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Treatment of Headache Associated With Subarachnoid Hemorrhage

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Treatment of Headache Associated with Subarachnoid Hemorrhage:
A Retrospective Electronic Health Record Review

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By

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Abstract

Background: Subarachnoid hemorrhage (SAH) patients experience significant headaches that can last weeks to years. The treatment for these headaches has not been effective in successful alleviation of pain. Understanding the present standard of care will help guide future medication modalities for these patients.

Conceptual Framework: The Neuman Systems Model was utilized as a framework in this study.

Methodology: A retrospective review of the electronic records of patients who experienced a subarachnoid hemorrhage (SAH) at an academic health system in the southcentral part of the United States was done to evaluate patient demographics and comorbidities. Variables included Hunt-Hess (HH) scores, intracranial pressures, aneurysm coiling, and patient-reported pain scores over the first ten days of hospital admission.

Results: A total of 203 patient electronic medical records were evaluated for this study. Maximum daily pain score was statistically significant on admission day 5, with a mean for Hunt-Hess I 5.47, Hunt-Hess II 7.0, and Hunt-Hess III 7.07. Acetaminophen administration (in milligrams) was 729.59 for HH I, 679.93 for HH II, and 338.82 for HH III on day one of admission. Admission day 10 was also statistically significant with HH I receiving (in milligrams) 437.75, HH II receiving 718.42, and HH III receiving 912.76. Morphine equivalent dosing for day one admissions were HH I 2.69, HH II 5.52, and 0.86 ($p=.009$).

Discussion: Those patients who presented to the hospital with a SAH with a HH I or HH II had similar intensity headache, but received more acetaminophen than HH III. On admission day 5, HH I experienced less headache than HH II or HH III.

Conclusion: Of the patients in the study, all HH classifications presented with similar headache. Patients with a HH I or HH II received more acetaminophen and opioids than HH III on admission day I. Those with a HH II and HH III had greater headache on admission day five than HH I, and received more acetaminophen.

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Introduction

The incidence of aneurysmal subarachnoid hemorrhage (aSAH) is approximately 10 to 15 people per 100,000 (D'Souza, 2015). Because of the acute cerebral injury, this population of patients experiences significant headaches that can last weeks to years. While the exact mechanism of headache remains unclear, it is believed to be related to hypertension, meningeal irritation from the accumulation of blood post-rupture, hydrocephalus, or vasospasm (Swope et al., 2014). Regardless if organic or mechanical in nature, the treatments for headache include acetaminophen, acetaminophen/butalbital/caffeine, intravenous magnesium, and opioids, however none of these have been effective in successful alleviation of pain. While there have been many articles published about the ineffectiveness of treatment, no new direction for medication or headache treatments has emerged.

According to Glisc et al., (2012), headaches after SAH occur for more than two weeks while patients are in the hospital setting. The mean scores of patient-reported headache remains nearly constant throughout the patients' treatment course, despite administration of varied treatment modalities. Glisc et al (2012) further states that this population's headache persisted in post-discharge follow-up, in some cases up to nine years. Unfortunately, understanding the exact cause of headache remains obscure and further complicates effective and reliable treatment.

Additionally, headache was the second leading cause for hospital readmission (Glisc et al., 2012). Readmission rates are particularly significant for hospital organizations as these rates impact reimbursement. The Centers for Medicare and Medicaid Services (CMS) and other insurance institutions have dramatically reduced or eliminated reimbursement for readmissions within thirty days for complications related to a previously treated illness. As such, the costs incurred by the hospitals increase dramatically.

Purpose

The purpose of this study was to determine the maximum daily patient-reported pain scores for those patients who experienced SAH, and to assess how medications were utilized in the treatment of headache for those in the study time frame from 2012-2017. Patient self-reported headache pain scores, medication administration for the treatment of pain, intracranial pressures stratified by Hunt-Hess scoring, and intracerebral interventions were evaluated for correlation. The data collected were acquired through the electronic health record utilizing the informatics division of UKCMC, which allowed for consistency of information obtained. The two electronic data warehouses utilized for this study included the Kentucky Appalachian Stroke Registry (KApSR) and The Center for Clinical and Translation Science (CCTS).

