Evaluation of antibiotic-impregnated shunt catheters in prevention of shunt infections: a systematic review

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Abstract

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Background: Cerebrospinal fluid (CSF) shunts remain among the most failure-prone life-sustaining medical devices implanted in modern medical practice, with failure rates of 30–40% at 1 year and approximately 50% at 2 years in pediatric patients. **Aim of the Work:** To study the effectiveness of antimicrobial impregnated catheters in preventing shunt and EVD infections and the impact of antibiotic impregnated catheters on mortality, and prevention colonization. **Methods:** The PubMed and Scopus databases were searched. Catheter implantation was classified as either shunting (mainly ventriculoperitoneal shunting) or ventricular drainage (mainly external [EVD]). Studies evaluating antibioticimpregnated catheters (AICs), silver-coated catheters (SCCs), and hydrogel-coated catheters (HCCs) were included. A random effects model meta-analysis was performed. **Results:** Thirty-six studies (7 randomized and 29 nonrandomized, 16,796 procedures) were included. The majority of data derive from studies on the effectiveness of AICs, followed by studies on the effectiveness of SCCs. Statistical heterogeneity was observed in several analyses. Antimicrobial shunt catheters (AICs, SCCs) were associated with lower risk for CSF catheter-associated infections than conventional catheters (CCs) (RR 0.44, 95% CI 0.35-0.56). Fewer infections developed in the patients treated with antimicrobial catheters regardless of randomization, number of participating centers, funding, shunting or ventricular drainage, definition of infections, de novo implantation, and rate of infections in the study. There was no difference regarding gram-positive bacteria, all staphylococci, coagulase-negative streptococci, and Staphylococcus aureus, when analyzed separately. On the contrary, the risk for methicillin-resistant S. aureus (MRSA, RR 2.64, 95% CI 1.26-5.51), nonstaphylococcal (RR 1.75, 95% CI 1.22-2.52), and gram-negative bacterial (RR 2.13, 95% CI 1.33-3.43) infections increased with antimicrobial shunt catheters. **Conclusion:** The use of antimicrobial shunt catheters reduces the risk for CSF infections in patients with hydrocephalus. Several subgroup analyses showed that factors related to study design, type of catheter, duration of catheter placement, and whether the procedure is a de novo implantation or a revision may affect this risk. Publication bias in the region of small negative trials was also observed.

Key words: antibiotic-impregnated shunt catheters, shunt infections

Introduction

Cerebrospinal fluid (CSF) shunting is a commonly used surgical procedure for the treatment of hydrocephalus. Infections are among the most common complications following shunt implantation occurring in 5% to 15% of procedures and they have been associated with increased morbidity; including lower intellectual ability, higher number of revision surgeries, prolonged hospitalization, and higher cost [1,2,3].

In addition, CSF shunt infections were identified as predictors of mortality, which in such cases ranges from 1.5% to 22% in individual studies [2].

The risk factors for shunt infections were younger age; including neonatal period and age less than 6 months, prematurity, and postoperative CSF leakage. The identified risk factors of shunt and or external ventricular drains (EVDs) are previous shunt insertion, duration of ventriculostomy for more than 5 days, previous craniotomy, and the etiology of hydrocephalus; including intraventricular and subarachnoid hemorrhage [2,3].

Several efforts have been made to reduce the incidence of shunt and EVD infections.

The development of antimicrobial-impregnated and -coated catheters (antimicrobial catheters) including antibiotic-impregnated catheters (AICs), silver-coated catheters (SCCs), and hydrogel-coated catheters (HCCs) has been among the most promising advances in this field. the effectiveness of antimicrobial catheters in reducing CSF catheter implantation infections remains controversial [4,5,6,7,8].

Additional topics in debate are whether antimicrobial catheters reduce the risk of infection in lower risk populations like adults, their impact on mortality, and whether they prevent colonization.

Aim of the work

To study the effectiveness of antimicrobial impregnated catheters in preventing shunt and EVD infections and the impact of antibiotic impregnated catheters on mortality, and prevention colonization.

Systematic review

Object

The aim of this study was to evaluate the effectiveness of antimicrobial-impregnated and -coated shunt catheters (antimicrobial catheters) in reducing the risk of infection in patients undergoing CSF shunting or ventricular drainage.

