

Systemic care in the acute management of patients with stroke

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Abstract

Early and effective systemic management plays an important role in the outcome of patients with stroke. Vigilant respiratory and hemodynamic monitoring and optimisation along with nutritional and metabolic correction goes a long way in improving results of definitive treatment in patients with stroke. This review discusses the systemic changes occurring after stroke and provides current evidence in the management of these factors, which significantly influence the outcome.

Key words: Cerebral oxygenation, intensive care, intracerebral haematoma, ischemia, stroke

INTRODUCTION

Derangements in the systemic physiology in the acute phase significantly influence the functional outcome of stroke. Up to 30% of all stroke patients deteriorate in the first 24 hours requiring close neurological, haemodynamic and respiratory monitoring and associated care.^[1] Dedicated stroke units or stroke intensive care units (ICUs) have been reported to improve the outcome after acute stroke.^[2]

Management of a patient with acute stroke revolves around factors that determine cerebral perfusion and oxygenation. While definitive treatment in the form thrombolysis for ischaemic stroke and surgical evacuation of haematoma in haemorrhagic stroke are in progress, efforts should be made to optimise cerebral blood flow (CBF) and oxygenation such that the neuronal loss and consequent long-term neurological deficits could be minimised. Figure 1

shows the role of optimising systemic physiology in maintaining the delicate balance between cerebral oxygen demand ($CMRO_2$) and oxygen supply. Jugular venous oxygen saturation ($SjvO_2$) (normal: 55-75%), is generally used as a gross approximation of adequacy of cerebral oxygenation. A low $SjvO_2$ value signifies oxygen delivery that is disproportionately low compared with the metabolic demands of the brain and hence, the threat of ischaemia. The converse is expected when the $SjvO_2$ is higher than 75%, which indicates that the cells are unable to utilise the oxygen, and there is a risk of infarction.

In a critically ill stroke patient, decrease in cerebral oxygenation (low $SjvO_2$ or a high $CMRO_2/CBF$) is related to a decrease in CBF or an increase in $CMRO_2$. Several reversible epiphenomena may contribute to this ischaemic/hypoxic process. These phenomena include arterial hypoxia, hypocapnia, systemic arterial hypotension, anaemia, raised intracranial pressure (ICP) and cerebral vasospasm. Correction of the $CMRO_2/CBF$ imbalance, thus, calls for optimisation of haemodynamic and respiratory variables and measures to maintain CBF and control ICP. Practical approaches to the management of these factors in a patient with acute stroke are discussed later.

RESPIRATORY CARE

Maintaining adequate tissue oxygenation is very important in the setting of acute stroke. Respiratory

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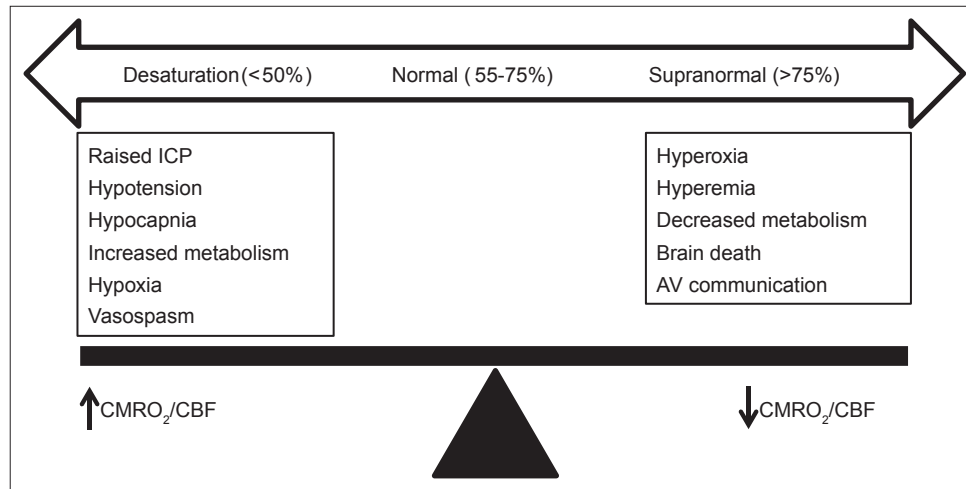


