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Original Article

Is Shunt Location a Risk Factor for the Development of *De Novo* Post-shunt Seizures?

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Abstract

Background: While ventriculo-extracranial shunting procedures have been the standard treatment option for hydrocephalus for a long time, their long-term morbidity, including the development of post-shunt *de novo* seizures, should be taken into account. This study aimed to investigate the rate and risk factors of the occurrence of *de novo* post-shunt seizures in patients with hydrocephalus.

Methods: In this retrospective longitudinal study, all patients with hydrocephalus who had ventriculo-peritoneal shunt insertion from 2014 to 2017 at Namazi Hospital, (Shiraz, Iran) were studied. Phone calls were made to all patients to obtain their postoperative seizure outcome and other data (e.g., sex, age at surgery, shunt insertion location, history of seizures before surgery, history of seizures after surgery, any other type of brain surgery, and the etiology of their hydrocephalus). The Pearson Chi Square was used for the analysis of binary variable (e.g., sex) differences, and the *t* test for the analysis of differences in the means of numerical variables (e.g., age). Bonferroni correction tests were also utilized. P values less than 0.05 were considered significant.

Results: A total of 114 patients were included in the study. Overall, 68 (60%) patients had a frontal location of shunt insertion and 46 (40%) had a parietal site. Twenty-four (21%) patients reported experiencing *de novo* post-shunt seizures, 15 of which had a frontal location and nine a parietal location for shunt insertion (P=0.824).

Conclusion: *De novo* post-shunt seizures are common occurrences. However, shunt location is not a significant risk factor for the development of *de novo* post-shunt seizures.

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Keywords ● Brain ● Epilepsy ● Seizures ● Neurosurgery

What's Known

- The comorbidity of epilepsy and hydrocephalus (HC) is mainly due to the underlying etiology; however, the treatment (i.e., shunting procedure) has also been implicated in the development of epilepsy in some patients.

What's New

- *De novo* post-shunt seizures are common occurrences. However, shunt location is not a significant risk factor for the development of *de novo* post-shunt seizures.

Introduction

Hydrocephalus (HC) is a cerebrospinal fluid (CSF) physiology disorder that causes abnormal enlargement of the cerebral ventricles. This disorder has various etiologies.[1] Congenital hydrocephalus, which frequently involves aqueduct stenosis, has a genetic etiology. Hydrocephalus can also be acquired, mainly as a result of pathological events affecting ventricular outflow, subarachnoid space function, or cerebral venous compliance. Treatment strategies may include shunt and endoscopic approaches.[1] Epilepsy is a major comorbidity in patients with HC and may have a serious impact on their outcomes.[2] The

comorbidity of epilepsy and HC is mainly due to the underlying etiology. However, the treatment (i.e., shunting procedure) has also been implicated in the development of epilepsy in some patients.[2-5] Despite the reproducibility of the observation of post-shunt *de novo* seizure occurrences in multiple studies,[2-6] the risk factors associated with such sequelae are contradictory in previous studies. For example, one study suggested that shunt location is very important.[3] This observation was not reproduced in any other study.[4] While ventriculo-extracranial shunting procedures have been the standard treatment option for HC for a long time,[1, 2] their long-term morbidity, including the development of post-shunt *de novo* seizures, should be taken into account.

The current study aimed to investigate the rate and risk factors of the occurrence of *de novo* post-shunt seizures in patients with HC. In specific, we hypothesized that shunt location is a significant risk factor for the development of *de novo* post-shunt seizures in patients with HC. The answer to this question could have significant practical implications.

Patients and Methods

The study was approved by the Review Board and the Ethics committee of Shiraz University of Medical Sciences (code: IR.SUMS.REC.1398.1287). In the current retrospective longitudinal study, all patients with HC who had ventriculo-peritoneal shunt insertion between 2014 and 2017 at Namazi Hospital, (Shiraz, Iran) were studied. There were no exclusion criteria at this stage. In the initial phase, we reviewed their medical records to obtain detailed clinical information such as sex, age at surgery, shunt insertion location, history of seizures before surgery, history of seizures after surgery, any other type of brain surgery, and the etiology of their HC. The shunt insertion location criteria were not known in this retrospective study (it was based on the decision of treating neurosurgeons).

In the second phase, the neurologist, the first author, made phone calls with all the patients to verify their medical information, as well as to obtain their postoperative seizure outcome (occurrence and frequency of seizures). The patients were asked if they agreed to share their information over the phone (no written consent was obtained). Patients who did not respond to our phone call, those not willing to participate, and patients who reported having seizures before their surgery were excluded. All data has been kept confidential.

Relevant clinical variables were summarized descriptively to characterize the study population.

Statistical Analysis

IBM-SPSS statistics (version 25, IBM Corp.-USA) was used for statistical analyses. Fisher's Exact test was used for the analysis of binary variable (e.g., sex) differences. The *t* test was used for the analysis of differences in the means of numerical variables (e.g., age), and Bonferroni correction tests were applied for statistical analyses. P values less than 0.05 were considered significant.