Methods Search Strategy, Study Selection, and data extraction

Systematic search of the PubMed and Scopus electronic databases using the following search terms: “antibiotic OR antimicrobial AND (cerebrospinal fluid OR ventriculo-peritoneal OR external ventricular drainage) AND (shunt OR catheter) AND infection.” Additional searches were performed with the keywords: “antibiotic AND shunt”, “external AND ventricular AND drainage”, “silver AND shunt”, “silver AND CSF”, “hydrogel AND shunt”, “hydrogel AND CSF”. We also reviewed the references of the primarily retrieved studies to identify additional potentially eligible studies.

A study was eligible for inclusion in the systematic review if it met the following criteria:, it provided comparative data regarding the development of infection or mortality in patients with any type of antimicrobial and conventional CSF shunt catheters, It was published in a peer- reviewed journal , It was written in the English language., Both primary insertion and revision procedures were considered eligible surgical interventions. , Randomized controlled trials (RCTs) and nonrandomized studies in adults, children, infants, or neonates were eligible.

A study was excluded if: 1) No control group was defined, 2) It was a case report or included fewer than 10 patients, 3) It was considered part of a bigger study (multiple publications).

The extracted data included study design, geographic region, type of catheters, duration of follow-up period, funding, population characteristics, type of neurosurgical procedure, and outcomes (infection, mortality).

Results

Characteristics of the included Studies

We identified a total of 36 studies that evaluated 16,796 procedures eligible for systematic review [9-10-11-12-13-14-15-16-17-18-19-20-21-22-23-24-25-26-27-28].

The main characteristics of included studies are presented in Table 1. Twenty nine studies were nonrandomized (19 retrospective and 10 prospective) and evaluated 15,335 procedures; 7 were randomized and evaluated 1461 procedures. There were 27 single-center studies and 9 multicenter studies. Eighteen studies were conducted in Europe, 9 studies in the US, 2 in Africa, 1 in Canada, 1 in Asia, 1 in Australia, and 1 in NewZealand. Three studies were international. Eleven studies were funded either by the manufacturer of the catheter or an independent source.

In 22 studies, a positive culture was considered definitive for shunt infection while in 13 studies the diagnosis of infection was based on the presence of symptoms, signs of infection, laboratory findings in CSF and/or blood, and positive cultures. One study did not provide a definition for CSF shunt infection. The populations across and within the studies were characterized by heterogeneity regarding the proportion of the causes of hydrocephalus and the risk factors for shunt infection.

Prevention of infections

The systematic review showed that the use of antimicrobial shunt catheters, was associated with lower risk for infection when compared with CCs (15,949 procedures,) [9-10-12-13-14-15-16-17-18-19-20-21-22-23-24-25-26-27].

Fewer CSF infections developed in the antimicrobial catheter group regardless of randomization, number of participating centers, funding (by the manufacturer or independent sources), shunting or ventricular drainage placement of the catheter, population age, definition of infections, and rate of infections in the study.

The risk of infection was lower in de novo placement but not in revision surgery.

There was no difference regarding gram-positive, staphylococcal, coagulase- negative streptococci (CoNS), and Staphylococcus aureus infections, separately.

On the contrary, the risk for methicillin-resistant S. aureus (MRSA) infection was higher with antimicrobial catheters than CCs.

Finally, patients treated with antimicrobial catheters had a higher risk for infection due to gram-negative bacteria and nonstaphylococcal species (data for a more detailed analysis according to specific pathogens were not available).

Antibiotic-impregnated catheters

Lower risk for infection was observed when AICs were compared with CCs for all types of CSF catheter implantation [12-13-14-15-16-17-18-19-20-21-22-23-24-25-33-27-28-29-32-33].

Subgroup analyses showed that AICs were associated with lower risk for infections regardless of randomization, number of participating centers in the study, funding (by the manufacturer or independent sources), shunting or ventricular drainage, early-onset infections in permanent shunting, age of studied population, definition of infection, de novo catheter implantation, and rate of infection in the participating center(s).

AICs were not associated with fewer infections in revision surgery in any type of implantation or late onset infections in permanent shunting.

Finally, no difference was observed when rifampin-minocyclin impregnated catheters were compared with rifampin-clindamycin impregnated catheters.

