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# Risk factors associated with bacterial growth in derivative systems from cerebrospinal liquid in pediatric patients

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## Abstract

**Objective:** *To determine risk factors associated with bacterial growth in systems derived from cerebrospinal fluid in pediatric patients.* **Methods:** *Case and controls study from January to December 2012, in patients aged < 16 years who were carriers of hydrocephalus and who required placement or replacement of derivative system. Cases were considered as children with cultures with bacterial growth and controls with negative bacterial growth. Inferential statistics with Chi-squared and Mann-Whitney U tests. Association of risk with odds ratio.* **Results:** *We reviewed 746 registries, cases n = 99 (13%) and controls n = 647 (87%). Masculine gender 58 (57%) vs. feminine gender 297 (46%) (p = 0.530). Age of cases: median, five months and controls, one year (p = 0.02). Median weight, 7 vs. 10 kg (p = 0.634). Surgical interventions: median n = 2 (range, 1-8) vs. n = 1 (range, 1-7). Infection rate, 13.2%. Main etiology ductal stenosis, n = 29 (29%) vs. n = 50 (23%) (p = 0.530). Noncommunicating, n = 50 (51%) vs. 396 (61%) (p = 0.456). Predominant microorganisms: enterobacteria, pseudomonas, and enterococcus. Non-use of iodized dressing OR = 2.6 (range, 1.8-4.3), use of connector OR = 6.8 (range, 1.9-24.0), System replacement OR = 2.0 (range, 1.3-3.1), assistant without surgical facemask OR = 9.7 (range, 2.3-42.0).* **Conclusions:** *Being a breastfeeding infant, of low weight, non-application of iodized dressing, use of connector, previous derivation, and lack of adherence to aseptic technique were all factors associated with ependymitis.* (Gac Med Mex. 2015;151:695-701)

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## Introduction

Hydrocephalus is produced when there is an unbalance between generation and resorption, or circulation, of cerebrospinal fluid (CSF), which causes an increase in ventricular size and in the CSF volume within and progressive intracranial hypertension (ICH), which can lead to coma and death[1].

CSF diversions (shunts) are used to decrease intracranial pressure, and are one of the most common neurosurgical procedures: in the United States, more than 40,000 shunts are implanted every year; in Mexico, these data are not available.

Shunt-associated CSF infection is one of the most frequent complications faced by pediatric neurosurgeons[2]. Highly variable incidences, ranging from 1.5 to 41%, have been described in permanent shunts. The incidence per operation is 2.7-14%, although in the latest series it is lower: 4.2-6.2% per patient[3,4,5].

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Different factors have been associated with CSF shunt infection[1]. Factors that increase risk include: the cause of hydrocephalus, age of the patient[5,6], sex, birth weight, weight at the moment of surgery[7], skin characteristics, surgical procedure duration longer than 60 minutes[8], presence of previous shunt systems and leaks after its placement (internal or external fistula). Risk is higher in children younger than 6 months and in preterm newborns. Children are more prone than adults to acquire CSF shunt infections due to several factors, including skin characteristics (less thickness), longer hospital stay, increased skin bacterial concentrations, an immature immune system[9], or more adherent bacterial strains. The rates of infection experienced by children younger than 6 months are usually 2 or 3 times higher than those observed in older children[10].

With regard to the surgical procedure, size of the wound, duration of surgery and surgical technique are referred factors that can increase the risk of infection.

Resident skin flora higher bacterial density, previous state and deficient preparation of the skin, as well as the time elapsed from shaving to incision, exposure of large cutaneous areas during the intervention, bacterial flora of the head and its modification by the use of antibiotics prior to surgery are factors that increase the risk for infection with multidrug-resistant microorganisms. Other important factors that have been referred are: change of gloves[11], multiple replacements, previous valvular system infection, neurosurgeon experience[10], catheter manipulation during the intervention, use of neuroendoscope, previous neurosurgery or associated procedures, number of staff members intervening in the procedure, since the more the unnecessary personnel, the higher the environmental contamination (procedures with more than 3 surgical staff physicians or nurses participating)[8]; time of the surgery, since the first hour scheduled in the operating room is better, and type of surgeries prior to the placement of a CSF shunt system[11,12,13].

With regard to the type of procedure, total replacement and system replacement after infection are those more closely related to infection[8].

In 62-80% of cases[1,14], the infection usually appears within the first month after surgery[15]. In a retrospective study of 840 cases, the mean was 19 days[11], in 90% at 6 months[12], in 28% at between 2 and 12 months, and in 10% after one year. In external ventricular drains (EVD), incidences up to 22% have been reported, although the most usual are 5-16%.