Figure 1: Factors affecting the cerebral oxygen demand and supply balance

care efforts should be directed at preventing cerebral hypoxia. The most common causes of hypoxia are airway obstruction, hypoventilation, irregular breathing patterns, aspiration pneumonia, pulmonary oedema and atelectasis. Patients with decreased consciousness or brain stem dysfunction (posterior circulation stroke) have the highest risk of airway compromise because of impaired oropharyngeal mobility and loss of protective reflexes. Medical complications occur in 59% of stroke patients, with pneumonia occurring in about a third of them and contributing to prolonged ICU/hospital stay and higher mortality (26.9% vs 8.2% with and without pneumonia).^[3] Elective intubation, frequent positional change, chest physiotherapy, humidification of inspired gases, good oral care, appropriate antibiotic therapy, prompt diagnosis and treatment of chest infection along with early mobilisation and swallowing rehabilitation go a long way in improving outcomes after acute stroke.^[3] Elective tracheal intubation apart from preventing aspiration pneumonia, also facilitates management of increased ICP or malignant brain oedema after stroke.^[4] Therefore, tracheal intubation may be considered when any of the above-mentioned respiratory abnormalities are not corrected by simple measures such as introduction of an oropharyngeal airway and administration of oxygen by mask. Tracheal intubation, however, is not without its risks in patients with stroke. Laryngoscopy and intubation may cause cardiovascular stress, intracranial hypertension and pulmonary aspiration. An ideal technique of intubation requires suppression of these responses with sedative/hypnotic drugs and cricoid pressure to prevent pulmonary aspiration. Attention must be paid to the hypotension that may be caused by the sedative drugs. Pragmatic choice of the sedative drugs and their dosages, a good intravenous access for administration of fluids/vasopressors in case of hypotension and adequate pre-oxygenation before intubation help to

prevent dangerous levels of hypotension and hypoxia that threatens the viability of the already vulnerable neurons. Despite these theoretical advantages of active respiratory management, views have been expressed on the futility of endotracheal intubation in stroke; studies have shown that 50% of intubated patients die within 30 days after stroke with pneumonia being the leading cause of death.^[5] A practical approach to this dilemma has been suggested by Gujjar *et al.*, who, advocate that mechanical ventilation may be provided for patients with severe stroke with the understanding that it could be withdrawn if there was no neurologic improvement or further deterioration. Defining, in advance, a specific degree of neurologic improvement within a predetermined time frame may serve to establish the futility of the situation. Mechanical ventilation may also be used in preparation for other, potentially useful but unproven interventions.^[6]

Hyperventilation, as an ICP control measure, has attracted the clinicians' attention for a long time. While the ability of hypocapnia to cause cerebral vasoconstriction and decrease in the ICP rapidly remains undisputed, its potential to cause cerebral ischaemia has come under closer scrutiny recently. Unless hyperventilation is specifically intended as a treatment strategy for intracranial hypertension that is not amenable for simpler measures, a ventilatory setting that achieves normocapnia ($\text{PaCO}_2 = 35 \text{ mmHg}$) and mild to moderate hyperoxia ($\text{PaO}_2 = 150\text{-}200 \text{ mmHg}$) and does not impose excessive work of breathing on the patient's respiratory muscles, is acceptable. Most often, mechanical ventilation is started in a controlled mode (either volume or pressure control) and then changed to an assisted mode (pressure support mode) as neurological improvement occurs. It is important to appreciate the effect of PaO_2 and PaCO_2 changes on CBF. CBF is linearly related to PaCO_2 in the range of 20-80 mmHg. In subjects with

intact vascular reactivity, hypercapnia causes cerebral vasodilation (with consequent increase in ICP) and hypocapnia causes cerebral vasoconstriction (with a possible reduction of ICP, but potential risk of cerebral ischaemia). In general, vascular reactivity to carbon dioxide is a robust response that is affected only by extreme degrees of pathology. Decrease in PaO₂ up to 60-50 mmHg has minimal effect on CBF. Any further decrease, however, is associated with a steep increase in CBF and ICP. Survival of the neurons in the penumbral zones is heavily dependent on a normal arterial oxygen tension or even a mild degree of hyperoxia. Therefore, it is ideal to target a PaO₂ of 100 mmHg or more during the acute phase.

