated reduced scalp bacterial growth, including fewer virulent Gram-positive strains, with the use of chlorhexidine wound dressings.[9] Despite this trial's small sample size, it was methodologically well designed using silver-coated

Table 2: Results from the SiLuDrain trial.

Silver-impregnated lumbar drain group (*n*=24)	Conventional lumbar drain group (*n*=24)
Two catheter occlusions	Five catheter occlusions
One drain-associated infection	Four drain-associated infections

Table 3: Results from the EVDAI study.

Chlorhexidine wound dressing group (*n*=28)	Conventional wound dressing group (*n*=27)
About 5.87 bacterial colony-forming units per cm^2 of the scalp	About 15.7 bacterial colony-forming units per cm^2 of the scalp
Four drain-associated infections	Seven drain-associated infections

EVDAI: External ventricular drain-associated infection

ventriculostomies as an effort to control for potential confounders associated with CSF infections.

Protocols for drain insertion and care can raise awareness of drain-associated CSF infection risk factors. Management of these risk factors, including multiple drain exchanges, frequent CSF samplings, and catheter duration, is essential to decrease patient morbidity and health-care-related costs associated with CSF infections and long-term likelihood of requiring permanent CSF diversion.

CONCLUSIONS

Two 2018 RCTs demonstrated that silver-coated drains were effective in decreasing Gram-positive bacterial adherence to catheter tips and subsequent colonization. They may not be as effective as antibiotic-impregnated drains in preventing Gram-negative bacterial colonization. Furthermore, antimicrobial-coated chlorhexidine dressings appear to be effective in suppressing scalp bacterial growth.

Disclaimer

The views and opinions expressed in this article are those of the author and do not necessarily reflect the official policy or position of the Journal or its management.

REFERENCES

1. Atkinson RA, Fikrey L, Vail A, Patel HC. Silver-impregnated external-ventricular-drain-related cerebrospinal fluid infections: A meta-analysis. J Hosp Infect 2016;92:263-72.
2. Atkinson R, Fikrey L, Jones A, Pringle C, Patel HC. Cerebrospinal fluid infection associated with silver-impregnated external ventricular drain catheters. World Neurosurg 2016;89:505-9.
3. Jakobs M, Klein S, Eigenbrod T, Unterberg AW, Sakowitz OW. The siLuDrain trial: A prospective randomized controlled trial comparing standard versus silver-impregnated lumbar drains. J Neurosurg 2018:1-8. [Epub ahead of print].
4. Keong NC, Bulters DO, Richards HK, Farrington M, Sparrow OC, Pickard JD, *et al.* The SILVER (Silver impregnated line versus EVD randomized trial): A double-blind, prospective, randomized, controlled trial of an intervention to reduce the rate of external ventricular drain infection. Neurosurgery 2012;71:394-403.
5. Konstantelias AA, Vardakas KZ, Polyzos KA, Tansarli GS, Falagas ME. Antimicrobial-impregnated and coated shunt catheters for prevention of infections in patients with hydrocephalus: A systematic review and meta-analysis. J Neurosurg 2015;122:1096-112.
6. Lackner P, Beer R, Broessner G, Helbok R, Galiano K, Pleifer C, *et al.* Efficacy of silver nanoparticles-impregnated external ventricular drain catheters in patients with acute occlusive hydrocephalus. Neurocrit Care 2008;8:360-5.
7. Lemcke J, Depner F, Meier U. The impact of silver nanoparticle-coated and antibiotic-impregnated external ventricular drainage catheters on the risk of infections: A clinical comparison of 95 patients. Acta Neurochir Suppl 2012;114:347-50.
8. Ramanan M, Lipman J, Shorr A, Shankar A. A meta-analysis of ventriculostomy-associated cerebrospinal fluid infections. BMC Infect Dis 2015;15:3.
9. Roethlisberger M, Moffa G, Fisch U, Wiggli B, Schoen S, Kelly C, *et al.* Effectiveness of a chlorhexidine dressing on silver-coated external ventricular drain-associated colonization and infection: A prospective single-blinded randomized controlled clinical trial. Clin Infect Dis 2018;67:1868-77.
10. Tunkel AR, Hasbun R, Bhimraj A, Byers K, Kaplan SL, Michael Scheld W, *et al.*2017 infectious diseases society of America's clinical practice guidelines for healthcare-associated ventriculitis and meningitis. Clin Infect Dis 2017;64:e34-65.

How to cite this article: Lo BW, Fukuda H, Miyawaki S, Tsang AC, Koyanagi M. Short review of randomized controlled trials for surgical neurology international: Part II – drain-associated cerebrospinal fluid infections. Surg Neurol Int 2019;10:39.