Theoretical Framework

The Neuman Systems Model was utilized as a conceptual base for this study. Within the framework for this study, the individual is considered a system whose external environment is constantly changing. Specific to this model, the "individual" could be a group, community, or a defined population (Bademli & Duman, 2017). The system's response to these changes is dynamic and interacts with their external environment. The model focuses on the individual in response to stressors within the environment, including all aspects such as psychological, physiological, spiritual, cultural, and sociocultural (Bademli and Duman, 2017). Understanding beliefs and structures that are unique to each individualized patient, when possible, aids in the way to best understand and interpret findings. The Neumann Systems Model is applicable to this population because the impact of the cerebral injury is specific to each individual and the factors that are associated with pain are relative to the individual and their previous experience with pain.

Literature Review

Evaluation for a subarachnoid hemorrhage (SAH) involves rating headache severity and level of consciousness, in addition to imaging with computed tomography (CT) and magnetic resonance imaging (MRI) for the volume of blood in the subarachnoid space. Patient level of consciousness is evaluated and scored utilizing the Hunt-Hess Classification, with scores ranging from I-IV (The Joint Commission, 2018). Frequently, patients present to the treating facility with a headache described as the most severe ever experienced and of significant intensity.

SAH is caused by a rupture of an aneurysm or leakage from an intracerebral vessel, causing blood to enter the subarachnoid space. Frequently associated with this is cerebral edema and intraventricular extension as blood moves into the ventricular space. As the blood migrates into additional areas, this leads to cerebral compression as well as meningeal irritation causing an exacerbation and prolongation of headache.

Establishing an effective and lasting treatment for headache associated with SAH has proven to be a challenge. Several medications are theorized to decrease the inflammation associated with SAH and subsequent headache, including intravenous magnesium, acetaminophen/butalbital/caffeine, acetaminophen, ibuprofen, ketorolac, morphine, and dexamethasone (Swope et al., 2014). However, no clinical studies were found that addressed the cause of headache and associated headache improvement with substantive results for future treatment. In order to understand any future medical intervention or treatment, establishment of a historical baseline for patients is of utmost importance. A review of the literature revealed only limited articles that presented information regarding the degree to which symptomatic headache control is treated in the inpatient hospital setting. Because of variance in patient conditions and individual patient perception of pain, it is difficult to assess the true cause of the headache and whether it is mechanical or organic in nature.

Hong et al., (2015) and Glisc et al., (2016) completed retrospective studies that followed patients for the purpose of evaluating the effectiveness of treatment of headache in patients that experienced SAH. The researchers determined that treatment of headache was ineffective throughout the course of hospitalization for these patients. Glisc et al., (2016) found that headache was the second leading cause for readmission to the hospital within 30 days. Hong et al., (2015) found that nearly 94% of patients had experienced headache pain improvement at 12 months. Both of these studies underscore the need for improved headache mitigation and control.

Magalhaes and Rocha-Filho (2013) performed a cohort study of 101 patients from 2009 to 2010 in which patients who presented with aSAH were followed for incidence of headache and associated medical treatments and interventions. Their study focused on the effects of embolization and craniotomy. The researchers found that 54% of those who underwent surgical craniotomies experienced lasting headaches for more than a month. Additionally, 25% of those who underwent arterial embolization experienced headache at one month follow up. Endovascular procedures, including angiography with intra-arterial coiling, stenting, or clipping were overall associated with greater increase and risk for headache (Magalhaes & Rocha-Filho, 2013).

Available literature underscores the need for further research as it relates to SAH, as no published study has identified a uniformly effective protocol for treating SAH-related headache. Providers in the medical facility where this study was conducted treat and manage patients in the tristate region for SAH. This project focused on historical data, with an emphasis on patients who were treated for SAH from 2012-2017.

Methods

Design

A retrospective medical record review was used to obtain data to evaluate the headache scores of patients with aneurysmal and non-aneurysmal subarachnoid hemorrhage who were admitted to the neurosurgery service line from 2012-2017. KApSR and CCTS were employed for the compiling of data that met the inclusion criteria for this study. Additional information collected included intracerebral interventions, specifically aneurysm coiling, and medication administration for the treatment of headache associated with subarachnoid hemorrhage; medications included acetaminophen, acetaminophen/butalbital/caffeine, ketorolac, intravenous magnesium, dexamethasone, and the morphine equivalent for the study time frame.

