Does duration and sampling of external ventricular drainage systems influence infection rate?

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Abstract
External ventricular drainage systems are often necessary in neurological and neurosurgical patients. The purpose of this literature review is to review the problem of external ventricular drain related infections resulting from repeated cerebrospinal fluid sampling and manipulation of the drain systems. The aim is to provide an appropriate improved protocol for care of patients undergoing external ventricular drainage treatment. Routine analysis of cerebrospinal fluid is often performed to diagnose external drainage related bacterial meningitis at an early stage. Nurses are routinely instructed to collect cerebrospinal fluid from ventricular catheters for analysis. Does the way in which sampling occurs relate to increased infection?

This literature review will discuss that prophylactic frequent cerebrospinal fluid sampling is of no benefit and increases infection risk and should be limited. It will also provide evidence that duration of the external ventricular drain (EVD) systems does not correlate with infection and therefore the EVD should stay in situ for as long as clinically needed or be removed if infected.

Key Words: Bacterial meningitis, cerebrospinal fluid sampling, external ventricular drain systems and central nervous system.

Background
External ventricular drainage (EVD) systems are used as temporary measures to provide reliable means of monitoring intracranial pressure (ICP) and controlling hydrocephalus (Arabi, Memish, Balkhy, Francis, Ferayan, Shimemeri & Almuneef, 2005). Hydrocephalus can be a common problem which occurs in neurosurgical patients (Arabi et al, 2005). The risk factors associated with developing external drainage related bacterial meningitis (ED-BM) are duration of drainage and drain related factors such as site leakage or frequent manipulation of the drain (Lopez-Cortes, Marquez-Arbizu, Jiminez-Meijas, Caballero-Granado, Rey-Romero, Polaina & Pachon, 2000). In order to obtain a diagnosis of ED-BM in patients with external drainage systems, routine analysis of cerebrospinal fluid (CSF) is performed. A diagnosis of bacterial meningitis can be made if there is an increased leukocyte count, high protein concentration and low glucose concentration (Shameen, Vinod-Kumar & Neelagund, 2008). It is currently unknown whether CSF analysis can be used to diagnose bacterial meningitis in patients undergoing EVD system usage or whether external factors influence the results. However, studies have found it difficult to make a comparison of the CSF of patients with EVDs, and those without EVDs due to the underlying disease (Blomstedt, 1987).

Micro-biological tests remain the gold standard for diagnosing ED-BM, however it is time consuming compared to leukocyte count and chemical analysis. CSF samples are collected routinely from EVD systems for laboratory tests. There have been several studies conducted that discuss the correlation between sampling and infection rate (Crane & King, 2015). However, there have been few studies conducted to identify the most appropriate site for cerebrospinal fluid collection in order to reduce the disruption of the closed EVD system and reduce the risk of infection. It is also controversial whether regular changes of EVDs can reduce CSF infection (Crane & King, 2015; Wong, 2011).

Discussion: Cerebrospinal Fluid Sampling
To investigate the value of several commonly used parameters for prediction and diagnosis of ED-BM in the literature of Rogier, Schade, Janke, Freet, Roel, Ronald, Gesku, Leo, Marc, Van Dijk, Joan, Voormolen, Hans &
Kuijper, (2006), a cohort study was performed in 230 patients who had EVDs to analyse the predictive and diagnostic value of routine CSF sampling. Daily CSF samples were obtained for analysis and the results have shown that leukocyte count, glucose and protein concentrations in the CSF of EVDs with ED-BM were comparable to those of patients with external drains without ED-BM in both groups. The results of CSF have shown that they were heterogeneous during the period of external drainage (Rogier, et al, 2006). Results of patients with ED-BM during the first days of infection were compared with the results of the control group without ED-BM; there were no statistical significant differences. The results were the same with CSF obtained in patients with ED-BM for the three days preceding an active infection when compared with the control group.

