Evaluation and Management of Cerebral Vasospasm after subarachnoid Hemorrhage

Abstract:

The constriction of the big and medium-sized cerebral arteries following aneurysmal subarachnoid haemorrhage (aSAH) is a well-described condition that most commonly affects the anterior circulation supplied by the internal carotid arteries. SAH is an uncommon yet life-threatening kind of stroke. Authors have used words like symptomatic vasospasm, delayed cerebral ischemia (DCI), transcranial Doppler vasospasm, and angiographic vasospasm to define vasospasm across the literature. Because posthemorrhagic vasospasm causes major neurologic morbidity and death, there has been a lot of interest and study into understanding its physiologic basis and creating effective preventative and treatment approaches. The triple-H therapy hemodynamic augmentation technique, which comprises hypertension, hemodilution, and hypervolemia, has been a key component of treatment. In this article we'll be looking at Cerebral Vasospasm after subarachnoid Hemorrhage, its causes, Epidemiology, Evaluation and most importantly management

Introduction:

The constriction of the big and medium-sized cerebral arteries following aneurysmal subarachnoid haemorrhage (aSAH) is a well-described condition that most commonly affects the anterior circulation supplied by the internal carotid arteries. In instances with aSAH, cerebral vasospasm leading to delayed cerebral ischemia (DCI) remains a prominent consequence and cause of morbidity. [1,2,3] Authors have used words like symptomatic vasospasm, delayed cerebral ischemia (DCI), transcranial Doppler vasospasm, and angiographic vasospasm to define vasospasm across the literature. Each definition has its own set of advantages and disadvantages. Symptomatic vasospasm affects 20% to 40% of SAH patients, and it usually refers to clinical worsening after other plausible reasons of deterioration have been ruled out. This is a subjective diagnosis that might be limited in low-

grade instances with small or unnoticeable differences in the examination. DCI is defined as symptomatic vasospasm, vasospasm-related infarction, or both. [4,5-9]

Because posthemorrhagic vasospasm causes major neurologic morbidity and death, there has been a lot of interest and study into understanding its physiologic basis and creating effective preventative and treatment approaches. The cause of cerebral vasospasm, on the other hand, is unknown. Although a variety of treatment techniques have been proven to have variable degrees of value in avoiding vasospasm and its subsequent neurologic sequelae, no one therapy approach has been proved to be universally helpful in preventing vasospasm and its following neurologic sequelae. [1]

In poor-grade instances, DCI allows for the identification of clinically relevant vasospasm with minimum neurological exams; nonetheless, infarcts caused by spasm must be separated from those caused by surgery, angiography, or other reasons. Furthermore, because DCI is a post-mortem diagnosis made after an infarct has been discovered, the number of therapeutic actions to prevent this result is restricted. Angiographic vasospasm can occur in up to 70% of patients, although the link between angiographic spasm and clinical symptoms can be shaky, and it's unknown how widespread or severe angiographic spasm must be to be clinically meaningful. [4]

The triple-H therapy hemodynamic augmentation technique, which comprises hypertension, hemodilution, and hypervolemia, has been a key component of treatment. Increases in mean arterial pressure (MAP) have been found to be helpful on their own and can be induced with a variety of drugs. Calcium-channel antagonists have been extensively studied for the prevention of vasospasm in aSAH, with nimodipine being recommended as the first-line pharmacological therapy for post-aSAH cerebral vasospasm prevention. Intra-arterial vasodilator medication and balloon angioplasty are two more invasive treatments for vasospasm that rely on the use of cerebral angiography. These techniques have been approved as appropriate for the treatment of symptomatic individuals who are not responding to hypertensive medication, according to guidelines. [1]

Etiology and Epidemiology:

Aneurysmal SAH is an uncommon yet life-threatening kind of stroke. Despite the fact that SAH accounts for just around 3% of all strokes and 5% of all stroke

fatalities, the young age of those affected implies that this event is responsible for a quarter of all years of life lost as a result of stroke. In the nearly 80 years after the first cases of SAH were detected in living people, advances have been made in our understanding of the pathogenesis of the disease, and the prognosis has vastly improved. From 1960 to 1992, case-fatality rates declined by 0.9 percent per year, adjusted for age and sex, according to a systematic assessment of 12 epidemiological studies of SAH. [10]

In a retrospective analysis of 1200 consecutive SAH patients, in-hospital mortality was 18 percent, with Hunt-Hess grade 4 or 5 patients having the greatest rates (24 percent and 71 percent respectively). Hemorrhage, aneurysmal re-rupture, and medical problems were the main reasons for the removal of life support. In around 80% of instances, a burst cerebral aneurysm causes non-traumatic SAH, which accounts for 5 to 10% of all strokes in the United States. Furthermore, data suggests that high-volume centres had better mortality outcomes than low-volume centres, which might be due to improved resource access (e.g., neurointensivists, surgical treatments, etc.). As a result, resource allocation and management are anticipated to be critical for improving outcomes for patients suffering from SAH and its consequences (e.g., vasospasm). [11-16]

The patient's initial neurological status is the most strong predictor of prognosis following aneurysmal SAH , while it's unclear how this contributes to delayed neurological deterioration. Initial global ischemia induced by aneurysm rupture, increased intracranial pressure (ICP), and reduced perfusion pressure are all factors in immediate brain damage after SAH. Lowered blood flow can occur without increasing ICP or after ICP has been reduced, and there is a drop in cerebral metabolism that accounts for at least some of the reduction in cerebral blood flow. Blood flow reductions assessed after SAH in rats were not enough to produce frank ischemia right away, but they were enough to sensitise tissue to later assaults. [10]

Evaluation:

Depending on the severity of the disorder and which cerebral arteries are most impacted, a physical examination may reveal a constellation of signs and symptoms of continuing vasospasm. Lethargy, disorientation, meningismus, and a new or worsening headache are examples of nonlocalizing symptoms.

The specific vascular implicated in focal neurologic impairments is as follows: [1]

- Disinhibition, confusion, mutism; lethargy, delayed sensitivity, abulia; leg loss of strength; with involvement of the recurrent artery of Heubner (a large ACA perforator), contralateral faciobrachial numbness without cortical findings; with participation of the recurrent artery of Heubner (a large ACA perforator), contralateral faciobrachial weakness without cortical results
- Hemiparesis, faciobrachial weakness, monoparesis; aphasia, apractagnosia; neglect; middle cerebral artery (MCA) distribution
- Visual disturbance, hemianopsia in the distribution of the posterior cerebral artery (PCA).

Vasospasm can be diagnosed by a variety of methods, including cerebral angiography, ultrasonography, and symptomatic assessment. Traditional cerebral angiography has a high specificity since the arteries may be immediately viewed, and it often demonstrates constriction and spasm of the cerebral arteries. The passage period of contrast through the vessels is usually slowed or increased. Although this is considered the gold standard for diagnosis, it is invasive, not always available, and comes with its own set of dangers. There is also evidence that computed tomography (CT) angiography and perfusion have a high sensitivity (75%) and specificity (93%) and can be used to diagnose vasospasm. Transcranial Doppler (TCD) is an essential method for identifying vasospasm because it employs ultrasonography to determine velocity across the middle cerebral artery. [11]

The Hunt-Hess scale can be used to assess the neurological condition of the patients at the time of admission. Clinically significant arrhythmia (defined as any cardiac arrhythmia other than sinus tachycardia, bradycardia, or sinus rhythm with premature atrial or ventricular complexes) should be recorded, as well as pulmonary edoema (diagnosed by clinical examination and chest X-ray), myocardial infarction (diagnosed by ECG, troponin values, and echocardiography), cardiac arrest, cerebral edoema (diagnosed by CT), fever The length of stay in the hospital and critical care unit also should be recorded. [4]