Sample

A convenience sampling method was used for selection of patients who presented with SAH in the study time frame. A total of 408 patients were in the data sample from KApSR. Exclusion criteria included death during admission and a Hunt-Hess classification of IV or V upon admission to the hospital. Data were evaluated for the first ten days of hospitalization. The inclusion criteria for this study were as follows: a diagnosis of SAH with a Hunt-Hess classification I, II or III, admission to the neurosurgery service upon time of hospital admission. A Hunt-Hess (HH) I classification indicates no neurological impairment, mild headache, and no nuchal rigidity. A HH II classification indicates full nuchal rigidity, moderate to severe headache, alert and oriented, and no neurological deficits other than cranial nerve palsy. A HH

III classification indicates lethargy or mild confusion with mild neurological deficits. Due to the neurological impairment and depressed level of consciousness and inability to provide feedback about headache, those with a Hunt-Hess IV or V were excluded from this study.

Setting/Agency Description

The study setting was a Level-1 trauma hospital and Comprehensive Stroke Center (per The Joint Commission certification), which delivers care to patients from a tristate area who experience subarachnoid hemorrhage, among multiple other illnesses and disease processes. The hospital has complete vascular neurology, cerebrovascular surgery, neurointerventional, and neurocritical care service lines which treat between 35 and 50 SAH per year.

Procedures

Institutional Review Board (IRB) approval was granted through the affiliated university. KApSR delivered patient demographics (including obesity, hypertension history, tobacco use, dyslipidemia, age, gender, and race). CCTS provided data that related to daily pain scales, charted average intracranial pressures on admission days 1-10, and dosage and frequency of analgesia administered.

Data Analysis

Data were analyzed using SPSS version 24. Descriptive and correlation analyses were done using patient demographic, classification of HH scoring, patient-reported pain scores, intracranial pressures, and incidence of aneurysm coiling with p=<.05 considered significant. Additionally, SAS was employed to complete a post-hoc analysis to determine correlation between the variable and patient demographic, if any. Any missing data for HH classification resulted in the exclusion of that participant from the statistical analysis.

Results

Demographics

A total of 203 patients remained after all exclusion criteria were applied. Significant data were missing for 31 of the 203 patients, leaving a total of 172 patient medical records for the study. The mean age of participants was 54.6 years with 62.3% of study subjects being female, and 89.9% being Caucasian/white. Additionally, 24.3% were obese (defined as a body mass index $\geq$ 30 kg/m^2), 85.5% had a history of hypertension, 53.4% used tobacco, and 24.3% were diabetic. (see Table 1 for additional demographic information).

Findings

There were 49 patients with a HH I, 76 patients with a HH II and 47 patients with a HH III for the study time frame, with data missing for four patients. Patient-reported pain scores were rated on a scale from 1-10. Maximum daily pain scores were analyzed on admission days 1, 5, and 10, and stratified by Hunt Hess classification. Day 5 of admission was the only time when a significant difference was noted between Hunt Hess classification, with a mean score of 5.47 (SD 2.94) for Hunt Hess I and 7.0 (2.88) and 7.07 (2.24) for HH II and III, respectively (p = .023). A post hoc analysis of the data revealed a significant difference between HH I and HH II and HH I and III, but not between HH II and HH III. There were no significant difference between the three HH classifications on admission days 1 and 10 (see Table 2).

Cumulative acetaminophen administration was compared for the three HH classifications. Post hoc analysis revealed a significant difference on admission day 1 (p = .01) with patients classified as HH I and II receiving more acetaminophen than HH III. On admission day 10, patients rated as HH II and HH III received significantly more acetaminophen than did patients with a HH I classification ($p=.02$)(see Table 2). The post hoc analysis showed that the morphine equivalent for admission day 1 was statistically different between the three HH classifications: HH I mean 2.69 (4.87); HH II mean 5.52 (11.67); and HH III mean 0.86 (2.76). Intravenous magnesium, ketorolac, and acetaminophen/butalbital/caffeine did not have a statistically significant impact in the treatment of patient-reported pain scores for the study time frame (see Table 2).

Aneurysm coiling, a treatment to prevent incidence of additional rupture, was performed in a total of 97 patients, accounting for roughly 24% of all 408 patients who presented with SAH during the study timeframe. Statistically significant findings as they relate to patient demographic and aneurysm coiling can be found in Table 3. As it relates to gender, fifty-seven percent of those who received an aneurysm coiling were women, compared to only 38% that were male ($p = .014$). Fifty-eight percent of the participants in this study who received an aneurysm coiling used tobacco, compared to 41% of non-tobacco users ($p= .02$). However, of those who received an aneurysm coiling, a medical history of diabetes showed an inverse relationship, with 55.5% not having the disease present, compared to a positive diabetic history at 34% ($p = .01$). There was no correlation between intracranial pressures by HH classification for this study time frame, (see Table 4). The relationship between HH classification and intracranial pressures from days 1 through 10 can be observed in Graph 1.