No difference was observed in risk for infections due to Staphylococcus spp. (regardless of the type of shunting), CoNS, S. aureus, or gram-positive bacteria, but the risk was higher for infection due to gram-negative bacteria, nonstaphylococcal species, and MRSA.

Silver-coated and hydrogel-coated catheters

Data regarding the comparative effectiveness of SCCs and CCs were available only for ventricular drainage catheter placement SCCs were associated with lower risk for infection compared with CCs [25-2934-36-37].

The difference was significant in the single multicenter, randomized trial but not in the analysis of 4 single-center, non-randomized studies.

SCCs were associated with lower risk for infection in nonfunded studies and in center(s) with a high rate of infection (> 10%), but no difference was found between SCCs and CCs with regard to population age, definition of infection, low rate of infection < 10%, or microbial etiology.

Two multi center studies (a randomized trial involving adults and a prospective cohort study involving children) evaluated HCCs compared with CCs for the prevention of shunt infections[12-28]. HCCs were not associated with fewer infections than CCs (689 procedures).

Silver-coated versus antibiotic-impregnated catheters SCCs were compared with AICs for ventricular drain- age in 2 studies (a randomized trial involving adults and a prospective cohort involving children and adults) [26-37].

No difference in the risk for infection was observed in either of these studies.

Mortality

Eleven studies provided data for all-cause mortality (1910 patients);[9-24-25-29-30-34-35-35-38-39].

8 studied AICs and 3 studied SCCs, all in comparison with CCs.

No data for mortality was available for HCCs.

When all types of antimicrobial catheters were compared with CCs, no difference was observed in all-cause mortality.

No difference in mortality was seen for AICs compared with CCs for ventricular drainage or shunting and no difference in mortality was seen for SCCs compared with CCs in ventricular drainage.

