REVIEW ARTICLE

IS CONSCIOUS SEDATION ASSOCIATED WITH BETTER OUTCOMES IN PATIENTS UNDERGOING ENDOVASCULAR TREATMENT FOR ACUTE ISCHEMIC STROKE?

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ABSTRACT: Advances in the management of stroke include endovascular procedures aimed at reperfusion of the occluded arteries in the brain. Although, there are no clear benefits of endovascular procedures over IV thrombolysis, endovascular procedure is most frequently employed. Depending on the institutional preferences, the procedure is carried out either under local anesthesia with conscious sedation or general anesthesia. In the absence of a prospective study, retrospective analyses have reported the better clinical outcomes with conscious sedation over general anesthesia. A meta-analysis of the retrospective studies showed higher rates of good functional outcome and recanalization and decreased rates of mortality and respiratory complications with conscious sedation compared to general anesthesia. Based on the available evidence and in the absence of a guideline, the Society of Neuroscience in Anesthesiology and Critical Care (SNACC) created a task force to provide expert consensus recommendations on the use of anesthesia during endovascular procedures. However, future prospective randomized control trials are warranted to evaluate the outcomes of retrospective studies.

INTRODUCTION: Stroke is a major healthcare problem that is silently turning into an epidemic among Indians. Stroke is the third major cause of mortality.[1] Most often patients surviving stroke carry the risk of disabilities in terms of physical dependence, cognitive decline, dementia, depression, and seizures.[1] The prevalence of stroke in rural and urban India is estimated at 84–262/100, 000 and 334-424/100, 000, respectively.[2] It has been projected that more than 1 million people per year will be affected by stroke.[3] Treatment aimed at restoring the blood flow to the ischemic brain is the basis of effective therapy for acute ischemic stroke. Intravenous (IV) thrombolysis with recombinant tissue plasminogen activator (rtPA) is the United States Food and Drug Administration (FDA)-approved treatment for acute ischemic stroke.[4] Moving a step further, nearly two decades ago, endovascular therapy with intra-arterial administration of thrombolytic agents for acute ischemic stroke was introduced. Later, endovascular treatment of acute ischemic stroke evolved through catheter-based drug administration, mechanical embolectomy, and angioplasty with stent placement.[4]

Three recent randomized trials [Interventional Management of Stroke (IMS) III, Mechanical Retrieval and Recanalization of Stroke Clots Using Embolectomy (MR RESCUE), and Synthesis Expansion: A Randomized Controlled Trial on Intra-Arterial Versus Intravenous Thrombolysis in Acute Ischemic Stroke (SYNTHESIS Expansion)] evaluating the efficacy of

endovascular treatment of acute ischemic stroke did establish any clinical benefit from endovascular treatment.[5, 6] Nevertheless, endovascular therapies are being used at a higher rate than IV thrombolysis and will continue to be used as a treatment option for acute ischemic stroke.[6, 7] Practically, endovascular therapies are administered either under general anesthesia or local anesthesia at the puncture site with conscious sedation. Each method of sedation has its own advantages and disadvantages and hence researchers have compared the clinical outcome of endovascular therapies under both the conditions of sedation.

Outcome of endovascular therapies under general vs. conscious sedation: Vessel recanalization is an important predictor of clinical outcome in the treatment of acute ischemic stroke. In the absence of a prospective study, retrospective studies report that general anesthesia has a negative impact on the clinical outcomes (such as neurologic, radiographic, or mortality) in patients undergoing endovascular therapy for acute ischemic stroke (Table 1).[7-16]

Table 1.A comparison of conscious sedation vs. general anesthesia during endovascular therapy in retrospective studies

Study	Treatment allocation	Vessels occluded	Endovascular procedure	Outcome measure	Outcome	Authors conclusion
Abou-Chebl A et al. 2010	980 patients at 12 stroke centers [conscious sedation (651) and general anesthesia (428)]	Anterior circulation strokes due to large-vessel occlusion	Intra-arterial. tissue plasminogen activator, mechanical thrombectomy, stent	Neurologic outcome and mortality	The use of GA was associated with poorer neurologic outcome at 90 days (odds ratio=2.33; 95% CI, 1.63-3.44; p<0.0001) and higher mortality (odds ratio=1.68; 95% CI, 1.23-2.30; p<0.0001) compared with conscious sedation.	Although there are no differences in hemorrhagic complications between the two groups, general anesthesia is associated with higher risk of poor neurologic outcome and mortality.