Evidence points out that the CSF contents of patients who have recently undergone neurosurgery are often abnormal (Forgacs, Geyer & Freidberg, 2001). The chemical irritation resulting from the presence of blood products in the CSF leads to chemical or aseptic meningitis and disturbs the glucose and protein concentration in CSF. It also increases CSF white blood cell count (Forgacs, et al, 2001). As the blood is reabsorbed from the CSF and infection subsides, chemical disturbances normalise in patients with EVDs that do not develop bacterial meningitis. Therefore, it is expected that CSF parameters will improve during the period of external drainage in patients who do not develop meningitis (Forgacs, et al, 2001).

When analysing the results for the 200 patients with EVDs who did not have ED-BM as a reference, it was found that only a small proportion of patients who developed ED-BM had abnormal values for one of the commonly analysed CSF parameters shortly before or during the course of ED-BM infection. This led to the conclusion that combining the results for different CSF parameters did not increase the diagnosis value of CSF analysis (Rogier, et al, 2006). However this reference has not fully analysed the predictive value for ED-BM.

Daily analysis of CSF was performed on 130 patients in the literature by Pfisterer, Muhlbauer, Czech & Reinprecht, (2003). The leukocyte count for both control group and patient group was found to be heterogeneous. There was no difference in leukocyte count between the patients with ED-BM and patients without ED-BM. However the literature does not state whether glucose and protein were analysed in the report.

To assess possible causes of risk factors for infection related to external ventricular drainage, a study was carried out by Hoefnagel & Dammers, (2008). The method involved two hundred and twenty eight patients in the period from January 1993 until April 2005 (over a 12 year period). Reviews were collected covering patient information, including disease demographics, external ventricular drain data and infection occurrence. The data was compared and included in a risk analysis study. Results of this study have shown that the mean age was 56 years. Analysis of both sexes has shown equal distribution. Most indications for insertion of EVD systems were for hydrocephalus caused by intraventricular haemorrhage which accounted for 48% of patients. Infection rate was 23.3% and the authors found that duration of the EVD systems was a risk factor for infection. Frequency of CSF sampling was also a risk factor for infection. The results indicate that there was a relatively high percentage of EVD-related infection (Hoefnagel & Dammers, 2008). Limitations to the study included selection bias and some missing values.

However, further analysis supported a relationship between the drain duration and frequency of CSF sampling. The risk for infection increases with the duration of the drain, hence it has been suggested that sampling of CSF should be done less frequently (Schade, Schinkel, Visser, Van Dijk, Voormolen & Kuijper, 2005). These studies lend support for the development of protocols for EVD management to reduce infection.

Discussion: Drain Duration
The most common complication of EVD systems is CSF infection (Kim, Uttley, Bell, Marsh, Moore, 1995). Neurosurgical patients with EVDs are at high risk for developing device related nosocomial infections (Lopez, et al, 2000). The use of closed drainage systems may decrease the rate of infection (Lucey & Myburgh, 2003). Efforts must be made to distinguish clinically relevant CSF infections from contamination and catheter colonisation (Lozier, Sciacca, Romagnoli & Connolly, 2002). Infection may lead to removal and replacement of a new EVD system. Predisposing patient factors associated with high risk of infection include craniotomies, depressed skull fractures, intraventricular haemorrhages, catheter duration, catheter
irrigation, site leaks and frequent sampling of CSF (Korineck, Reina, Boch, Rivera, De Bels & Puybasset, 2005).

Mayhall, Archer, Lamb, Spadora, Baggett, Ward & Narayan (1984), recommend elective revision of external ventricular drainage system on day five post insertion to reduce the risk of infection. However, other larger studies have revealed that the duration of the EVD in a patient has no effect on the risk of infection (Lo, Spelman, Bailey, Cooper, Rosenfeld & Brecknell, 2007). To evaluate the roles of duration a catheter remained inserted and that of multiple catheter insertions in the literature of Lo, et al, (2007), a study was carried out at the Alfred Hospital in Victoria, Australia. Data was obtained for patients who had undergone EVD system placement between the period of October 2002 and May 2004 from the intensive care database. A record was kept for each patient, including age, conscious state, diagnosis, presence or absence of an open skull fracture, diabetes mellitus status and bacteremia within fourteen days of EVD insertion. The outcome measure of death prior to discharge was also recorded.