Concerns have been expressed about the effect of positive pressure ventilation and positive end expiratory pressure (PEEP) in particular, on ICP and cerebral perfusion. PEEP up to 12 mmHg has been shown to significantly decrease mean arterial pressure and in turn cerebral perfusion pressure (CPP) with negligible effect on ICP in patients with acute stroke.^[7]

Sedation and/or neuromuscular blockade are necessary to facilitate mechanical ventilation in all patients with stroke. Opioids (morphine, fentanyl) and benzodiazepines (midazolam) are commonly used for this purpose. Of late, dexmedetomidine is being increasingly used in neurologically critical patients, as it has a favourable haemodynamic and respiratory profile and it facilitates frequent neurological assessment. Most often, sedatives are given as continuous infusions. Some centres prefer to use hypnotic drugs such as thiopentone or propofol as continuous infusions. Both the drugs, apart from providing hypnosis, also decrease the ICP, but have a tendency to cause systemic hypotension, which may adversely affect CPP and CBF. Muscle relaxants are to be used sparingly. Both succinyl choline and rocuronium offer ideal conditions for smooth and rapid intubation. But succinylcholine may cause hyperkalaemia, cardiac arrhythmias and transient increase in ICP. Vecuronium, rocuronium and atracurium are the competitive neuromuscular blocking agents that are commonly used as continuous infusions. These drugs cause minimal hemodynamic changes.

HAEMODYNAMIC MANAGEMENT

In health, autoregulatory mechanisms maintain CBF constant over a CPP range of 50-150 mmHg. In this physiological range, any increase in CPP causes cerebral vasoconstriction and a decrease, causes cerebral vasodilatation. At CPP values below or above this autoregulatory range, CBF becomes pressure-passive. The autoregulatory range is shifted rightward in chronically hypertensive individuals, which implies that

in these patients the lowest CPP compatible with normal CBF is higher than in normal individuals.

CBF autoregulation is impaired after stroke. Such impairment occurs both in the cerebral hemisphere with stroke and the contralateral hemisphere too.^[8] In the absence of autoregulation, blood pressure becomes a crucial parameter that affects the blood flow to the potentially vulnerable penumbra.

The strategies of blood pressure management differ between ischaemic and haemorrhagic stroke. Hypertension is prominent during the initial phase, irrespective of the nature of the stroke. Risks *vs* benefits of correcting such hypertension have been extensively debated. Uncontrolled hypertension leads to cardiac de-compensation, and increase in brain oedema in ischaemic stroke and extension of haematoma in intracerebral haemorrhage. In contrast, aggressive control of hypertension worsens cerebral ischaemia. The international stroke trial showed a 'U' shaped relation between blood pressure and mortality in patients with ischaemic stroke.^[9] Excessively high or low values are associated with poor outcome; for every 10 mmHg increase in systolic BP (SBP) >150 mmHg, mortality increased by 3.8% and for every 10 mmHg decrease in BP <150 mmHg, mortality increased by 17.9%.^[10]