Discussion

The purpose of this study was to evaluate the effectiveness of the treatment of headache associated with SAH. Treatment of headache associated with SAH involves the administration of multiple medications. In this study, acetaminophen and opioids proved to be more effective in the treatment of headache than other medications.

Study findings revealed that women who are Caucasian/white and who used tobacco were more likely to require an aneurysm coiling than other ethnicities who presented with a SAH during the study time frame. In line with these results, Lindbohm et al., (2016) found that out of 65,521 individuals who were followed in Finland, women who smoked were three times more likely to have a SAH than non-smokers. While this current study did not evaluate the comparison of smokers and non-smokers, the findings do suggest that women have a higher incidence of SAH and the need for aneurysm coiling than men.

Cumulative acetaminophen dosage for day one was statistically significant in that HH I and HH II required more medication than HH III. The disparities in acetaminophen administration could be related to the difference in levels of alertness at the time of admission, since HH I and HH II patients are more alert and able to report headache pain. The morphine equivalent dosage findings were the same as acetaminophen on day one of admission, with HH I and HH II receiving a greater amount of medication than HH III.

On admission day ten there were no significant differences in maximum daily pain scores, but there was a significant difference in acetaminophen administration, with HH II and HH III patients receiving higher mean doses of medication than HH I. This finding would suggest that HH I required less medication to control headache pain than did HH II and HH III. Related to this finding, Swope et al., (2014) found that pain intensity increased over the first seven days of admission after a SAH. Their study, which had a slightly different grouping of HH classifications (HHI - II and HH III-IV), compared daily pain scores and the incidence of vasospasm which did determine correlation of the two study variables.

Increased intracranial pressure (ICP) is also a prognostic tool in quality outcome for those patients who experience SAH. This study did not evaluate all five HH classifications for the correlation of headache, as the study criteria were dependent upon patient-reported pain scoring which is only possible with HH I-III. However, in the three HH classifications that were evaluated, there was no statistically significant differences in HH I-III and ICPs throughout the ten days of evaluation of this study. This could be due in part to the understanding that those with HH I-II are not as likely to have a need for ICP monitoring as those who are classified as a HH III, IV or V. In this study, an average of 17.7% of HH I, 26.7% of HH II, and 88.6% of HH III had intracranial pressure monitoring for the study time frame. In a study by Wang et al., (2104) the researchers found a statistically significant difference in ICP and HH classification, with a higher HH classification being associated with increased ICP ($p < .001$).

Limitations

As this was a retrospective review, the researcher was unable to randomize patient selection. Additionally, information was obtained only from one medical center, limiting the number of possible participants. The electronic data warehouses utilized for the study only extracted information that had been charted, regardless of missing or incomplete information. Data was missing for 31 participants, resulting in a lower overall sample. Further, data were not collected following discharge to evaluate for headache resolution or continuation or medication that abated pain associated with SAH. Also, the data compilation only consisted of information for patients within the first ten days of hospital admission. Frequently, patients who experience SAH are hospitalized for more than three weeks and continue to experience headache that requires medication administration.

An additional limitation is that this study did not account for the Fisher score of each patient. The Fisher grading scale classifies SAH by the degree of blood in the subarachnoid space and it can help predict the likelihood of cerebral vasospasm (Lindvall et al., 2009). The

Fisher scale is used in correlation with HH classification when a patients presents to an admitting facility with a SAH. Additional limitations are that this study did not account for incidence of cerebral vasospasm in the study window or for the development of hydrocephalus, both of which can increase intracranial pressures and associated headache.

Summary and Recommendations

For this study population, women were more likely than men to have a SAH. Cigarette smokers were more likely to require an aneurysm coiling. Additionally, the data in this study suggests that patients who present with a subarachnoid hemorrhage for a Hunt Hess I, II and III classification have headaches that are best treated with an opioid or acetaminophen. It is suggested that other medications could be administered for the treatment of headache and evaluated for comparison in a future study.