Results have shown that there were two hundred patients who had EVD systems inserted during this period whilst in the intensive care unit. This group of patients had a mean age of 41 years (ranging from 15-87 years). Seventy-four per cent had traumatic brain injuries; nineteen per cent of these patients had open skull fractures. The remaining patients had presented with spontaneous subarachnoid or intraventricular haemorrhage. None of these patients had a primary diagnosis of intracranial or spinal sepsis or any recorded infection within fourteen days of admission. In these patients, twenty one had nosocomial EVD-associated CSF infections. Five patients had positive cultures for infection in their CSF but no other evidence of infection was considered for colonisation of the EVDs. Diabetes, patient’s age and the presence of a skull fracture did not present any significant risk factors for infection (Lo, et al, 2007).

The literature is conflicting as to whether drain duration increases risk of EVD associated infections (Pfisterer, et al, 2003). This is reported by Sundberg, Kjellquist, Lumberg & Ponte, (1972) and has not changed since that period. They analysed 1586 patients and found that prolonged drain insertion was not a risk factor. Routine changing of EVD catheters after five days did not reduce the risk of CSF infection and did not improve outcome (Winfield, Rosenthal, Kanter & Casella, 1993).

However, the work by Mayhall, et al, (1984) presents a stark contrast to these findings. Despite these disagreements, there has been agreement that EVD-associated CSF infection is often acquired at the time of insertion when skin organisms enter the sterile intracranial compartment (Khanna, Rosenblum, Rock & Malik (1995). Retrograde colonisation may also occur as a result of continued externalisation of the cerebrospinal space during sampling (Khanna, et al, 1995).

Conclusion

Study results have shown that frequent analysis of CSF has no predictive value for ED-BM. Routine chemical analysis of CSF samples to screen patients with EVDs for ED-BM has shown no additional value. The analysis of an isolated CSF sample in a patient in whom ED-BM is suspected also has no additional value due to unclear cut-off levels. This lends support to diagnosis of ED-BM based only on the results of microbiological cultures. It may be worthwhile to reduce the frequency of CSF sampling on patients with EVDs. The risk for infection increases with the duration of the drain, hence it has been suggested that sampling of CSF should be done less frequently.

It has been proven in the literature reviewed that there is a well-established relationship between the duration of EVDs and the occurrence of EVD-related infections. Studies have shown that using standard protocols helps to reduce the rate of infection. Using closed drainage systems may also decrease the rate of infection. Sample size has not been mentioned in the results and this may be a limitation of the literature. Routine CSF sampling should be avoided, unless there is suspicion of infection, in the presence of fever of unknown origin or mental status change. Multiple external drain insertion is associated with an increase in infection rate. This practice should be abandoned. There has not been much change in the technique of EVDs throughout the years, hence earlier literature still applies. From a nurse’s perspective, a standard protocol for clinically managing EVD systems should be established and no routine CSF samples should be undertaken unless necessary. The EVD system should also be handled under strict aseptic practice.
References


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Leptomeningeal Carcinomatosis: Cerebral spinal fluid tumours.

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Abstract
Leptomeningeal Carcinomatosis (LC) is the dissemination of cancer, commonly breast, lung, melanoma, acute lymphoblastic leukaemia and Non-Hodgkin lymphoma occurring through either direct extension from surrounding tumours or metastasis of a preexisting, parenchymal central nervous system tumour. A rise in the diagnosis of leptomeningeal disease has been seen with increased survival rates of cancer due to improved medical treatment, with 5-8% of patients with cancer going on to develop LC.

Leptomeningeal Carcinomatosis spreads to the meninges, the outer covering of the brain and spinal cord, directly migrating into the cerebral spinal fluid (CSF), arachnoid and pia mater. This migration of tumour cells occurs throughout the arachnoid vessels or choroid plexus into the surrounding outer layers extending into the CSF. On entry into the CSF, tumour cells are infiltrated in a diffuse or multifocal manner where the leptomeninges cover the surface of the brain and spinal cord. This covering causes the meninges to become irritated causing patients to exhibit signs of photophobia, neck stiffness, neurological decline and cranial nerve defects. LC has a significant morbidity and mortality rate with a median survival of 4-6 weeks if untreated and 2-3 months if treated. Diagnosis is based on analysis of the cerebral spinal fluid, through detection of positive cytology of LC tumour cells, elevated protein and CSF pressures. Magnetic resonance imaging findings identify areas of meningeal enhancement indicative of meningeal irritation.