In patients with intracerebral haemorrhage (ICH), a recent multicentre study showed that SBP >150 mmHg doubled the risk of death or dependency.^[11] Earlier, evidence has also shown that persistent high blood pressure will result in expansion of the haematoma and poor outcome.^[12] However, concerns about ischaemia in the peri-haematoma brain tissue, limited the enthusiasm for aggressive reduction of blood pressure in acute ICH. The American Heart Association/American Stroke Association (AHA/ASA) guidelines recommend aggressive control of SBP >200 or MAP >150 mmHg guided by frequent blood pressure monitoring (every 5 min). In patients with elevated ICP, the recommended MAP is <130 mmHg for the first 24 hours and in patients without suspected elevated ICP, the MAP goal is <110 mmHg. After a de-compressive craniotomy, the recommended MAP is 100 mmHg.^[13] As data to guide management of the lower limits of blood pressure after ICH are non-existent, a MAP is >90 mmHg with a CPP >70 mmHg is recommended in all cases.^[14] A recent study, which compared the haematoma volume at 24 hours between aggressive blood pressure reductions versus standard ASA, recommended blood pressure control, observed a 22.6% difference (13.7% vs 36%, respectively) in haematoma expansion.^[15] The anti-hypertensive agents recommended are short acting intravenous drugs like labetalol, esmolol, nicardipine and enalapril over nitroglycerin or nitroprusside.^[13] The latest AHA/ASA guidelines (2010) suggest that

lowering of SBP to 140 mmHg (within 1 hour) is probably safe.^[16]

In acute ischaemic stroke, though elevated blood pressure improves penumbral perfusion, if rapid and sustained, it may lead to cerebral oedema and haemorrhagic transformation.^[14] However, for patients who are not candidates for thrombolytic therapies and have critical vascular stenosis, blood pressure augmentation is the only way to perfuse the penumbra. The AHA/ASA 2007 guidelines recommend treatment of hypertension when SBP >220 mmHg or DBP >120 mmHg with a maximum reduction of 15% in the first 24 hours in patients who are not candidates for thrombolytic therapies and to SBP <185 mmHg and DBP <110 mmHg in candidates for thrombolytic therapy. Though hypotension is relatively rare after stroke, its presence should alert the clinician to look for and correct hypovolemia and a decreased cardiac output state. Inotropes and vasopressors have been successfully used to augment the blood pressure after the above measures have failed.^[4,17]

TEMPERATURE MANAGEMENT

Temperature at admission in acute stroke patients has a correlation with the outcome, with higher temperatures being associated with worsened outcome. A 1°C spontaneous hypothermia has been shown to double the odds of good outcome after ischaemic stroke.^[18] The beneficial role of therapeutic hypothermia both in ischaemic and haemorrhagic stroke patients has been inconsistent in clinical studies, despite promising findings in experimental conditions.^[19] A high incidence of brain oedema and herniation during rewarming, bradycardia, thrombocytopenia and pneumonia have been reported in these studies. Various factors like the degree and duration of cooling, the re-warming rate and the method of rewarming have all been implicated for varying results of hypothermia in the numerous studies. While the beneficial role of hypothermia is doubtful, the need for control of hyperthermia cannot be overemphasised. The current AHA/ASA guidelines suggest aggressive management of fever in acute stroke patients with antipyretics like acetaminophen (up to 6000 mg/day), aspirin and ibuprofen. It also described that temperature >38°C may not respond to the antipyretics. Seeking and treating the possible source of fever is a more prudent option. The guidelines do not recommend therapeutic hypothermia for patients of stroke.^[4]

GLUCOSE MANAGEMENT

About a third of patients with stroke manifest with hyperglycaemia and the presence of hyperglycaemia

is associated with increased infarct size and poor outcome.^[20] In a systematic review of observational studies examining the prognostic impact of hyperglycaemia in acute stroke, the relative risk of in-hospital or 30-day mortality was 3.07 (95% CI, 2.50-3.79) in non-diabetic patients and 1.30 (95% CI, 0.49-3.43) in those with diabetes.^[21] Therefore, management of glucose during early phase forms an important part of acute care of stroke. Whether the effective regulation of glucose results in improvement of outcome and what is the acceptable target glucose level that needs to be maintained within the first 24 hours of stroke, remain inconclusive. In a large clinical trial by GIST-UK group, of the 464 acute stroke patients who were treated with the glucose potassium insulin (GKI) infusion, 30% died within 90 days compared with 27.3% among the 469 patients who received saline ($P = 0.37$).^[22] The recent guidelines advocate initiating insulin therapy at glucose level >200 mg/dl and maintaining it between 140 and 180 mg/dl within the first 24 hours of stroke.^[4] Till date, studies have not been able to elucidate whether acute hyperglycaemia in stroke is a cause of neurological deterioration or it is just an epiphenomenon related to the severity of stroke.^[23] In either case, it is reasonable to actively treat hyperglycaemia during the acute phase of stroke without focusing on the specific insulin regimen or the time course for achieving the target. Caution should be exercised to avoid hypoglycaemia by continuously monitoring the glucose levels throughout the clinical course.^[24] Similar suggestions have been made in patients with haemorrhagic stroke too.^[16]

