Continous local Intra –arterial Nimodipine administration in severe symptomatic vasospasm after spontanous subarachnoid hemorrhage:a meta-analysis

A Meta-Analysis

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By

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List of Abbreviations

CCBS : Clcium channel blockers

CONSCIOUS : Clazosentan to overcome neurological ischemia and infarcts occurring after subarachnoid hemorrhage.

CT : Computed tomography.

CTA : Computed tomographic angiography.

DCL **:** disturbed conscious level.

EVD : external ventricular drain.

FDA : Food and drug administration.

GCS : Glasgow Coma Scale.

IMASH : Intravenous magnesium sulfate for aneurysmal subarachnoid hemorrhage.

ISAT : International subarachnoid aneurysm trial .

MMBE : Multisession matched mask bone elimination.

NF-B : Nuclear factor-B.

SAH : Subarachnoid hemorrhage.

STASH : Simvastatin in aneurysmal subarachnoid hemorrhage.

US **:** United States.

WFNS : World Federation of Neurological Surgeons.

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Introduction

Subarachnoid hemorrhage (SAH) is bleeding into the subarachnoid space (the area between the arachnoid membrane and the pia mater surrounding the brain) **(Abraham et al., 2016)**. SAH is a potentially life threatening condition. Hemorrhage may occur as a result of a head injury or spontaneously (usually from a ruptured cerebral aneurysm). Spontaneous subarachnoid hemorrhage occurs in about one per 10,000 people per year. Females are more commonly affected than males. While it becomes more common with age, about 50% of people present under 55 years old. It is a form of stroke and comprises about 5 % of all strokes **(Carpenter et al., 2016).**

Risk factors for spontaneous cases included high blood pressure, smoking , family history, alcoholism and cocaine use **(van Gijn et al., 2007).** Sudden headache is the most characteristic symptom of subarachnoid hemorrhage. Headache from subarachnoid hemorrhage is generally diffuse and often described by patients as by far the most severe headache they have ever had **(Linn et al., 1998).**

On admission two-thirds of all patients have depressed consciousness, of whom half are in coma **(Brilstra et al., 2000).**

Neck stiffness is a common symptom, caused by the inflammatory response to blood in the subarachnoid space **(Vermeulen et al., 1990).**

Seizures at onset of the hemorrhage occur in one of every14 patients with SAH **(Butzkuevenh et al., 2000).**

Vomiting is not a distinctive feature either because almost half the patients with non-hemorrhagic thunderclap headache also report vomiting at onset **(Linn et al., 1998).**

CT scanning is the first investigation if SAH is suspected **(Boesiger et al., 2005).** In an important small minority of patients (about 3%) with sudden headache and normal head CT scan within 12 hours the cerebrospinal fluid shows xanthochromia (metabolites of haemoglobin) **(O'Neill et al., 2005).**

Angiographic studies in general serve not only to identify one or more aneurysms as potential causes in a patient with subarachnoid hemorrhage, but also to study the anatomical configuration of the aneurysm in relation to adjoining arteries, which allows optimum selection of treatment (coiling or clipping) **(Chappell et al., 2003).**

Management involves general measures to stabilize the patient while also using specific investigations and treatments. These include the prevention of rebleeding by obliterating the bleeding source, prevention of a phenomenon known as vasospasm, and prevention and treatment of complications such as hydrocephalus, seizures, deep venous thrombosis and stress ulcer **(van Gijn et al., 2007).**

Aim of the Work

To evaluate the effect of continous local Intra – arterial nimodipine administration in severe symptomatic vasospasm after spontanous subarachnoid hemorrhage on mortality and morbidity (symptomatic cerebral ischemia).

Risk Factors and Pathophysiology of Subarachnoid Hemorrhage

According to a review of 51 studies from 21 countries, the average incidence of subarachnoid hemorrhage is 9.1 per 100,000 annually. Studies from Japan and Finland show higher rates in those countries (22.7 and 19.7, respectively), for reasons that are not entirely understood, South and Central America, in contrast, have a rate of 4.2 per 100,000 on average **(Schussp et al., 2013).**

To identify the pathophysiology of spontaneous subarachnoid hemorrhage an idea should be taken about circle of Willis as most of aneurysms arises from it . The circle of Willis is a part of the cerebral circulation and is composed of the following arteries :

- Anterior cerebral artery (left and right)
- Anterior communicating artery
- Internal carotid artery (left and right)
- Posterior cerebral artery (left and right)
- Posterior communicating artery (left and right)

The middle cerebral arteries, supplying the brain, are not considered part of the circle **(Purves et al., 2008).**

Origin of arteries:

