

Efficacy of Antimicrobial-Impregnated External Ventricular Drain Catheters: A Prospective, Randomized, Controlled Trial

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Abstract

Background: Insertion of External Ventricular Drain (EVD) is associated with considerable risk of Cerebrospinal Fluid (CSF) infection which is a life-threatening complication. Infection occurs when microorganisms colonize along the catheter surface.

Aim of Study: The aim of this study is to compare the safety & efficacy of EVD catheters impregnated with Clindamycin & rifampin with those of standard control catheters for prevention of the catheter-related infections.

Subjects and Methods: The prospective study was conducted on forty patients between April 2013 – November 2014. All patients were randomly assigned to undergo placement of an EVD with a catheter impregnated with Clindamycin & rifampin or a standard non-impregnated catheter (control group). Each group included twenty patients. Standard silicone catheter was the EVD used in both cohorts. Patients diagnosed with a known or suspected CSF infection were excluded from this study. Initial cell counts and cultures were obtained from the CSF, repeated at intervals (72 hours) and at time of Catheter removal. CSF infection rate and its impact on the clinical outcome were evaluated in both groups.

Results: Among this series of forty patients with EVDs, three had an EVD-associated CSF infection in the control group giving an infection rate within this group of 15% per patient. Only one case in the Antibiotics-impregnated Catheter (AIC) group had CSF infection. Positive CSF cultures were obtained on day 10, 12 & 14 respectively. Organism isolated from CSF cultures was mainly gram-negative infection. AIC group showed a significant low infection rate compared to the uncoated one ($p < 0.001$).

Conclusion: The Catheters impregnated with the antibiotic combination of Clindamycin and rifampin appears to be safe and effective in reducing the risk of infectious complications associated with the placement of an EVD.

Key Words: *External ventricular drain – CSF infection – Antibiotics impregnated Catheter.*

Introduction

EXTERNAL ventricular drain catheter has a major importance in the treatment of patients experiencing head trauma, subarachnoid hemorrhage, and other causes of increased Intracranial Pressure (ICP). The catheter provides a reliable means of ICP monitoring and controlling elevated pressure through draining the Cerebrospinal Fluid (CSF) [1]. These benefits can be offset by catheter-related complications as CSF infection which is a potentially life-threatening complication.

Insertion of External Ventricular Drain (EVD) is associated with considerable risk of CSF infection which reaches up to 27% of patients with EVDs [2]. Coagulase-negative Staphylococcus is the most common bacteria isolated in the patients with EVD-related infections, others include Enterococcus, Enterobacter and Staphylococcus aureus [3]. Infection occurs when microorganisms colonize along the catheter surface. Systemic Antibiotic prophylaxis (SAP) is a widely used strategy to prevent EVD-related infections. However, SAP may not significantly lower the incidence of infection [4]. The antimicrobial-impregnated catheter has emerged as an alternative strategy [5]. Several papers have documented the controversial debate of the role of using the antimicrobial-impregnated ventricular catheters (AIC) in decreasing adherence of microbes to the catheter surface thus preventing the clinical infection [6].

Although, there is no universally accepted practice standard for the use of coated catheters for prevention of the clinical infection [7]. The aim of the present study was to review the Efficacy of Clindamycin and rifampin-impregnated external ventricular drain catheters in preventing of these catheter-related infections.

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Subjects and Methods

This prospective randomized controlled trial was performed at Cairo University Hospital and SKMC between April 2013 – November 2015. Hospitalized patients who required insertion of an EVD catheter were all eligible for the study. The exclusion criteria included patients allergic to Clindamycin or rifampin, infection at the catheter insertion site, suspected CSF infection, dermatitis, pregnancy and CSF catheter placement within the previous one month. All enrolled patients or their legal guardians gave informed consent. Forty patients were enrolled in the study protocol divided into 2 groups. Patients in the control group were randomly assigned to undergo the placement of an EVD with standard non-impregnated No. 9 French silicone catheter while the other group operated upon using No. 9 French silicone catheter which is impregnated with Clindamycin & rifampin. Standard protocols for EVD placement identically were used for both catheter types'. Initial cell counts and cultures were obtained from the CSF, repeated at intervals (72 hours) and at time of Catheter removal. CSF Infection rate and its Impact on the clinical outcome were evaluated in both groups.