Jumaa et al. 2010	126 patients [conscious sedation (73) and general anesthesia (53)]	Acute stroke due to middle cerebral artery-M1 segment occlusion	Intra-arterial. tissue plasminogen activator and mechanical thrombectomy	Clinical and radiographic outcomes (final infarct volume, Modified Rankin Scale score ≤2 and In-hospital death)	No significant differences primary outcome were observed between the two groups (general anesthesia with intubation state vs. nonintubated state	Treating patients in nonintubated state appears to be as safe as treatment in intubated state but may result in more favorable clinical and radiographic outcomes
Nichols et al. 2010	75 patients [conscious sedation (26) and general anesthesia (49)]	Anterior circulation strokes	Intra-arterial. tissue plasminogen activator, low-energy ultrasound	Clinical outcomes including successful angiographic reperfusion and the occurrence of clinical complications	Patients in the lower sedation category fared better [higher rate of good outcomes ($p<0.01$), lower death rates ($p=0.02$), and higher successful angiographic reperfusion rates ($p=0.01$)] Clinical complications (infection rate) was higher in patients receiving	Patients not receiving sedation exhibited better clinical outcome in terms of higher rates of successful angiographic reperfusion and fewer complications.

					heavy sedation or pharmacologic paralysis (p=0.02).	
Sugg et al. 2010	66 patients [conscious sedation (57) and general anesthesia (9)]	Acute stroke due to internal carotid, middle cerebral and vertebrobasilar occlusion	Mechanical thrombectomy	Time to groin puncture, the length of the procedure, or revascularization rates, good outcome, and mortality	There were no differences between groups in the time to groin puncture, the length of the procedure, revascularization rates, or mortality Good outcome was significantly better in the nonanesthetized patient group (50.9% versus 11.1%, p=0.155) but was not controlled for other factors	Mechanical embolectomy in nonanesthetized patients is effective and should be considered an option in the treatment of the patient with acute ischemic stroke.

Davis et al. 2012	96 patients [conscious sedation (48) and general anesthesia (48)]	Stroke involving middle cerebral artery occlusion, extracranial internal carotid occlusion, intracranial carotid "T" occlusion, and basilar artery occlusion	Intra-arterial. tissue plasminogen activator and mechanical thrombectomy	Modified Rankin Score of 0-2 for 3 months poststroke	The relative risk of good outcome with local anesthesia was 3.2 (1.5– 6.8) Mortality was more likely in the patients that received general anesthesia than in those managed with local anesthesia (relative risk: 2.3, or 1.1–3.7; p=0.039)	Patients receiving general anesthesia for treatment are less likely to have a good outcome than those receiving local anesthesia.
Hassan et al. 2012	136 patients [conscious sedation (83) and general anesthesia (53)]	Not specified	Endovascular technique not specified	Modified Rankin score of ≥ 3 and in-hospital mortality	Poor outcome at discharge (odds ratio 2.9, 95% CI 1.2-7.4) (p=0.0243) and in-hospital mortality (odds ratio 4.5, 95% CI 1.5-12.5) (p=0. 0.0046) were significantly higher among	Since the rate of death and disability appears to be high, caution to be exercised when intubating stroke patients for endovascular treatment