Microorganism isolates vary according to the pathogenesis of infection and the type of shunt. The most common are: *Staphylococcus epidermidis* and *Staphylococcus aureus* in 60-80%[1,11,12]. Gram-negative bacilli (10-25% of cases) are usually nosocomial pathogens or are isolated in devices draining CSF to the peritoneal cavity *(Escherichia coli, Pseudomonas aeruginosa, Enterobacter* spp and *Klebsiella pneumoniae).* Polymicrobial isolates are common (10-18%)[1,12], sometimes with enterobacteria or anaerobic microorganisms (suggestive of hollow viscus perforation by distal catheter)[1]. *Candida* is identified as a causative agent in 1% of these infections[16]. Patients infected with *S. aureus* usually have an early onset (first 15 days post-surgery), whereas those infected by coagulase negative staphylococci have a late onset (more than 15 days)[8].

In external drainages, used in cases of intraventricular hemorrhages, gram-positive cocci are isolated in 25-56%. The rest are gram-negative bacilli, usually nosocomial and multidrug-resistant, isolated in patients admitted to the intensive care unit.

The purpose of the study was to identify risk factors associated with bacterial growth in CSF shunt systems in pediatric patients with hydrocephalus.

## Material and methods

Case-control study in patients assessed from January to December 2012 in a pediatric tertiary care reference hospital.

### *Selection criteria*

Patients younger than 16 years, with cranial computed tomography-confirmed hydrocephalus, who were under the care of the Neurosurgery Department of the UMAE Pediatrics Hospital of the CMNO and who required CSF shunt system placement or replacement were included. Patients with a micoorganism isolated from CSF by means of culture were considered to be cases, and patients without such growth were regarded as controls. Patients with suspected shunt system colonization or infection at enrollment and with data consitent with fever, irritability, food rejection, catheter trajectory erythema, evidence of CSF leak or purulent discharge from the surgical wound were excluded. Patients with lost or incomplete records were eliminated.

### *Study development*

All patients who had had a CSF shunt system placed by the Neurosurgery Department of this hospital, provided they had no evidence of central nervous system

**Table 1. Distribution by age groups and sex of children with cerebrospinal fluid shunt**

| | Cases (n = 99) | Controls (n = 647) | p-value |
|---|---|---|---|
| Gender | | | |
| Male, n (%) | 58 (57) | 297 (46) | 0.530 |
| Female, n (%) | 42 (43) | 350 (54) | |
| Weight in kg, median (range) | 7 (2-56) | 10 (2-58) | 0.634 |
| Age | | | |
| 1-28 days | 18 (18) | 132 (20) | 0.269 |
| 29 days-2 years | 55 (56) | 229 (36) | |
| 2-6 years | 7 (7) | 92 (14) | |
| 6-12 years | 12 (12) | 135 (21) | |
| Older than 12 years | 7 (7) | 59 (9) | |

Proportion differences with the chi-square test, median differences with the Mann Whitney U-test.

prior to the placement or replacement of the device, were identified in the daily census. Once the patient was identified, the medical chart was requested from the medical records deparment of this hospital. Data retrieved from the medical record were fed into an Excel database. Relevant statistical analysis was carried out according to variables' characteristics.

## *CSF culture*

It was carried out by the neurosurgeon using a sterile technique in the operating room at the moment of placement or replacement of the shunt system. An air-tight container was used to carry the sample and was sent to the emergency laboratory for immediate seeding. Tha sample was cultured using chocolate agar medium, with electronic reading performed at 72 hours and serial readings every 24 hours up to a maximum period of 2 weeks.

## *Sample size calculation*

No sample calculation was carried out, since all patients found in the census that met the characteristics for either case or control were included. Nonprobability consecutive sampling.

## *Statistical analysis*

Descriptive analysis for qualitative variables by means of frequencies and percentages. Quantitative variables were analyzed using means and ranges according to the non-symmetric data distribution curve. The chi-square test was used for inferential analysis to assess proportion differences. Inferential statistics with Mann Whitney's U-test was used for median differences. The qualitative variables normality distribution characteristics were analyzed with the Kolmogorov-Smirnoff test. The odds ratio (OR) was calculated to determine the strength of association of factors related to the presence of shunt system infection. The statistical package SPSS, version 20.0 for Windows (Chicago, Ill), was used for data analysis. Statistical significance was considered with a p-value < 0.05.