The statistical paragraph in material and methods:

Data were statistically described in terms of mean \pm Standard Deviation (\pm SD), or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between pre and post-operative data was done using paired *t*-test for matched samples. For comparing categorical data, McNemar test was done. *p*-values less than 0.05 was considered statistically significant. All statistical calculations were carried out using the computer program SPSS (Statistical Package for the Social Science; IL, SPSS Inc., Chicago, USA) Version 15 for Microsoft Windows.

Results

Among the forty patients enrolled in this cohort, standard non-AIC was inserted in the first group (control group) while the one impregnated with 0.15% clindamycin & 0.054% rifampicin was inserted in the second group (AIC group). Systemic intravenous Antibiotics were used in the two groups as long as the ventricular catheter is insitu.

The CSF samples collected using a sterile technique, were all sent for the gram stain and routine bacterial cultures as well as cell counts & levels of protein and glucose. Infection was defined as a positive CSF culture. The Catheters were daily

inspected for any evidence of infection at the catheter insertion site, erythema, tenderness, pain, suppuration or swelling.

After Catheter removal, cultures were obtained from the tip of the catheters. Positive culture was defined as colonization. All the patients were followed-up for one week after the catheter was removed because the CSF infection diagnosed within that period could have been related to the catheter itself. Patient characteristics are shown in (Table 1).

Table (1): Patient characteristics.

Data	Control	AIVC
No. of patients	20	20
Mean age (y)	53.6	46.3
<i>Sex:</i>		
Male %	48.2%	43.6%
Female %	51.8%	56.4%
<i>Neuropathology:</i>		
Head injury	11	10
Hypertensive bleed	5	6
Venous sinus thrombosis	2	
Aneurysmal Subarachnoid Hemorrhage	1	1
Brain Neoplasm	1	1
Intraventricular Hemorrhage	–	2
<i>Place of Catheter insertion:</i>		
OR	5	4
ER	3	–
ICU	12	16
Mean no. of days Catheter remained in place	9.2	11.4

Among this series of forty patients with EVDs, three patients (15%) had an EVD-associated CSF infection in the control non-AIC group. Only one case (5%) in AIC group had positive CSF culture. Cultures were obtained on day 10, 12 & 14 respectively. Organisms responsible Included Coagulase negative staphylococci (n=2), Acinetobacter (n=1) and Staphylococci epidermidis (n=1).

There were three positive cultures of ventricular catheter tips not associated with CSF infection in the control non-AIC group. The organisms cultured were Coagulase negative staphylococci (n=2), Staphylococci epidermidis (n=1). AIC group showed a significant low infection rate compared to the uncoated one ($p < 0.037$). Table (2) shows the organisms isolated from CSF and ventricular catheter tips cultures.

Table (2): Organisms isolated from cultures.

	Control	AIVC
• From CSF:	Coagulase negative staphylococci Acinetobacter Staphylococci epidermidis	Coagulase negative staphylococci
• From ventricular catheter tips:	Coagulase negative staphylococci Staphylococci epidermidis	–

Discussion

Cerebrospinal fluid infection is a common sequale after the insertion of external ventricular drains. Prophylactic removal & replacement of a catheter after few days of placement was the idea mentioned in several studies. It was first suggested by Mayhall et al. [8]. He examined 172 patients and mentioned that there is a statistically significant risk for Catheter infection if the ventricular catheter remained more than 5 days insitu. That was challenged by Medical College of Virginia's retrospective research which included 611 patients with head injuries, the study stated that the rate of infection did not decrease in the patients whose catheters were exchanged prior to 5 days than those whose had the exchange at more than 5-day intervals, thus no benefit was achieved from prophylactic catheter exchange [9]. That was agreed by a study from Hong Kong which conducted a randomized study on 103 patients needed EVD placement for more than 5 days, the study revealed that infection rate did not show difference between patients who had catheter removal and exchange every 5 days and those that did not [10].

In our study we used a different strategy to overcome the increased risk of the infection occurred with the insertion of EVD. We assessed the efficacy of EVD catheters impregnated with Clindamycin and rifampin compared to the standard non-impregnated catheters for the prevention of catheter-related infections without exchanging the catheters every several days to avoid bacterial colonization on it. In our research, external ventricular catheters in both groups used for the means of ICP monitoring and controlling the elevated pressure by draining cerebrospinal fluid.

Our study which was conducted on 40 patients, demonstrated that AIC was associated with lower rate of CSF infection than the standard one. Three patients (15%) had an EVD-associated CSF infection in the control non-AIC group. Only one case (5%) in AIC group had CSF infection. There were three positive cultures of tips of the ventricular catheter without evidence of CSF infection in the control non-AIC group.