					intubated patients	
Langner et al. 2013	124 patients [conscious sedation (105) and general anesthesia (19)]	Anterior circulation and in the posterior circulation strokes	Mechanical thrombectomy	Conversion from conscious sedation to general anesthesia, recanalization rate, infarct volume and peri- and post-procedural complications	There were no significant differences for recanalization rate and complications between the two groups. The mean procedure time was significantly shorter in patients treated under CS ($p<0.01$)	Endovascular stroke therapy with conscious sedation is feasible, can be performed safely and is faster than with general anesthesia
Whalin et al. 2014	216 patients [conscious sedation with α2 adrenergic agonist dexmedetomidine (83) and general anesthesia (133)]	Anterior circulation strokes		Radiographic angiographic variables, hemodynamic changes	Hemodynamic changes during the procedure was significant with general anesthesia	Dexmedetomidine can be safely administered in patients undergoing endovascular reperfusion therapies.
Li et al. 2014	109 patients [conscious sedation (74) and general anesthesia	Acute stroke due to intracranial arterial occlusion	Mechanical thrombectomy, intra-arterial. tissue plasminogen activator	Clinical outcome	The duration of the procedure and the time-to-revascularization from	Prospective randomized control trials are warranted to evaluate the effects of conscious

	(35)]				symptom onset were significantly longer in the general anesthesia group. Mortality was higher in the GA group compared with the CS group (40% vs. 22%, p=0.045)	sedation and general anesthesia on the clinical and radiographic outcomes.
Abou-Chebl et al. 2014	281 patients [conscious sedation (85) and general anesthesia (196)]		Solitaire stent	90-day modified Rankin Scale, mortality, and symptomatic intracranial hemorrhage	Recanalization (thrombolysis in cerebral infarction ≥2b; 72.94% versus 73.6%; p=0.9) and rate of symptomatic intracranial hemorrhage (7.1% versus 11.2%; p=0.4) were similar between the groups Modified Rankin Scale ≤2 was	The clinical outcomes and survival are significantly better in patients treated with local anesthesia, without increased symptomatic intracranial hemorrhage risk.

					achieved in more local anesthetic patients [52.6% vs.35.6% (odds ratio, 1.4 (1.1-1.8); p=0.01]	

A recently published systematic and meta-analysis reviewed nine studies (from table1) related to the use of general anesthesia and conscious sedation in stroke patients undergoing endovascular treatment.[17] The study assessed recanalization rate, good functional outcome (mRS≤2), asymptomatic and symptomatic intracranial hemorrhage, death, vascular complications, respiratory complications, procedure time, time to groin, and time from symptom onset to recanalization. Patients receiving general anesthesia (six studies) had a higher average National Institute of Health Stroke Score (NIHSS) score. The odds of death [odds ratio (OR)=2.59; 95% CI, 1.87–3.58] and respiratory complications (OR=2.09; 95% CI, 1.36–3.23) were higher among patients undergoing endovascular procedure under general anesthesia. The odds of lower odds of good functional outcome (OR=0.43; 95% CI, 0.35–0.53) and successful angiographic outcome (OR=0.54; 95% CI, 0.37–0.80) was lower among patients undergoing endovascular procedure under general anesthesia. There was no difference in procedure time (p=0.28) between the two groups. The outcome of the meta-analysis showed that conscious sedation was associated with higher rates of good functional outcome and recanalization and decreased rates of mortality and respiratory complications compared to general anesthesia.[17]

Anesthesia for endovascular therapies: Points to ponder: Literature on the anesthetic management of endovascular treatment of acute ischemic stroke is limited. However, retrospective studies have shown favorable outcomes with conscious sedation. Current practice is largely driven by institutional preferences on the type of anesthesia for endovascular treatment.[18] The basic challenges is the deciding the type of anesthesia for acute ischemic patients undergoing endovascular procedure is related to individual patient factors such as assessment of neurologic status, airway, ability of the patient to cooperate with the procedure, anticipated technique and procedure time, and planned post procedure care.[19] In addition, the general risks of the type of anesthesia also plays an important role in decision making.