The neuroscience nurse role in the patient care includes providing a supportive environment and thorough assessment of vital and neurological signs. Treatment aims to improve or maintain a patient’s neurological status while prolonging survival and palliation. The literature review will highlight the diagnosis, progression and treatment for LC to further increase awareness and inform neuroscience nurses of increasing trends in management.

Key Words: Leptomeningeal carcinomatosis, meninges, cerebral spinal fluid, tumour.

Introduction
Leptomeningial carcinomatosis (LC) was first identified in the 1870 by Ebert in a patient with lung cancer, and was named in 1902 by Sieffert as meningitis carcinomatosa (Schiff, Kesari & Wen, 2008). Sixteen thousand patients globally will be diagnosed with LC each year (Abrey, 2002). There has been a significant rise in the incidence of LC since 1970, thought to be due to improvements in the diagnostic techniques and neuro imaging available in today’s healthcare system (Schiff, Kesari & Wen, 2008). The rise in diagnosis is the direct result of patients surviving their primary cancer. Hence there is a need for health professionals to be aware of LC and the clinical presentation, in order to provide appropriate care and interventions along with the potential for future research and cure.

Currently epidemiological studies suggest that 3-8% of patient with solid tumours will develop leptomeningeal metastasis (LM) throughout their illness (Abrey, 2002). Twenty per cent of patients are diagnosed on autopsy. These are patients undiagnosed and asymptomatic (Le Rhun, Taillibert & Chamberlain, 2013). It was determined that the rise in diagnosis is due to increased survival rates of cancer as a result of improved medical treatment. All cancers have the potential to metastasise into the meninges causing LM. The leading primary cancers associated with LM include lung cancer (10-26%), melanoma (5-25%), gastrointestinal (4-14%), cancer of unknown primary (1-7%) and breast cancer (12-35%) (Le Rhun et al 2013).
The brain and spinal cord are surrounded by three membranes referred to as the meninges, composed of the dura mater being the pachymeninges, arachnoid mater and pia mater referred to as the leptomeninges. The space between is referred to as the subarachnoid space, containing the CSF and the Circle of Willis providing arterial blood supply. Approximately 140ml of cerebral spinal fluid surround the brain and spinal cord at any one time, replenishing approximately five times a day (Hickey, 2014). CSF is produced in the choroid plexus of the third, fourth and lateral ventricles. Tumours cells gain entry into the CSF and subarachnoid space by metastatic seeding. Entry is gained by hematogenous spread to the choroid plexus onto the leptomeninges, primary hematogenous metastasis through leptomeningeal vessels, metastasis from the Batson venous plexus, retrograde dissemination, centripetal extension or direct extension from contiguous tumour deposits (Gleissner & Chamberlain, 2006; Le Rhun et al 2013). Once tumour cells have invaded the leptomeninges, the flow of CSF causes the seeding and infiltration of tumour cells in a diffuse and multifocal manner (Le Rhun et al 2013). Greatest infiltration occurs in the basal cisterns and dorsal surface of the spinal cord and cauda equina.

Case Study

Patient X presented to hospital with increased confusion, ataxia and lower limb mild weakness. Histology included breast cancer where a left mastectomy and lymph node clearance was completed in the 14 months prior to diagnosis. Symptoms of leptomeningeal metastases are caused by pressure from the metastases placed on the nerves that run across the meninges in both the head and the spine. This includes those running from the spinal cord out to the body, and is dependent on the location of the metastases. Symptoms that occur simultaneously in both the head and the spine suggest a diagnosis of leptomeningeal metastases (LM). Leptomeningeal metastases can also cause hydrocephalus, a condition that occurs when the metastatic cancer interferes with the flow of cerebrospinal fluid around the brain. As the spinal fluid continues to be produced, an increase in the intracranial pressure is then seen as the arachnoid villi are no longer able to effectively reabsorb the CSF.