FLUID AND ELECTROLYTE MANAGEMENT

Fluid management in stroke patients requires a systematic approach with regular assessment of clinical and biochemical markers of dehydration and over-hydration. Patients with stroke may present with signs of over-hydration or under-hydration. Initial dehydration is hyperosmolar, caused by an inadequate intake of water due to drowsiness, dysphagia, reduction in thirst, or presence of infection. Dehydration, leading to haemoconcentration and a reduction in blood pressure, can worsen the ischaemic process and also predispose the patient to stroke recurrence. Stroke patients with high plasma osmolality levels on admission have lower survival rates.^[25] The conventional approach of keeping stroke patients dehydrated in order to prevent cerebral oedema is deleterious to the ischaemic brain. Hyponatraemia is a common finding in patients with stroke affecting about 16% of the stroke patients. Further, it has been shown to be associated with both increased in-hospital mortality and death at 3 and 12 months.^[26] Therefore, attempts should be maintained to maintain homeostasis of sodium and other electrolytes.

Some fundamental principles to be adopted in the fluid management of patients with cerebral ischaemia are: (a) hypotonic solutions should be avoided, (b) rapid changes in serum osmolality have an overwhelming influence on brain oedema; even a minor decrease in serum osmolality may increase the brain water content, (c) hyperglycaemia during acute phase of stroke can be deleterious to the injured brain and should be avoided. There are no studies that examined the effect of the type and quantity of fluid on the outcome of stroke. Studies on volume expansion and haemodilution up to a haematocrit of 30% demonstrated improved CBF and perfusion of potentially viable penumbral tissue, but they are currently not recommended as these measures did not improve the mortality.^[4]

Cerebral ischaemia or haemorrhage is almost always accompanied by raised ICP. Mannitol effectively reduces ICP and also appears to benefit brain metabolism.^[27] Hypertonic saline (HTS) (3% and 7.5% NaCl) is being increasingly used for control of raised ICP in stroke patients with some studies suggesting that the initial ICP reduction is more rapid with HTS than with mannitol.^[28] Apart from its beneficial effect on the injured brain, HTS has been shown to attenuate the stroke associated increase in lung water content in an experimental model. These findings provide an opportunity for a potential therapeutic role in the management of neurogenic pulmonary oedema in stroke patients.^[29] HTS by reducing the extracellular lung water and improving the cardiac output and systemic vascular resistance can enhance oxygen delivery and perfusion to the injured brain.^[30] Increase in extracellular lung water can compromise gas exchange and thereby cerebral oxygenation. If this is associated with hypotension caused by diuretics, mannitol or dehydration, it can be deleterious in both forms of stroke.

PREVENTION OF VENOUS THROMBO-EMBOLISM (VTE)

Intermittent pneumatic compression and elastic stockings along with low dose subcutaneous low-molecular-weight heparin (LMWH) or unfractionated heparin (UH) after 1-4 days of haemorrhagic stroke is recommended in patients who are immobile.^[16] These recommendations are based on the two CLOTS trials, which found the elastic stockings to be ineffective in preventing VTE in patients with stroke.^[31,32] In patients with acute ischaemic stroke and immobility who do not have contraindication for anticoagulants, either LMWH or UH is recommended as these agents reduce VTE by about 75%.^[4]