Management:

Nimodipine: is a dihydropyridine drug that inhibits voltage-gated calcium channels and causes arterial smooth muscle to dilate. With a half-life of around 9 hours, it is the sole FDA-approved medication for vasospasm. Its anti-CVS benefits are most likely due to its neuroprotective qualities as compared to arterial smooth muscle cell relaxation. Nimodipine has a low complication risk and may have excellent angiographic response and clinical outcomes. Furthermore, nimodipine may lower the incidence of subsequent cerebral ischemia following aneurysmal haemorrhage. The safety and efficacy of nimodipine were recently demonstrated in a meta-analysis done in 2011, in which treatment of nimodipine was linked to a substantial reduction in CVS following aneurysm rupture. [17]

Haptoglobin in (CSF): The predominant haemoglobin binding protein in plasma is haptoglobin. Toxic byproducts such as reactive oxygen species can be produced when free haemoglobin is liberated from red blood cells. Haptoglobin, on the other hand, attaches to free haemoglobin quickly and prevents the harmful biochemical processes. Humans have two haptoglobin alpha chain alleles, each of which may form three different kinds of haptoglobin dimers (alpha1-alpha1, alpha1-alpha2, and alpha2-alpha2). Although alpha1 and alpha2 have identical haemoglobin binding affinities, alpha1 can more effectively prevent the harmful oxidative processes caused by free haemoglobin. As a result, it's been claimed that people with alpha2 are more prone to inflammation, oxidative damage, and even vasospasm. [11]

The hemodynamic augmentation method: known as triple-H treatment, which comprises hypertension, hemodilution, and hypervolemia, has been an essential component of the current therapeutic alternatives. By raising mean artery pressure (MAP) and lowering blood viscosity, this method was supposed to increase brain perfusion. Patients with vasospasm have been proven to benefit from increases in MAP alone, and a variety of medicines have been researched and used to achieve this aim. The chief pressors used in this situation are phenylephrine, norepinephrine, and dopamine. The most data appears to support the use of phenylephrine; multiple trials have demonstrated that it is useful in individuals with maintained left ventricular function. Other drugs, such as vasopressin, may be used as a supplement to help with treatment. [1,18-23]

Verapamil: The CCB verapamil, like nimodipine, inhibits voltage-gated calcium input into arterial smooth muscle cells. According to the literature, verapamil has been used to treat cardiac vasospasm for a long time. Its usage in the treatment of refractory coronary spasm is both safe and efficacious, as well as convenient and affordable. Alana et al. prospectively evaluated participants with vasospasm who were scheduled for cerebral angiography with likely IA verapamil injection, and their findings contradicted previous publications that claimed IA verapamil had no systemic hemodynamic effects. Mikeladze et al. described a female patient who received selective IA verapamil for the treatment of CVS following a severe subarachnoid parenchymal haemorrhage caused by an internal carotid artery bifurcation aneurysm, with satisfactory clinical results. [17,24-27]

Retrievable stent angioplasty: For severe or refractory vasospasm, endovascular treatment such as balloon angioplasty has demonstrated to be effective. Early and frequent endovascular therapy has been shown to lower the likelihood of delayed cerebral ischemia and, as a result, improve functional outcomes. Prophylactic balloon angioplasty can dramatically reduce the requirement for urgent rescue treatment for symptomatic vasospasm, according to a randomised study with 175 patients. The dangers and disadvantages of balloon angioplasty, on the other hand, should be considered. The endothelial wall is mechanically stretched and the extracellular matrix is disrupted during balloon angioplasty, resulting in enhanced cerebral blood flow. [11]