Clinical presentation occurs in a pleomorphic and multifocal manner with neurological signs and symptoms emerging over days to weeks. Symptoms correlate to the region of malignant cell infiltration in the central nervous system (CNS). The clinical manifestation of LM can be caused by several different pathophysiological mechanisms and can be characterised into the following main categories:

- cerebral hemisphere dysfunction causing a mass effect due to the invasion of the leptomeninges and associated inflammation thus a raised intracranial pressure (ICP) and occlusion of CSF flow occurs.
- cranial nerve and spinal cord symptoms: Through direct involvement of the tumour.

A recent study described the signs and symptoms of 150 patients with solid tumour LM (Clarke, Perez, Jacks, Panageas & DeAngelis, 2010; Clarke 2012; Demopoulos & Brown, 2014). Between 30-50% of patients describe headache as their initial symptoms (see Table 1). Headaches can be associated with raised ICP or meningeal irritation resulting in neck stiffness and pain, along with signs of nuchal rigidity. Headaches occurring due to a raised ICP are known to be associated with nausea, vomiting and dizziness.

| Table 1 (Above): Initial symptoms of LM as reported by patients. |
These symptoms commonly occur in wave patterns caused by changes in position due to arachnoid villi failing to reabsorb CSF thus resulting in hydrocephalus. Altered mental status accounts for 11% of presenting symptoms with confusion, forgetfulness, disorientation, lethargy or personality changes the most common. These changes in mental state are referred to as an encephalopathy, the result of hydrocephalus, seizure activity, cerebral dysfunction or a combination of those. When cranial nerves are directly invaded by malignant cells within the subarachnoid space, cranial neuropathy occurs. The first intervention in diagnosis is a lumbar puncture to obtain a CSF specimen. Malignant cells are detected in 70-89% of CSF specimens (Le Rhun et al, 2013). Repeated samples are often necessary as only 50% of patients with LM on initial lumbar puncture exhibit positive cytology. Patients are 25% more likely to have positive cytology on second lumbar puncture. Multiple lumbar punctures are often required due to the meningeal dissemination, where tumour cells are localised in the brain rather than the spinal cord hence movement of CSF must occur in order to obtain a positive sample. Therefore negative CSF cytology is directly related to the flow of malignant cells within the spinal cord CSF when lumbar punctures are taken.

Clinical finding on CSF analysis includes, an elevated opening pressure of > 200mm Hg in 57% of patients, decreased glucose concentration, high protein concentration, lymphocytic pleocytosis and a positive cytology for malignant cells (Chamberlain, 2008; Drappatz & Batchelor, 2007; Palma, Fernandez-Torron, Estève-Belloc, Fontes-Vilalta, Hernandez, Fernandez-Hidalgo, Gallego Pérez-Larraya & Martinez-Vila, 2013). A positive MRI assessment of an undiagnosed patient includes a whole CNS scan where a complete neuraxis and A T1 C+ gadolinium enhancement is completed in order to obtain the primary diagnosis (Drappatz & Batchelor, 2007).

Typical findings include a thin diffused enhancement along the contours of the gyri and sulci with multiple nodular deposits in the subarachnoid space in 30-50% of cases (Le Rhun et al, 2013). LM enhancement can be found in cerebellar folia, cortical surface, basal cisterns and ventral surface along the brainstem, indicating abnormal thickening and enhancement. However these are not the most common sites of LM. Between 15-25% of patients present with spinal enhancement, showing linear or nodular enhancement along the spinal cord or cauda equina where clumping of nerve roots can be seen (Le Rhun et al, 2013). CT is an uncommon practice due to poor diagnostic value, with significantly reduced sensitivities of 23-38% when compared with the MRI.