Table (1): Characteristics of studies included in systematic review

							Definitions of Infection				
Authors & Year	Study Design	Region, Study Period or Duration	Population, Age (mean/range)	Type of Implantation: Type of Catheters	No. of Procedures/ Patients	Funding*	Symptoms, Signs, or Other Laboratory Exams	Cultures	Primary Outcome	Frequency of Infection in Both Arms	Follow-Up Duration
Kandasamy et al., 2011	MC, prospective cohort	Europe, NR	Children <16 yrs	S: AICs,‡ CCs	2544/NR	None	+	+	CSF S infection	7.27%	5–47 mos
Kaufmann et al., 2004	MC, RCT	Canada, NR	Adults, >18 yrs	VD: HCC, CCs¶	NR/158	Funded	–	+	CSF VD infection	8.22%	NR
Keong et al., 2012	MC, DB RCT	Europe, Jun 2005–Sep 2009	Adults, 18–84 yrs	VD: SCCs, CCs	278/278	None	+	+	CSF VD infection	16.90%	NR
Kestle et al., 2011	MC, prospective cohort	International, Jun 2007–Feb 2009	Children	S: HCC, CCs	531/NR	Funded	+	+	CSF S infection	7.72%	6–12 mos
Lackner et al., 2008	SC, prospective cohort	Europe, Jun 2006–Jan 2007	Adults, >18 yrs	VD: SCCs, CCs	NR/39	Funded	–	+	CSF VD infection	12.82%	NR
Lajcak et al., 2013	SC, retrospective cohort	Europe, Jan 2006–Dec 2008	Children & adults, 1–89 yrs	VD: SCCs, CCs	402/402	None	–	+	CSF VD infection	7.21%	NR
Lane et al., 2014	SC, retrospective cohort	Africa, NR	Children, 11.3 mos	S: AICs,‡ CCs	160/160	Funded	+	+	CSF S failure (death, revision or removal of shunt)	9.37%	7.6 mos, 113 patients
Lemcke et al., 2012	SC, prospective cohort	Europe, Jul 2003–Jun 2006	Children & adults, 53.6 yrs/12–84 yrs	VD: AICs,‡ SCCs, CCs	96/95	None	–	+	CSF VD infection	10.41%	19 days
Mikhaylov et al., 2014	SC, retrospective cohort	US, Jul 2007–Jul 2009	Adults	VD: AICs,‡ CCs	145/145	None	–	+	CSF VD infection	6.89%	NR
Muttaiyah et al., 2010	SC, prospective cohort	New Zealand, Jul 2005–Aug 2007	Children & adults, 1 mo–87 yrs	VD: AICs,‡ CCs	144/120	None	–	+	CSF VD infection	8.33%	NR
Parker et al., 2009	SC, retrospective cohort	US, Jan 1997–Dec 2007	Children & adults, 6.5 yrs/1 day–20 yrs	S: AICs,‡ CCs	1072/NR	None	–	+	CSF S infection	7.46%	AICs (34.6 mos), CCs (72.3 mos)
Pattavilakom et al., 2007	SC, prospective cohort	Australia, Jul 1995–Jun 2005	Children & adults	S: AICs,‡ CCs	794/NR	None	+	+	CSF S infection	4.91%	15 mos/6–42 mos/min 6 mos
Pople et al., 2012	MC, RCT	International, Nov 2004–Sep 2010	Adults, >18 yrs	VD: AICs,‡ CCs	357/357	Funded	+	+	CSF VD infection	19.6%	NR
Abla et al., 2011	SC, prospective cohort	US, Jan 2007–Jun 2008	Adults, 58.4 yrs/18–89 yrs	VD: AICs†‡	129/129	None	–	+	CSF VD infection	0%	NR
Albanese et al., 2009	SC, retrospective cohort	Europe, Oct 2005–Oct 2007	Adults,§ 61.8 yrs/40–79 yrs	S: AICs,‡ CCs	18/18	None	–	+	CSF S infection	38.8%	Min 12 mos
Aryan et al., 2005	SC, retrospective cohort	US, Apr 2001–Apr 2003	Children, 4.5 yrs/6 mos–17 yrs	S: AICs,‡ CCs¶	78/NR	None	+	+	CSF S infection	10.25%	14–37 mos
Eymann et al., 2009	SC, retrospective cohort	Europe, Jan 2002–Dec 2007	Children, 2 days–100 mos	S: AICs,‡ CCs	56/56	None	–	+	CSF S infection	7.14%	6–75 mos
Eymann et al., 2008	SC, retrospective cohort	Europe, 1998–2006	Adults, 18–88 yrs	S: AICs,‡ CCs	269/269	No	–	+	CSF S infection	1.85%	Min 6 mos
Farber et al., 2011	SC, retrospective cohort	US, 2004–2009	Adults, 60 yrs/21–93 yrs	S: AICs,‡ CCs	500/500	Funded	–	+	CSF S infection	2.6%	12 mos
Fichtner et al., 2010	SC, retrospective cohort	Europe, Jun 2003–Dec 2006	Children & adults, >16 yrs	VD: SCCs, CCs	NR/160	None	–	+	CSF VD infection	3.75%	NR
Govender et al., 2003	SC, RCT	Africa, NR	Children & adults,** 1 mo–72 yrs	S: AICs,‡ CCs	135/110	None	+	+	CSF S infection	9.62%	9–28 mos
Gutiérrez-González et al., 2010	SC, retrospective cohort	Europe, Jan 2004–Oct 2006	Children & adults	S: AICs,‡ CCs VD: AICs,‡ CCs	231/NR	None	–	+	CSF S & VD infection	12.55%	PS Min 90 days TS Min 5 days
Harrop et al., 2010	SC, prospective cohort	US, 2003–2008	Children & adults	VD: AICs,†‡ CCs	1634/NR	None	–	+	CSF VD infection	2.81%	NR
Hayhurst et al., 2008	MC, retrospective cohort	Europe, Jan 2002–Dec 2006	Children, 1 day–18 yrs	S: AICs,‡ CCs	291/215	None	+	+	CSF S infection	9.96%	8–42 mos
James et al., 2014	SC, retrospective cohort	Europe, 14 yrs	Children, 0–17 yrs	S: AICs,‡ CCs	2092/NR	None	+	+	CSF S infection	7.64%	Min 24 mos
Kan & Kestle, 2007	SC, retrospective cohort	US, Jun 2003–Oct 2005	Children	S: AICs,‡ CCs¶	160/129	None	–	+	CSF S infection	6.87%	Min 9 mos, AICs (11.6 mos), CCs (13.8 mos)

(continued)