Magnesium: Magnesium sulphate was originally used to suppress uterine smooth muscle contractions in pre-eclamptic pregnant women. It's a noncompetitive calcium antagonist with a number of essential vascular and neuroprotective properties. By inhibiting the voltage-dependent calcium channel and reducing glutamate release as well as calcium entry into the cell, magnesium causes vasodilation. Magnesium also inhibits the generation of reactive oxygen species and attenuates the action of certain powerful vasoconstrictors, such as endothelin 1. [17]

Multimodality monitoring: MMM (multimodality monitoring) is one of the most recent advances in neurosurgical critical care treatment for patients with neurological illnesses. Intracranial pressure (ICP) has traditionally been utilised for invasive monitoring. ICP, on the other hand, has limits since it does not depict the

entire cerebral environment. ICP and cerebral perfusion pressure (CPP) have been shown in a number of clinical investigations to not always identify brain hypoxia and ischemia. Cerebral ischemia can develop in the context of normal ICP and CPP, according to clinical trials employing jugular venous catheters or a brain oxygen tension (PbtO2) monitor. [11]

There's Multiple technique approaches for managing of The Vasospasm. One which for seizure prevention, all patients can be given nimodipine every 4 hours and phenytoin perioperatively. To keep central venous pressure above 5 mm Hg, all patients can be given 0.9 percent normal saline at a rate of 1 mL/kg per hour, with an additional 5 percent albumin solution. Digital subtraction angiography can be performed on all patients on admission, as well as between SAH days 4 and 8 in patients with poor-grade status (Hunt-Hess grade 3–5), or as needed to evaluate neurological deterioration or new infarction on CT, or for accelerated TCD values in patients with good-grade status. Every day, all of the patients can have standardised serial neurological exams done without sedation. Head CT scans can be done on an as-needed basis for clinical reasons only. [4]

Why did clazosentan's reduction in angiographic vasospasm not transfer into a similar reduction in delayed neurological deterioration or improved outcome? One theory is that the treatment's favourable benefits are counterbalanced by medication toxicity. Although there was no indication of significant hypotension or other adverse effects in first analysis, more evaluation of the trial data is needed to evaluate the toxic consequences. Another possibility is that the contribution of angiographic vasospasm to poor result is too little or that the outcome measurements are too insensitive to show an effect in a CONSCIOUS-1-sized trial (about 400 patients). However, given infarction is strongly connected to bad result, and trials with nimodipine demonstrate that a reduction in infarcts is associated with improved outcome, this hypothesis does not appear to be plausible. [10]

Patients with symptomatic vasospasm or DCI can be given vasopressors (usually phenylephrine or norepinephrine) to keep their systolic blood pressure between 180 and 220 mm Hg, adjusted to clinical response, or inotropes to keep their cardiac index >4.0 L/min per metre squared with milrinone or dobutamine as needed. To keep a positive fluid balance and a central venous pressure of >8 mm

Hg, normal saline and 5% albumin solution can be given, and blood transfusions were given to keep a goal haemoglobin of >10 mg/dL. On patients who have symptomatic spasm or DCI, angiography can be regularly conducted. Angioplasty or intra-arterial chemical vasodilation with papaverine or verapamil can be used as endovascular treatments for vasospasm. [4]

Advances in diagnosis and therapy, most notably the use of nimodipine, intensive care management, hemodynamic adjustments, and endovascular neuroradiology operations, have improved the prospects for these patients, although the results are still unsatisfactory. The endothelin receptor antagonist clazosentan has been shown to significantly reduce vasospasm in recent clinical studies, although patient outcomes have not improved. [28]

Conclusion:

The constriction of the big and medium-sized cerebral arteries following aneurysmal subarachnoid hemorrhage is without doubt one of the most serious conditions, despite being rare case it's high mortality that attracted most of the attention, a lot of management techniques are available. Notably Nimodipine is the sole FDA-approved medication for vasospasm. Moreover, The triple-H therapy hemodynamic augmentation technique, which comprises hypertension, hemodilution, and hypervolemia, is a key component of treatment. We hope in the future more research is done on multiple management techniques that's available.

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