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Table 1. *Patient Demographics*

Characteristics	Mean (SD) or n (%)
Age	54.6 (13.1); range = 20-89
Gender	
Female	124 (62.3%)
Male	75 (37.7%)
Ethnicity	
White	177 (89.39%)
Black/African American	12 (7.07%)
Others	6 (3.54%)
Obesity	
No	146 (75.7%)
Yes	47 (24.3%)
Hypertension	
No	28 (14.5%)
Yes	165 (85.5%)
Tobacco	
No	90 (46.6%)
Yes	103 (53.4%)
Diabetes	
No	146 (75.7%)
Yes	43(24.3%)
Dyslipidemia	
No	127 (65.8%)
Yes	66 (34.2%)

Table 2: *Pain by Hunt Hess and Medication Administration*

Pain Scores and Medication Administration				
	Hunt Hess 1	**Hunt Hess 2**	**Hunt Hess 3**	***p***
Maximum Daily Pain Score	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	
Day 1	6.08 (2.1)	6.91(2.67)	5.48(3.64)	.094
Day 5	5.47 (2.94)[a]	7.00 (2.88)[b]	7.07 (2.24)[b]	.023
Day 10	5.21(3.4)	5.97(2.77)	5.2(3.29)	.55
Cumulative Tylenol Dose				
Day 1	729.59 (863.7)[a]	679.93(677.95)[a]	338.82(541.95)[b]	.010
Day 5	1008.16(1074.31)	1197.37(9.33.24)	1223.94(846.98)	.46
Day 10	437.75(710.03)[a]	718.42(955.76)[a,b]	912.76(728.73)[b]	.021
Dexamethasone, number of times administered				
Day 1	0.06(0.31)	0.18(0.62)	0.02(0.14)	.12
Day 5	0.61(1.41)	0.68(1.35)	0.42(1.05)	.56
Day 10	0.06(0.42)	0.21(0.82)	0.21(0.85)	.49
Morphine Equivalent				
Day1	2.69(4.87)[a]	5.52(11.67)[a]	0.86(2.76)[b]	.009
Day 5	10.08(22.77)	13.38(22.38)	7.75(10.21)	.30
Day 10	4.43(11.56)	8.98(23.55)	8.47(15.87)	.39
Fioricet (number of administrations)				
Day 1	1.5(1.22)	1.87 (1.45)	1 (-)	.78
Day 5	3.5(1.87)	3.86 (1.68)	3 (-)	.69
Day 10	3.0 (2.08)	3.0 (1.29)	4 (1.0)	.59
Intravenous Magnesium, 4 grams (number of administrations)				
Day 1	1.0 (-)	1.14(0.37)	1.0 (-)	.60
Day 5	1.0 (-)	1.23(0.43)	1.11(0.33)	.52
Day 10	1.0(-)	1.25(0.5)	.29	.29

Table 3: *Coiling and Comorbidities Correlation*

Comorbidities and Coiling Correlation			
	Coiling		
	Yes (n=97) **Mean (SD) or n (%)**	**No (n=96)** **Mean (SD) or n (%)**	***P***
Age	55.0 (13.6)	54.7 (13.0)	.91
Gender			
Female	69 (57%)	52 (43%)	.014
Male	28 (38.0%)	44 (61.1%)	
Obesity			
Yes	22 (46.8%)	25 (53.2%)	.59
No	75 (51.4%)	71 (48.6%)	
Tobacco			
Yes	60 (58.3%)	43 (41.7%)	.02
No	37(41.1%)	53 (58.9%)	
Diabetes			
Yes	16(34%)	31 (66%)	.01
No	81(55.5%)	65 (44.25%)	
Dyslipidemia			
Yes	28 (42.4%)	38 (57.6%)	0.1
No	69 (54.3%)	58 (45.7%)	
Hypertension			
Yes	82(49.7%)	83 (50.3%)	.70
No	15 (53.6%)	13 (46.4%)	

Table 4: *Intracranial Pressure by Hunt Hess Classification*

Intracranial Pressure (ICP) by Hunt Hess Classification				
	Hunt Hess 1	**Hunt Hess 2**	**Hunt Hess 3**	***p***
Average Daily ICP	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	
Day 1	9.7(5.60)	10.55(4.38)	9.60(3.08)	.65
Day 5	7.85 (4.16)	8.28(4.07)	8.76(4.72)	.81
Day 10	6.20(2.80)	9.84(4.70)	7.91(4.68)	.12

Graph 1: *Hunt and Hess and ICP Correlation*