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Guest Editorial

Cerebrovascular Spasm Following Subarachnoid Haemorrhage: Is Sildenafil Promising?

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Cerebrovascular spasm (CVS) following subarachnoid haemorrhage (SAH) is a well-known phenomenon with significant morbidity and mortality. It usually occurs within 3 - 21 days after the initial SAH resulting in delayed cerebral ischemia (DCI) in about 30 - 40% of cases and subsequent strokes, deterioration of Glasgow coma scale, neurological deficits and mortality. Risk Factors for CVS include higher modified Fischer grade of SAH, age, hypertension. CVS can be diagnosed either clinically or radiographically (cerebral angiography, transcranial doppler). Current management guidelines of CVS: First, maintaining euvolemia, inducing hypertension if normal at baseline (level 1 evidence). Second, Cerebral angiography with angioplasty or Cerebral angiography with intraarterial vasodilators (papaverine, verapamil, nicardipine, nitroglycerine) (level 2 evidence) [1,2].

Many theories are discussed about the Pathogenesis of CVS. Blood components play a role in CVS: Oxyhaemoglobin increases vasoconstriction, haemoglobin decreases the levels of nitric oxide, PDGF causes vascular proliferation and impaired vasodilation. In addition, increased production of endothelin-1 is claimed to cause CVS. Also, sympathetic overactivity found in some research to have a role [1].

Some recent research studies suggest Sildenafil can be an option for management of CVS. Mechanism of Sildenafil action is that it inhibits phosphodiesterase 5 (responsible for cGMP breakdown) resulting in accumulation of cGMP and subsequent protein kinas activation with decreasing calcium levels and smooth muscles relaxation. Other animal studies are showing sildenafil effects on CVS: reversal of CVS, improving angiogenesis, improving neurological outcome, decreasing endothelin 1 (vasoconstrictor) [2].

Most research studies regarding the role of sildenafil in CVS are mainly on animal models with few studies on human subjects. A Phase 1 prospective non-randomized trial on 12 human subjects postulates that sildenafil can be a safe and effective choice for CVS. During the trial phase 1, they administered 10 mg of Sildenafil IV over 30 minutes to 5 SAH patients (CVS diagnosed) then after ensuring safety, they increased the dose to 30 mg IV over 30 minutes in the other 7 patients in Phase 2 of the trial. Side Effects were tolerable with minimal effects on intracranial pressure, cardiac rhythms, pulmonary, neurologic status and the main side effect was hypotension. According to the study, the degree of hypotension was tolerable and not life threatening. Their results are promising as 8 of 12 patients had positive angiographic response (3 in low dose group and 5 in high dose group) [2].

Other groups investigated the role of sildenafil in CVS. A group in India did a feasibility study and concluded that sildenafil may be effective in refractory symptomatic vasospasm but more effective trials on humans needed [3]. Another group did an experiment on 24 rabbits divided into 4 groups (1st group sham- surgery, 2nd group SAH, 3rd group like 1st group but received sildenafil, 4th group like 2nd group but received sildenafil) and their results that sildenafil can reverse CVS but doesn't affect the apoptotic process [4]. In addition, some other studies with interesting results are paving a way for more powerful well organized randomized studies to prove the effectiveness and safety of sildenafil in CVS after SAH [5-9].

In our point of view, Sildenafil use in the management of CVS following SAH can be a promising discovery for many reasons. First, the current management modalities using cerebral angiography are invasive with a risk of morbidity and mortality. Second, it is cost effective (sildenafil is a cheap drug in comparison to the high cost of performing cerebral angiography with angioplasty or intraarterial vasodilators). Third, it is time saving (imagine giving a deteriorating patient sildenafil over few minutes vs transferring him to a catheterization lab to perform angiography). Fourth, FDA approved the drug for other indications like pulmonary hypertension, sexual dysfunction so it is considered relatively a safe drug with tolerable side effects. On the other hand, Recent trials results can't be generalized. They are mostly on animals, very few on human subjects. So, we need more organized powerful greater sample size randomized studies to legalize and prove the usage of sildenafil in CVS after SAH.

Now, do you agree with us Sildenafil for CVS after SAH can be a breakthrough?!

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