## *Ethical considerations*

The study was founded on the international investigation regulations established by the declaration of Helsinki of 1975; this protocol was considered without risk for the patient; being a study based on a review medical records, it did not entail any ethical implications and, therefore, it did not require informed consent. The protocol was submitted to the hospital's Local Committee of Research and Ethics in health for review, and was approved under the registry number R-2012-1302-41.

## Results

Ninety-nine (13%) out of 746 patients were identified with positive cultures, whereas 647 (87%) had no germs isolated. Ages ranged from 1 day of life to 16 years. Median age of the group with bacterial growth was 5 months, whereas in the goup without, it was 1 year, with a p-value of 0.25. The age group where the highest risk for having infectious complications was observed was the infants; these data are shown in table 1.

**Table 2. Hydrocephalus etiology by case and control groups in pediatric patients according to bacterial growth**

| | Cases (n = 99) | Controls (n = 647) | p-value |
|---|---|---|---|
| Aqueductal stenosis, n (%) | 29 (29) | 150 (23) | 0.530 |
| Intraventricular hemorrhage, n (%) | 23 (23) | 267 (41) | |
| Arnold Chiari II, n (%) | 20 (20) | 142 (22) | |
| CNS infections, n (%) | 9 (9) | 10 (2) | |
| Posterior fossa tumor, n (%) | 5 (5) | 64 (10) | |
| Trauma, n (%) | 4 (4) | 0 (0) | |
| Brainstem tumor, n (%) | 2 (2) | 14 (2) | |
| Dandy Walker, n (%) | 2 (2) | 0 (0) | |
| Arnold Chiari III, n (%) | 1 (1) | 0 (0) | |
| Hemorrhage due to art. malformation, n (%) | 1 (1) | 0 (0) | |
| Hygroma, n (%) | 1 (1) | 0 (0) | |
| Supratentorial tumor, n (%) | 1 (1) | 0 (0) | |

Proportion differences with the chi-square test.

**Table 3. Hydrocephalus type, time elapsed between shaving and surgery and number of interventions by study groups in pediatric patients with hydrocephalus**

| | Cases (n = 99) | Controls (n = 647) | p-value |
|---|---|---|---|
| Hydrocephalus type | | | |
| Communicating, n (%) | 49 (49) | 233 (36) | 0.456 |
| Non-communicating, n (%) | 50 (51) | 395 (61) | |
| Hygromas, n (%) | 0 (0) | 13 (2) | |
| Other, n (%) | 0 (0) | 6 (1) | |
| Shaving-surgery elapsed time | | | |
| < 6 hours, n (%) | 96 (97) | 634 (98) | 0.590 |
| > 6 hours, n (%) | 3 (3) | 13 (2) | |
| Interventions, median (range) | 2 (1-8) | 1 (1-7) | 0.050 |

Proportion differences with the chi-square test, median differences with the Mann Whitney U-test.

The main hydrocephalus etiology in patients with bacterial growth was aqueductal stenosis, whereas in the control group, it was intraventricular hemorrhage; however, differences were not significant between both groups, as shown in table 2.

Hydrocephalus in both groups was of the non-communicating type; however, there were no significant differences. Time elapsed between shaving and surgery, in most cases, was less than 6 hours with no differences shown between groups, as shown in table 3.

CSF characteristics such as appearance and cellularity are shown in table 4, where differences in both groups are observed, reflecting on statistical difference. We observed higher cellularity in the group of cases, with crystal-clear appearance predominating on both groups. Having a CSF with more than 11 cells entailed an OR of 2.8 (95% CI: 1.65-4.34), and more than 51 cells, an OR of 5 (95% CI: 2.8-9.3).

Among the microorganisms isolated from CSF, skin gram-positive bacteria with 51% and *Enterococcus* with 6% were predominant, followed by gram-negative microorganisms; *Pseudomonas* and enterobacteria with 18 and 17%, respectively, and others less frequently, as shown in table 5.