Pros and cons of general anesthesia and local anesthesia: In comparison to general anesthesia, local anesthesia with conscious sedation has several advantages, which include: less chance of delayed recanalization, provision for performing neurologic assessments at different stages during the procedure, shorter stay in intensive care unit (ICU), and earlier mobilization. On the contrary, conscious sedation has several disadvantages which include compromise on

airway protection and patient discomfort, which may lead to lack of cooperation and uncontrolled movements during the procedure. The latter reason is the strong indication for performing endovascular procedures under general anesthesia as the procedure is easier and safer to perform in a motionless patient.[9] Of the several reasons for poorer outcome with general anesthesia, hemodynamic instability and hypotension, delays in treatment, prolonged intubation with or without neuromuscular blockade, or neurotoxicity of the anesthetic agent itself are some of the cited reasons.[19]

Perception of the treating interventional neurologists: To understand the sedation practices in acute ischemic stroke, McDonagh et al. conducted a survey among 68 active members of the Society of Vascular and Interventional Neurology (SVIN).[20] Nearly three-fourth of the respondents (71.4%) was interventional neurologists practicing for 1-5 years. The most frequent type anesthesia used was general anesthesia (involvement of an anesthesia team), then conscious sedation (administered by a nurse), monitored anesthesia care (involvement of an anesthesia team), and finally local analgesia alone. They perceived that general anesthesia eliminated movement, the procedure was safer and efficacious. According to them, risk of time delay, propagating cerebral ischemia due to hypoperfusion or other complications and lack of adequate anesthesia workforce were the limitations of general anesthesia.[20]

Limitations of the retrospective studies: Literature data shows that patients generally had a poorer outcome under general anesthesia when compared to conscious sedation. This observation probably needs to be taken with a pinch of salt because in most of the studies, patients receiving general anesthesia were sicker (i.e., higher baseline values on the neurologic stroke scale) at baseline than patients receiving local anesthesia and/or sedation.[21] Hence, they had more likelihood of higher post procedure stroke volume, morbidity, and mortality. An additional contributor to poor outcome with general anesthesia is the peri-procedural hypotension that could have adversely contributed to loss of cerebral autoregulation and reliance on collateral circulation.[21]

SNACC expert consensus: The Society of Neuroscience in Anesthesiology and Critical Care (SNACC) created a task force to provide expert consensus recommendations on anesthetic management of endovascular treatment of acute ischemic stroke.[18] The recommendations on the choice of anesthetic technique advocates individual customization of the anesthetic technique in coordination with the neurointerventionalist.

- Uncooperative patients, patients with elevated neurological severity, who unable to protect their airways (such as those with posterior circulation stroke, depressed level of consciousness, or compromised respiration) may receive general anesthesia.
- Patients with anterior circulation stroke who can protect their airway and are cooperative may receive either local anesthesia with sedation or general anesthesia.
- Anesthesiologists should be prepared to convert patients from local anesthesia to general anesthesia, if required.

CONCLUSION: Stroke is a major epidemic with significant mortality and morbidity. Reperfusion of the occluded arteries is achieved with IV thrombolysis with rtPA or through endovascular treatment procedures. Endovascular treatment procedures done under conscious sedation or general anesthesia have different impact on the clinical. This observation was made from retrospective studies. In the absence of prospective randomized controlled trials, the SNACC have issued consensus guidelines on the use of anesthesia for endovascular treatment procedures in stroke patients. Currently, the choice of anesthesia during these procedures is still mostly dependent on individual or institutional preferences. General anesthesia may be suitable for patients with severe deficits, compromised airway, or bulbar dysfunction and continuous sedation may be suitable for those with milder deficits or those with feeble hemodynamic status. Until randomized controlled trial data on the use of general anesthesia vs. conscious sedation during acute ischemic stroke interventions provides the highest level of evidence to guide therapy, the choice of anesthesia should be customized to individual needs.

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