The left and right internal carotid arteries arise from the left and right common carotid arteries. The posterior communicating artery is given off as a branch of the internal carotid artery just before it divides into its terminal branches - the anterior and middle cerebral arteries. The anterior cerebral artery forms the anterolateral portion of the circle of Willis, while the middle cerebral artery does not contribute to the circle. The right and left posterior cerebral arteries arise from the basilar artery, which is formed by the left and right vertebral arteries. The vertebral arteries arise from the subclavian arteries. The anterior communicating artery connects the two anterior cerebral arteries and could be said to arise from either the left or right side. All arteries involved give off cortical and central branches. The central branches supply the interior of the circle of Willis, more specifically, the Interpeduncular fossa. The cortical branches are named for the area they supply **(Purves et al., 2008).**

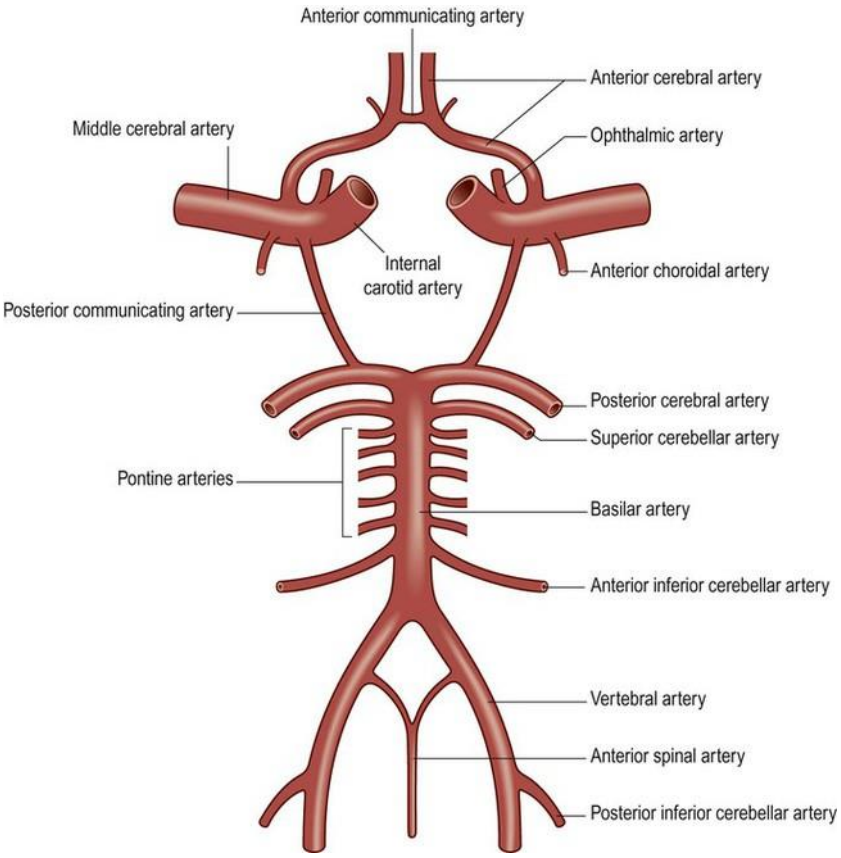

Figure (1): Circle of Willis (Purves et al., 2008).

Intracranial aneurysms are not congenital, as was once believed, but develop in the course of life. The best estimate of the frequency of aneurysms for an average adult without specific risk factors is 2.3% this proportion increases with age.**(Rinkel et al., 1998)**.

Saccular aneurysms arise at sites of arterial branching, usually at the base of the brain, either on the circle of Willis itself or at a nearby branching point. Most intracranial aneurysms will never rupture. The rupture risk increases with the size of aneurysm **(Feigin et al., 2005).**

Although the group of people at risk for SAH is younger than the population usually affected by stroke, the risk still increases with age. Young people are much less likely **(Feigin et al., 2005),** than middle-age people (risk ratio 0.1 or 10 percent) to have a subarachnoid hemorrhage. The risk continues to rise with age and is 60 percent higher in the very elderly (over 85) than in those between 45 and 55. Risk of SAH is about 25 percent higher in women over 55 compared to men at the same age, probably reflecting the hormonal changes that result from the menopause, such as a decrease in estrogen levels **(DeRooij et al., 2007).**

Behavioral risk factors for spontaneous subarachnoid hemorrhage (SAH) include hypertension, smoking, alcohol abuse, and the use of sympathomimetic drugs (eg, cocaine). The risk of SAH is increased by the presence of an unruptured cerebral aneurysm (particularly those that are symptomatic, larger in size, and located either on the posterior communicating artery or the vertebrobasilar