In the group with bacterial growth, face mask was inadequately worn by the assistant in 77%, whereas in the control group, face mask was correctly worn by the assistant in 99.7%, with the difference being statistically

**Table 4. Cerebrospinal fluid characteristics in pediatric patients according to bacterial growth**

| | Cases (n = 99) | Controls (n = 647) | p-value |
|---|---|---|---|
| Cells found, median (range) | 6 (0-6560) | 3 (0-522) | 0.035 |
| 0-10, n (%) | 58 (57) | 537 (83) | 0.047 |
| 11-50, n (%) | 11 (11) | 71 (11) | |
| 51-250, n (%) | 12 (12) | 32 (5) | |
| > 251, n (%) | 9 (9) | 6 (1) | |
| Appearance | | | |
| Crystal clear, n (%) | 60 (61) | 454 (70) | 0.050 |
| Xanthochromic, n (%) | 18 (18) | 65 (10) | |
| Hemorrhagic, n (%) | 7 (7) | 52 (8) | |
| Turbid, n (%) | 5 (5) | 13 (2) | |
| Not reported, n (%) | 9 (9) | 65 (10) | |

Proportion differences with the chi-square test.

significant ($p < 0.005$) and OR of 97; 95% CI: 23-422. Failure to use wound dressing with iodine after surgery implied 2.6-fold higher risk of infection than when it was used (95% CI: 1.8-4.3). The use of connector during the procedure also implied 6.8-fold higher risk for infection than when not used, as shown in table 6.

## Discussion

CSF shunt infection is one of the most common complications faced by pediatric neurosurgeons[2]. Highly variable variations have been described in permanent shunts, ranging from 1.5 to 41%[3,4,17]. Our study yielded a 13.2% infection rate. Peña et al.[18], in a retrospective study conducted in Chile from 1998 to 2008, reported rates as variable as from 4.1 to up to 50%.

The most common cause of hydrocephalus in Mexico is Chiari's malformation, followed by prematurity-related intraventricular hemorrhage[1,19]. In our study, acqueductal stenosis was documented at first place, followed by Chiari's malformation and then by prematurity hemorrhage, consistent with findings reported by Peña and Fortanelli[20] in a study very similar to ours conducted in our country.

In our study, there were 99 cases, the mean was 32 days, and in 98% of cases it occurred within the first 6 months, which is consistent with reports in the literature.

Isolated microorganisms vary according to the pathogenesis of infection and type of shunt. In our study, most commonly isolated microorganisms were *Staphylococcus epidermidis* and *Staphylococcus aureus,* enterobacteria, *Pseudomonas* and *Enterococcus,* which is consistent with reports in international literature[1,11,12].

**Table 5. Distribution of main microorganisms isolated from CSF in children with CSF shunt**

| Microorganism | No. | % |
|---|---|---|
| Gram-positive | | |
| *S. epidermidis* | 31 | 31.3 |
| *S. haemolyticus* | 2 | 2.0 |
| *S. aureus* | 18 | 18.2 |
| *E. faecium* | 3 | 3.0 |
| *E. faecalis* | 2 | 2.0 |
| *Enterococcus spp* | 1 | 1.0 |
| *S. viridans* | 2 | 2.0 |
| Gram-negative | | |
| *E. coli* | 8 | 8.1 |
| *E. cloacae* | 6 | 6.1 |
| *E. aerogenes* | 1 | 1.0 |
| *Klebsiella pneumoniae* | 1 | 1.0 |
| *Proteus mirabilis* | 1 | 1.0 |
| *Haemophilus spp* | 1 | 1.0 |
| *Pseudomonas aeruginosa* | 18 | 18.2 |

Factors that increase the risk for CSF shunt infection referred in the literature include the cause of hydrocephalus, age of the patient[10,17,21], sex, birth weight and weight at the moment of surgery[7]. In our study, there were statistically significant differences between weight and age of patients in the group of cases, with weight and age being lower with regard to the control group. Infection rates experienced by children younger than 6 months are usually 2 or 3-fold higher than those observed in older children[6]. Our study revealed that being younger than 2 years implied 2.2-fold higher risk for ventricular ependymitis. We found no