**Prognosis**

The overall prognosis for a patient with LM is poor; patients have an expected survival rate of 4-6 weeks if untreated and 4-6 months if treated. Research indicated that 14% of LM cases occur as a result of an advanced primary breast cancer with no well-established prognostic makers for patients with LM other than the presence of malignant cells within the CSF and low performance in Karnofsky performance status scale (Palma, et al 2013).

**Treatment**

Due to current poor prognostic outcomes, treatment aims to reduce mortality through improving and stabilising the patient’s neurological status, while maintaining neurological quality of life (Gleissner & Chamberlain, 2006). Current treatment plans are comprised of intrathecal or systemic chemotheraphy and focal radiation therapy with the goal to reduce size of tumours and growth. Statistically 20% of patients who receive treatment will respond (Demopoulos & Brown, 2014; Palma et al, 2013). Suitable patients will undergo insertion of a ventriculo-peritoneal shunt to alleviate hydrocephalus symptoms.

Chemotherapy is the only treatment which allows for simultaneous treatment of the brain and spinal cord. Intrathecal administration is defined as injecting chemotherapy into a cerebral access device inserted surgically or via repeated lumbar punctures (Demopoulos & Brown, 2014). Intrathecal administration allows for an even distribution throughout the subarachnoid space and is not required to cross the blood brain barrier (Drappatz & Batchelor, 2007). Access devices avoid the risk of epidural or subdural hematomas. Methotrexate and thiopeta are the most effective chemotherapies in the treatment of LM patients with metastasis from primary breast cancer (Demopoulos & Brown, 2014; Drappatz & Batchelor, 2007). Chemotherapy is administered initially twice weekly for three weeks then weekly for four week followed by monthly (Demopoulos & Brown 2014).

Radiation therapy involves field radiotherapy...
to symptomatic sites of the disease, bulky disease and sites where CSF flow is obstructed. The aim is to shrink tumour cells, stabilise neurological symptoms, establish disease and sites where CSF flow is obstructed at symptomatic sites of the disease, bulky aperients.

A high fibre diet, adequate oral intake and neck is bent forwards (Demopoulos, 2014). When the spine to the tips of the feet, when the therapy is currently the choice of treatment. CSF flow (Demopoulos, 2014). Combination tumours and assisting in the restoration of radiation therapy is better at treating large bulky skin tension and Lhermitte’s sign - an electrical signal running from the back of the cervical spine to the tips of the feet, when the neck is bent forwards (Demopoulos, 2014).

When selecting patient treatment options, chemotherapy or radiation therapy is considered and each play a significant role in the treatment of LM. Research indicates that intra CSF chemotherapy is better on smaller LC tumours due to the thickness of cells and diffusion capacity (Demopoulos, 2014). Radiation therapy is better at treating large bulky tumours and assisting in the restoration of CSF flow (Demopoulos, 2014). Combination therapy is currently the choice of treatment.

Nurse’s Role
When nursing a patient with LM the holistic approach is essential due to the array of symptoms a patient can display. Leg weakness and difficulty walking are common symptoms, thus ongoing assessment of mobility status including the need for walking aids, wheelchairs or hoisting devices. Referral to an occupational therapist before discharge is also important. Regular speech and swallowing assessments should be performed, as LM can increase the risk of aspiration as cranial nerve deficits impair the ability to chew and swallow. Constipation is a significant issue for LM patients as decreased mobility, pain medications and chemotherapy contribute to constipation (Drappatz & Batchelor, 2007). Nursing staff should commence a bowel regime including a high fibre diet, adequate oral intake and aperients.

Conclusion
As health professionals, it is important to note that in 3-8 % of patients with solid tumours, the chance of developing LM is a real consideration. In Patient X’s case, due to a delayed diagnosis and intervention, prognosis and outcome was poor.

MRI and lumbar puncture allows for earlier diagnosis and intervention, while chemotherapy and radiation therapy improve longevity and quality of life. Nurses are critical to the care of the LM patient. An understanding of the disease process and care required will ensure quality of life during the progression of the disease. With cancers increasing in today’s society and certain treatments readily available, health professionals will have an increased awareness of LM, therefore with the ability to identify and treat earlier.

Reference List