PREVENTION OF SECONDARY STROKE

The antiplatelet agents aspirin and clopidogrel are efficacious in the secondary prevention of stroke. Aspirin

irreversibly acetylates the cyclooxygenase enzyme suppressing production of thromboxane A₂ and inhibiting activation and aggregation of platelets. Aspirin results in relative risk reduction of about 15% for secondary stroke. The major adverse effect of even low dose therapy (<325 mg/day) is gastrointestinal haemorrhage. Clopidogrel inhibits adenosine diphosphate-induced activation and aggregation of platelets by irreversibly blocking P₂Y receptor on platelet membrane. A 75 mg dose of clopidogrel has been shown to be more effective than 325 mg of aspirin in preventing secondary stroke. Cilostazol, a phosphodiesterase 3 inhibitor, prevents inactivation of cyclic adenosine monophosphate and irreversibly inhibits platelet aggregation and is shown to be more effective in the dose of 200 mg/day in preventing secondary stroke with minimal bleeding risk.^[33]

NUTRITION

Fifty percent of patients with severe stroke are malnourished at 2-3 weeks after the stroke and this is associated with higher rate of complications and poorer functional outcomes.^[1] Nasogastric feeding with a 30° head end elevation can be initiated within 3-4 days of occurrence of stroke to supplement nutrition. It may be continued until the swallowing function is assessed and found adequate. Though dysphagia resolves in most of the patients, early gastrostomy might help in a select few in whom improvement in swallowing function is unlikely.^[1]

SOME IMPORTANT ASPECTS OF MONITORING

Given the impact of systemic physiology on outcome of stroke, monitoring of patients with acute stroke becomes critical for early detection of haemodynamic, respiratory and neurological changes. Those patients with acute stroke, who are not intubated, should be monitored by pulse-oximetry to maintain a target oxygen saturation of at least 92% and if required supplemental oxygen (2-4 l/min) should be provided. If the oxygen saturation is not maintained, the cause should be investigated by an arterial blood gas and a chest X-ray. Patients with stroke also are at the risk of developing myocardial infarction and arrhythmias. Insular stroke in particular, results in increased cardiac complications due to disturbances in autonomic nervous system function. Elevated myocardial enzymes and electrocardiographic changes (ischaemia/arrhythmia) are common, necessitating close cardiovascular monitoring. Routine non-invasive cardiac event recording after acute stroke enhances detection of paroxysmal atrial fibrillation (44% vs 4% in standard monitoring) and facilitates early anticoagulation.^[34] High body temperature, high

blood glucose and high systolic blood pressure have been shown to be associated with poor outcome and frequent monitoring and optimisation of these systemic parameters is likely to improve outcome in these patients.^[35] The AHA/ASA guidelines recommend vigilant cardiovascular monitoring for at least 24 hours after acute stroke.^[4] Significant benefits on outcome have been documented from intensive monitoring and systemic interventions based on monitoring.^[36]

STROKE MANAGEMENT: INDIA SCENARIO

Awareness about stroke interventions among patients is low. Even general practitioners have a limited comprehension; hence the low referral rates in the window period for thrombolysis. Aaron *et al.*, in their study found that only one-third of the general practitioners were well-informed about sugar control and management of blood pressure.^[37] Thrombolysis and even mechanical clot removal are being carried out in the country. But these specific treatments are limited to major centres.^[38,39] Therefore, there is a need for a nation-wide survey of the current practices and drawing up a roadmap for improving the awareness among general public and practitioners regarding prompt referral and early intervention. Dedicated stroke care units providing early thrombolysis and a holistic pre- and post-procedural critical care are likely to improve outcomes following stroke.

In conclusion, a good systemic care targeted at maximising oxygen and nutrient delivery to the brain, goes a long way in preserving the viability of the 'threatened' neurons and improves neurological outcomes after stroke.