**Table 6. Bacterial growth-associated risk factors in cerebrospinal fluid shunts in pediatrics**

| Risk factor | OR | 95% CI |
|---|---|---|
| Time since shaving | 1.4 | 0.40-4.50 |
| Failure to use wound dressing with iodine | 2.6 | 1.80-4.30 |
| No wound dressing | 1.25 | 0.47-3.30 |
| Linear incision | 0.67 | 0.40-1.19 |
| Same incision | 1.68 | 0.83-3.35 |
| Tunnel (relief) | 0.45 | 0.16-1.13 |
| Use of connector | 6.8 | 1.9-24 |
| VP shunt | 2.3 | 0.54-9.8 |
| Non-VP shunt | 0.43 | 0.10-1.84 |
| Type of valve (pellet) | 1.9 | 0.60-5.80 |
| Type of valve (diaphragm) | 0.53 | 0.17-1.65 |
| Washing of the system | 1.26 | 0.58-2.78 |
| Washing with antibiotic | 1.53 | 0.69-3.42 |
| Inadequate prophylaxis | 0.93 | 0.60-1.42 |
| Prophylaxis (cephalotin 50 mg/kg) | 1.08 | 0.61-1.94 |
| Prophylaxis (cefotaxime 50 mg/kg) | 0.98 | 0.46-2.10 |
| Received doses | 1.16 | 0.54-2.50 |
| System replacement | 2 | 1.30-3.10 |
| Replacement of gloves during surgery | 1.2 | 0.72-2.02 |
| Anesthesiologist without face mask | 1.40 | 0.80-2.50 |
| Circulating nurse without face mask | 1.29 | 0.74-2.25 |
| Assistant without face mask | 97 | 23-422 |
| Surgical scrub technician without face mask | 2.65 | 0.50-13.8 |
| Non-closed doors | 0.93 | 0.57-1.53 |
| Not morning surgical shift | 1.18 | 0.73-1.89 |
| Morning shift | 0.85 | 0.53-1.37 |

CI: 95% confidence interval.

significant difference between sexes, consistent with observations reported by Peña and Fortanelli[18,20].

Most experts recommend antimicrobial prophylaxis. The choice of antibiotics will depend on the isolates and their susceptibility; in this study, susceptibility records were not avaiable in the Neurosurgery Department database. Cephalotin or cefotaxime at 50 or 100 mg/kg/day divided in 3 doses was used as first-line prophylactic regimen; however, in the group with isolates, 64% of patients had received it, which did not represent any protection for them. Statistically significant difference was demonstrated between the regimens used in both groups; however, the characteristics of the study do not allow measuring which regimen is more effective in infection prevention. Something similar happened in the Chilean study, where antimocrobial prophylaxis with cefazolin (30 to 50 mg per kg of weight) at the start of the anesthetic procedure was not shown to be a protective factor. There were no differences in the prophylaxis administered to cases and controls, and there were no intensified prophylactic treatments in neither of both groups[18]. This can be explained because the cephalotin dose could have been insufficient, which instead of representing protection, could have promoted microbial flora selection and favor microorganism isolation. It would be useful to consider a study allowing to determine which prophylactic antibiotic regimen is more adequate for our pediatric population based on isolates and culture analyses.

In addition, a multifactorial, more detailed analysis should be pereformed in order to characterize which varibles are likely to have more weight, as well as to identify and separate some factors that might explain this behavior, such as the cases with multiloculated hydrocephalus or recurrent hydrocephalus, which could mask chemoprophylaxis protecting effects.

On the other hand, since the susceptibility patterns of the recorded isolates were not known, the extent of its influence could not be determined, since there could have been antimicrobial multiple resistance, especially in cases that required several shunt system replacements and that were exposed to different antibiotic regimens for shunt system-associated ependymitis.

According to the results of a study carried out in this hospital, in the past few years, micoorganisms of the ESKAPE group, as well as four-monthly reports from the Microbiology Department, methicillin susceptibility for *S. aureus* was 35%, for *S. epidermidis* was 90%, and for *Pseudomonas* there is decreased susceptibility for most antimicrobial groups, including carbapenems[22].

With regard to face mask use by circulating nurses and surgical assistants as a protective or risk factor, there are no previous reports in similar studies, since it is assumed that when being inside the surgical act it should worn by the entire staff.

Several risk factors for infectious complication were identified, with age and weight at the moment of surgery referred to as the most important of all the explored ones, as well as the number of interventions undergone by the patient, the use of connector, operating-room staff not following surgical protocol basic measures, iodized dressing not applied after the event, in addition to inefficacious antibiotic prophylaxis, which show areas of opportunity susceptible to intervention in order to reduce the rate of infection associated with health systems.

The study has important limitations owing to its characteristics; however, the number of patients and surgical events exceeds those reported in a similar study in a pediatric hospital of our country and another 10-year foreign study. However, we consider that a cohort study is required to confirm the reported findings and this way carry out preventive actions that allow for infection rate to be reduced.

In conclusion, infants had the highest risk when ventriculoperitoneal shunting was performed in comparison with older children; the more the number of surgeries, the higher the risk of infection; pleocytosis higher than 10 was associated with the risk of having bacterial growth; however, CSF culture is the gold standard for the diagnosis of ependymitis; non-adherence to asepsis and surgery protocol basic measures by the surgical team is associated with higher risk for bacterial growth. The use of cephalotin or cefotaxime requires further review in a more detailed analysis.

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