Authors & Year	Study Design	Region, Study Period or Duration	Population, Age (mean/range)	Type of Implantation: Type of Catheters	No. of Procedures/ Patients	Funding*	Definitions of Infection: Symptoms, Signs, or Other Laboratory Exams	Definitions of Infection: Cultures	Primary Outcome	Frequency of Infection in Both Arms	Follow-Up Duration
Richards et al., 2009	MC, retrospective registry	Europe, NR	Children & adults	S: AICs NR, CCs	1988/NR	Funded	–	–	CSF S infection	3.87%	Min 9 mos
Ritz et al., 2007	SC, retrospective cohort	Europe, 2 yrs	Children & adults	S: AIC,‡ CCs	598/258	None	–	+	CSF S infection	2.50%	NR
Rivero-Garvia et al., 2011	SC, retrospective cohort	Europe, 2000–2006	Children, <16 yrs	VD: AICs,‡ CCs	458/NE	None	–	+	CSF VD infection	3.27%	NR
Steinbok et al., 2010	MC, prospective registry	International, Jan 2006–Jan 2008	Children & adults, 0–84 yrs	S: AICs,‡ CCs	433/433	Funded	+	+	CSF S infection	3.23%	Max 90 days
Tamburrini et al., 2008	SC, prospective cohort	Europe, Nov 2000–Mar 06	Children	VD: AICs,‡ CCs	91/91	None	–	+	CSF VD infection	16.48%	NR
Winkler et al., 2013	SC, RCT	Europe, Feb 2011–Jun 2012	Adults, 56.5 yrs/18–80 yrs	VD: AICs,‡ SCCs	61/40	Funded	+	+	CSF VD Infection	18%	15 days, 3–30 days
Woernle et al., 2011	SC, retrospective cohort	Europe, Aug 2007–Jun 2009	Children & adults,§ 2–89 yrs	VD: AICs,‡ CCs	124/NE	None	–	+	Hemorrhage, infection & malplacement of catheters	11.29%	NR
Wong et al., 2010	SC, RCT	Asia, Apr 2004–Dec 2008	Adults, >18 yrs	VD: AICs,‡ CCs	184/184	Funded	–	+	Nosocomial infections	2.17%	>3 mos
Wright et al., 2013	SC, retrospective cohort	US, Feb 2007–Nov 2008	Adults, 53.8 yrs/>18 yrs	VD: AICs NR, CCs	98/98	Funded	+	+	CSF VD infection	16.32%	NR
Zabramski et al., 2003	MC, RCT	US, Dec 1998–Mar 2001	Adults, >18 yrs	VD: AICs,† CCs	288/288	Funded	–	+	CSF VD infection	5.2%	NR

DB = double-blinded; MC = multicenter; NE = not estimable; NR = not reported; PS = permanent shunting; S = Shunting; SC = single center; TS = temporary shunting, VD = ventricular drainage.
* Any type of funding from the manufacturer of the catheter or any other independent source was included.
† Minocycline/rifampin impregnated.
‡ Clindamycin/rifampin impregnated.
§ Patients with higher risk for infection included.
¶ Presoaked with bacitracin.
** Including 6 HIV patients.

Discussion

This systematic Review sought to investigate the protective effectiveness of antimicrobial catheters in reducing CSF shunting–associated infections in comparison with CCs.

The majority of the included studies (28 studies, approximately 90% of included procedures) evaluated AICs, followed by SCCs; only 2 studies evaluated the effectiveness of HCCs.

Antimicrobial catheters were associated with lower risk for infection compared with CCs regardless of randomization status, number of participating centers, funding, permanent or temporary catheter placement, de novo implantation, population age, timing of infection development, definition of infection, and rate of infections in the individual studies.

Although no difference in the development of infections due to gram-positive bacteria, all staphylococci, CoNS, or S. aureus was observed, anti- microbial shunt catheters were associated with higher risk for MRSA, non-staphylococcal, and gram-negative bacterial infections.

It should be emphasized that only half of the included studies provided data regarding either specific bacterial species or gram-positive and gram-negative status. Since the majority of the studies evaluated the effectiveness of AICs,

The outcomes of the subgroup analyses regarding AICs were similar to that of the primary analysis. In addition, in a sensitivity analysis after the exclusion of studies with large populations (more than 1000 procedures), AICs were still associated with lower risk for infections.