Results

A total of 114 patients [48 women (42%) and 66 men (58%)] met the inclusion criteria and entered the study. Their mean age at the time of the shunt surgery was 46±101 months (range: 0-79 years) and their postoperative follow-up period was 38±10 months (range: 2-5 years). Overall, 68 (60%) patients had a frontal location of shunt insertion, and 46 (40%) had a parietal site. Twenty-four (21%) patients reported experiencing *de novo* post-shunt seizure(s). There was no difference between frontal versus parietal shunt locations (P=0.824). Factors that were potentially associated with the occurrence of *de novo* post-shunt seizures are shown in table 1. Among the 24 patients who reported experiencing *de novo* post-shunt seizures, three had a single seizure, six had well-controlled

Table 1: Factors potentially associated with the occurrence of *de novo* post-shunt epileptic seizures

Variable		Patients with *de novo* post-shunt seizures (N=24)	Patients without *de novo* post-shunt seizures (N=90)	P value
Sex	Female	3 (13%)	45 (50%)	0.001[1]
	Male	21 (87%)	45 (50%)	
Age at surgery (Mean±SD) (month)		56±62	43±109	0.585[2]
Etiology of hydrocephalus	Congenital	10 (42%)	59 (66%)	0.058[1]
	Acquired	14 (58%)	31 (34%)	
Other brain surgery		6 (25%)	15 (17%)	0.379[1]
Shunt location	Frontal	15 (63%)	53 (59%)	0.818[1]
	Parietal	9 (37%)	37 (41%)	

*After Bonferroni correction, significant predictive value is 0.01. [1]Fisher's Exact test; [2]*t* test

seizures (i.e., no seizure in the past 12 months), and 15 had uncontrolled seizures (i.e., having seizures in the past 12 months despite receiving antiepileptic drugs for 13 months or after the discontinuation of their drugs in two months).

Discussion

In this study, we observed that *de novo* seizures occur in 21% of patients with HC, who receive ventriculo-extracranial shunting procedures. This rate is similar to that in one previous report,[5] while it is higher in another study.[3] The development of *de novo* post-shunt seizures could be directly related to shunt implantation.[5] *De novo* seizures may also happen following other types of brain surgery.[7-10] This observation has significant clinical and practical implications. First, it is reasonable to consider using alternative CSF diversionary techniques, when they are clinically appropriate,[3] or using alternative procedures, such as endoscopic third ventriculostomy (ETV), to treat HC, when anatomically possible.[5] In newborns with HC, initial treatment with ETV is preferable to the implantation of a shunt. In adults with HC, ETV failed sooner than shunt therapy; nonetheless, ETV was more efficient.[11] In addition, the incidence of complications and mortality is higher with the shunting procedure.[12] Secondly, it is important to identify the risk factors that predispose patients with HC to the development of *de novo* post-shunt seizures. Many studies have previously tried to provide a list of these risk factors.[2-6] The most consistent risk factor for the development of *de novo* post-shunt seizures in the literature is shunt complications (e.g., shunt infection).[5] We did not investigate shunt complications in our study.

Shunt location was not a significant risk factor for the development of *de novo* post-shunt seizures in patients with HC in our study. One previous study suggested that shunt location is important in the development of *de novo* post-shunt seizures in patients with HC.[3] However, this observation was not reproduced in any other study.[4] A recent study comparing complications and revision rates following frontal versus parietal approaches for ventricular shunt placement in patients with idiopathic normal pressure HC found that shunt location may not have a significant impact on complications and revision rates, and either approach is reasonable.[13] This is consistent with our findings.

We observed that sex was a significant risk factor for the development of *de novo* post-shunt seizures in patients with HC. The development rate of *de novo* post-shunt seizures in men (32%) was five times higher than in women (6%). In one previous study, the authors observed that men had greater odds for multiple revisions than women.[14] The relationship between male sex and shunt complications/sequels is an intriguing observation and should be explored in future studies.

Age at the time of the shunting procedure was not associated with the development of *de novo* post-shunt seizures in our study. This is consistent with the findings of a previous study.[3] Etiology of HC was not associated with the development of *de novo* post-shunt seizures in our study either. Similarly, one study has suggested that there is no significant association between shunt malfunction and the etiology of the HC or patient's age.[15] However, the association between the original cause of HC and the development rate of epilepsy is a controversial issue in the literature.[5] This issue should be resolved in future studies.

Our study has a limitation; the retrospective design of our study restricted our ability to differentiate between *de novo* post-shunt provoked versus unprovoked seizures. In addition, we did not investigate some of the potentially important risk factors, including shunt complications.

Conclusion

In conclusion, *de novo* post-shunt seizures are common occurrences and require serious attention. When possible, it is reasonable to consider using alternative techniques instead of ventriculo-extracranial shunting procedures. If performing ventriculo-extracranial shunting procedures is mandatory, it is important to try to prevent and minimize the risk factors for the development of *de novo* post-shunt seizures. It seems that shunt location is not a significant risk factor for the development of *de novo* post-shunt seizures in patients with HC.

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Authors' Contribution

H.B: Acquisition, analysis, and interpretation of data, revising it critically for important intellectual content; M.S.M: Acquisition, analysis, and interpretation of data, revising it critically for

important intellectual content; M.B: Acquisition, analysis, and interpretation of data, revising it critically for important intellectual content; A.A.A: Study concept and design, acquisition, analysis, and interpretation of data, drafting the manuscript; All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interest: None declared.

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