George et al., [11] in his series which enrolled 184 patients, he mentioned that antibiotic impregnated catheter coupled with systemic antibiotics could prevent colonization. Among the patients whom were randomly assigned to receive both antibiotic impregnated catheters and conventional ones, four CSF infections were found, one was in the AIC group (1%) and three were in the conventional group (3%). Seven positive ventricular catheter tips cultures without evidence of CSF infection were reported. Two of them were in the AIC group and five were in the non-AIC conventional group.

Xiang et al., [12] demonstrated in his research that the rates of CSF infection were 3.6% in AIC patients and 13.7% in the standard catheters patients. A significantly lowered rate of catheter bacterial colonization was noticed for antimicrobial-impregnated catheters. That agrees with our results which indicated that AIC group showed a significant low infection rate compared to the uncoated one. Another study from Italy performed by Tamburrini et al., [13,14] mentioned that positive CSF cultures rates were significantly lower in the patients treated with AIC compared to patients treated with the uncoated catheters (2.1% vs. 31.8%).

We detected the Organisms responsible for Catheter related infection in our study, for CSF infection the list included Coagulase negative staphylococci, Acinetobacter and Staphylococci epidermidis but for catheter tip infection, Coagulase negative staphylococci, Staphylococci epidermidis were isolated.

In other studies, as the one done by Margaret et al., [15] organisms isolated were coagulase negative staphylococci, staphylococci epidermidis, Acinetobacter and Serratia isolated in the CSF. Organisms cultured from ventricular catheter tips included coagulase negative staphylococci, methicillin resistant Staphylococcus aureus (MRSA), diphtheroid and Acinetobacter.

In George et al., [16] study the mean number of days Catheter remained insitu were 10 days for both groups, in our research it was 9.2 for non-AIC group and 11.4 for AIC group. There were no

differences in CSF infection rates related to duration of catheter placement among the groups.

Several studies including our series revealed that there is a relationship between using AIC and reduction of positive CSF cultures. This fact forms an argument for using the antibiotic impregnated catheters especially these catheters are available, and are equivalent to the local antibiotic prophylaxis.

Conclusion:

Antibiotic-impregnated catheters with a combination of Clindamycin & rifampin appears to be safe and effective in decreasing the risk of the infectious complications associated with the EVD placement.

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فعالية قساطر البطين الخارجى المشبعة بمضادات الميكروبات: تجربة مستقبلية عشوائية محكمة

يرتبط إدخال البطين الخارجى بخطر كبير للإصابة بالتهاب السائل النخاع الشوكى وهو مهدد للحياة. تحدث العدوى عندما تستعمر الكائنات الحية الدقيقة على طول سطح القسطرة.

الهدف من هذه الدراسة هو مقارنة سلامة وفعالية القساطر المشربة مع كليندامايسين وريفامبين مع قسطرة التحكم القياسية للوقاية من العدوى المرتبطة القسطرة.

أجريت هذه الدراسة الإستطلاعية على أربعين مريضا. تم تعيينهم بشكل عشوائى للخضوع لوضع قسطة مشربة مع كليندامايسين وريفامبين أو قسطة غير مشربة قياسية (مجموعة المراقبة). تضم كل مجموعة عشرين مريضا. كانت قسطة السيليكون القياسية هى المستخدمة فى كلا الأفواج. تم إستبعاد المرضى الذين تم تشخيصهم بعدوى السائل النخاع الشوكى أو مشتبه بها من هذه الدراسة. تم الحصول على تعداد الخلايا الأولية والمسحات من السائل النخاع الشوكى، وتكررت على فترات (٧٢ ساعة) وفى وقت إزالة القسطرة. تم تقييم معدل الإصابة السائل النخاع الشوكى ونتائج السريرية فى كلا المجموعتين.

أظهرت النتائج من بين هذه السلسلة من المرضى الأربعين، كان ثلاثة منهم مصابين بالعدوى السائل النخاع الشوكى فى المجموعة الضابطة مما أعطى معدل الإصابة ضمن هذه المجموعة من ١٥٪ لكل مريض. حالة واحدة فقط فى مجموعة القسطرة المشبعة بالمضادات الحيوية كان لديها عدوى السائل النخاع الشوكى.

وقد إستنتجنا أن القسطرة المشربة مع مجموعة المضادات الحيوية من كليندامايسين وريفامبين تكون آمنة وفعالة فى الحد من مخاطر المضاعفات المعدية المرتبطة بوضع قسطة البطين الخارجى.