However, AICs were not more effective than CCs in randomized trials and in reducing the occurrence of late infections. Despite the trend toward lower risk for infection with the use of AICs in an analysis with a large sample size, the lack of statistical significance indicates that further studies are required to define the patient populations that would benefit more from this intervention.

The presence of publication bias in the area of small trials with negative results is also an issue that needs to be addressed.

The finding that AICs were not associated with prevention of late-onset infections (developing more than 6 months after catheter placement) in permanent shunting denotes that AICs exert their protective effectiveness during the first months after their implantation. However, it has been noted that early shunt infections account for approximately 70% of all episodes.

Other interventions, and possibly stricter adherence to infection control measures and surgical techniques, are required to reduce the incidence of late-onset infections.

Five studies evaluated the effectiveness of SCCs for ventricular drainage; SCCs were associated with lower risk for infections in all studies and in the single available randomized trial.

Overall, far fewer data were available for SCCs. It is possible that the non–statistically significant lower risk for development of infection in the SCC arm was due to the smaller sample size. However, it is note- worthy that statistical heterogeneity was not observed in these analyses.

Limited data were also available for the comparative effectiveness of SCCs and AICs as well as of AICs with different antibiotics (rifampin/ clindamycin–impregnated vs rifampin/ minocycline–impregnated catheters). Although the antimicrobial spectrum of these combinations is quite similar for gram-positive bacteria, the comparative effectiveness could be evaluated in the future.

There are several concerns regarding the use of antimicrobial shunt catheters. The first is the cost-effectiveness of such an approach, which depends on the incidence of infections in an institution, the infection control measures, the surgical technique and expertise, the cost of catheters, and the cost of treatment of a possible subsequent infection in a given country.

Klimo et al., in a cost-effectiveness analysis of AICs compared with CCs, concluded that the yearly cost savings from the use of AICs ranged from $90,000 to over $1.3 million in the US [40]. In this analysis it was estimated that the total cost to treat a shunt infection accounted for up to $50,000, while the additional cost of AICs compared with CCs was up to $400 per kit. [41]. However, the authors acknowledged that in other countries where the cost to treat an infection is lower, the approach might not be cost-effective.

Limited data regarding the cost of other types of antimicrobial shunt catheters did not allow a cost saving analysis compared with conventional catheters. The second concern is the probability of a shift toward more virulent strains than CoNS.

In this systematic Review, AICs were associated with lower risk for any infection for both CSF shunting and ventricular drainage but higher risk for MRSA, nonstaphylococcal, and gram-negative bacterial infections. A large study performed in children showed that when CCs were used, CoNS were the predominant pathogen, accounting for approximately 52% of isolated pathogens, followed by S. aureus (31.6%), Streptococcus or Enterococcus spp. (8.8%), gram-negative organisms (4.4%), and Propionibacterium acnes (2.2%). When AICs replaced CCs, S. aureus became the predominant pathogen (40%), followed by Streptococcus or Enterococcus spp. (20%), P. acnes and CoNS (both 16%), and gram-negative organisms (4%). [17].

Although we were not able to study in depth the reasons behind this finding, one could assume that this is probably due to inactivity of antibiotics used in AICs against such bacteria. Nosocomial MRSA strains are probably not susceptible to rifampin, minocycline, and clindamycin in most settings, while Pseudomonas aeruginosa strains are definitively not susceptible. Similarly, the susceptibility of Acinetobacter spp. and multidrug-resistant Enterobacteriaceae to the aforementioned antibiotics is expected to be low. This shift toward more virulent pathogens than CoNS is an issue that warrants further study,

Since few of the included studies provided data for these comparisons, especially in settings where the incidence of MRSA or multidrug-resistant gram-negative bacteria is high. In addition, the impact of this shift on mortality should be explored.

The third issue is development of infections in patients who require replacement of catheters. Data regarding development of infections after de novo implantation showed that antimicrobial catheters reduce the risk for infections, but no difference was observed after revision implantation.

Moreover, 1 study showed that patients requiring revision surgery with AICs who had an AIC implanted during the first operation had a higher infection rate (11.7%) than those undergoing primary AIC insertion (1.6%) and those undergoing revision of CCs using AICs (2.5%) [17].

The systematic Review showed no difference in all-cause mortality between patients treated with antimicrobial or conventional shunt catheters. Some might argue that for an infection with considerable mortality, the intervention could not be considered successful. However, we should bear in mind that antimicrobial catheters are used for prevention and not for treatment of infections. Factors such as the primary offending organism (CoNS in CSF shunt infections, which are less virulent than other bacteria), the antibiotics or other antimicrobials used in manufacturing the catheters, rates of mortality (provided in only 11 of the 36 included studies, range 0%–23.3%) and infection (range 0%–38% in the included studies) in the medical center(s) where the study was performed, the time end point used in every study (which ranged from 3 days up to 7 years), and all-cause or infection-related mortality all deserve significant attention. Several systematic reviews in other fields of infectious diseases have failed to show a difference in mortality after the implementation of a preventive measure, despite a significant reduction in infection rate. [36-41-42-43] To our knowledge, 4 systematic reviews have been published thus far [44-45-46-47]. They included patients with ventricular drainage or shunt catheter implantation and concluded that antimicrobial catheters were more effective than CCs in preventing shunt infections. Besides the addition of recently published data, the present analysis out - weighs the former ones for several other reasons. First, it included a greater number of studies (36 compared with 19,[46] 11,[45] 14,[44] and 8[47]) and consequently procedures (almost 17,000 compared with 6171,[46] 1649,[45] 9049,[44] and 2991[150]). It included more randomized trials (7 compared with 3,[46] 1,[15] 1,[48] and 4[47]), thus increasing the quality of its outcomes, and showed that randomized and nonrandomized studies have produced similar outcomes in most of the performed analyses. Several subgroup analyses were performed to study the heterogeneity (either statistically proven or suspected due to the different populations included) and provided support for further studies. The previous systematic reviews studied mainly the effects of age, number of participating centers, gram-positive or gram- negative bacteria, and study design on the development of infections. This systematic review also evaluated the effects of randomization, shunting or ventricular drainage catheter placement, funding, staphylococcal and nonstaphylococcal species, gram-positive and gram-negative bacteria, CoNS, S. aureus and MRSA, timing of infection development, clinical or microbiological diagnosis, the effectiveness of different types of antimicrobial catheters, and rates of infection in the participating centers. However, the majority of the data referred to AICs, and a lot fewer data were available for SCCs and HCCs. Finally, this systematic Review provides a comprehensive review regarding the use of antimicrobial shunt catheters. The most important limitation of the present systematic Reviews is that they included mainly nonrandomized studies. Although residual confounding that could have affected the outcomes of the systematic review of nonrandomized studies cannot be ruled out, the similar findings in the subgroup analyses of randomized (although a marginally nonsignificant difference was observed in AICs probably due to smaller sample size) and nonrandomized studies reduce this possibility. Second, both clinical heterogeneity and statistical heterogeneity were present. Statistical heterogeneity ranged from 0 (no heterogeneity) up to 67% (considerable heterogeneity), even in subgroup analyses. The patients' demographic and clinical characteristics (including age and the etiology of hydrocephalus), the definition of shunt infection, and perioperative prophylaxis varied in the included studies; few of them provided adjusted results and therefore a systematic review of adjusted data were not feasible. Furthermore, ventricular drainage and shunt catheter placements are different surgical interventions that are associated with infections with different microbial etiology. The main cause of shunt-related infections is contamination due to skin flora during surgery, while the main cause of the ventricular drainage–related infections is retrograde colonization of the distal part of the catheter [147]. Nevertheless, subgroup analyses did not show differences in outcomes of ventricular drainage and shunting. Finally, the differences in infection rate among the studies reflect the differences in the definition of shunt-associated infections as well as differences in infection control and surgical techniques or expertise.

Conclusions

Based mainly on data from nonrandomized, single- center, retrospective studies, this systematic review showed that the use of antimicrobial shunt catheters reduce the risk for CSF infections in patients with hydrocephalus. Several subgroup analyses showed that factors related to study design, type of catheter, duration of catheter placement, and whether the procedure is a de novo implantation or a revision may affect this risk.

Publication bias in the region of small negative trials was also observed.

In addition, a higher risk for infections due to more virulent bacteria than CoNS, namely MRSA and gram-negative bacilli, was observed. Due to the small number of studies providing data on such infections in the systematic review, this issue warrants further study. The choice as to whether antimicrobial catheters will be employed in an institution depends on both medical and financial variables.

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