REFERENCES

- Summers D, Leonard A, Wentworth D, Saver JL, Simpson J, Spilker JA, *et al.* American Heart Association Council on Cardiovascular Nursing and the Stroke Council. Comprehensive overview of nursing and interdisciplinary care of the acute ischemic stroke patient: A scientific statement from the American Heart Association. *Stroke* 2009;40:2911-44.
- Bershad EM, Feen ES, Hernandez OH, Suri MF, Suarez JL. Impact of a specialized neurointensive care team on outcomes of critically ill acute ischemic stroke patients. *Neurocrit Care* 2008;9:287-92.
- Hilker R, Poetter C, Findeisen N, Sobesky J, Jacobs A, Neveling M, *et al.* Nosocomial pneumonia after acute stroke implications for neurological intensive care medicine. *Stroke* 2003;34:975-81.
- Adams HP, Zoppo GD, Alberts MJ, Bhatt DL, Brass L, Furlan A, *et al.* Guidelines for the early management of adults with ischemic stroke. *Stroke* 2007;38:1655-711.
- Grotta J, Pasteur W, Khwaja G, Hamel T, Fisher M, Ramirez A. Elective intubation for neurologic deterioration after stroke. *Neurology* 1995;45:640-4.
- Gujjar AR, Deibert E, Manno EM, Duff S, Diringner MN. Mechanical ventilation for ischemic stroke and intracerebral hemorrhage: Indications, timing, and outcome. *Neurology* 1998;51:447-51.
- Georgiadis D, Schwarz S, Baumgartner RW, Veltkamp R, Schwab S. Influence of positive end-expiratory pressure on intracranial pressure and cerebral perfusion pressure in patients with acute stroke. *Stroke* 2001;32:2088-92.
- Eames PJ, Blake MJ, Dawson SL, Panerai RB, Potter JF. Dynamic cerebral autoregulation and beat to beat blood pressure control are impaired in acute ischaemic stroke. *J Neurol Neurosurg Psychiatry* 2002;72:467-72.
- Leonardi-Bee J, Bath PM, Phillips SJ, Sandercock PA. IST Collaborative Group. Blood pressure and clinical outcomes in the International Stroke Trial. *Stroke* 2002;33:1315-20.
- Potter J, Robinson T, Ford G, James M, Jenkins D, Mistri A, *et al.* CHHIPS Trial Group. CHHIPS (Controlling Hypertension and Hypotension Immediately Post-Stroke) pilot trial: Rationale and design. *J Hypertens* 2005;23:649-55.
- Zhang Y, Reilly KH, Tong W, Xu T, Chen J, Bazzano LA, *et al.* Blood pressure and clinical outcome among patients with acute stroke in Inner Mongolia, China. *J Hypertens* 2008;26:1446-52.
- Ohwaki K, Yano E, Nagashima H, Hirata M, Nakagomi T, Tamura A. Blood pressure management in acute intracerebral hemorrhage: Relationship between elevated blood pressure and hematoma enlargement. *Stroke* 2004;35:1364-7.
- Broderick J, Connolly S, Feldmann E, Hanley D, Kase C, Krieger D, *et al.* American Heart Association, American Stroke Association Stroke Council, High Blood Pressure Research Council, Quality of Care and Outcomes in Research Interdisciplinary Working Group. Guidelines for the management of spontaneous intracerebral hemorrhage in adults: 2007 update: A guideline from the American Heart Association/American Stroke Association Stroke Council, High Blood Pressure Research Council, and the Quality of Care and Outcomes in Research Interdisciplinary Working Group. *Stroke* 2007;38:2001-23.
- Hocker S, Morales-Vidal S, Schneck MJ. Management of arterial blood pressure in acute ischemic and hemorrhagic stroke. *Neurol Clin* 2010;28:863-86.
- Anderson CS, Huang Y, Wang JG, Arima H, Neal B, Peng B, *et al.* Intensive blood pressure reduction in acute cerebral hemorrhage trial (INTERACT). A randomized pilot trial. *Lancet Neurol* 2008;7:391-9.
- Morgenstern LB, Hemphill JC 3rd, Anderson C, Becker K, Broderick JP, Connolly ES Jr, *et al.* American Heart Association Stroke Council and Council on Cardiovascular Nursing. Guidelines for the management of spontaneous intracerebral hemorrhage. *Stroke* 2010;41:2108-29.
- Aiyagari V, Gorelick PB. Management of blood pressure for acute and recurrent stroke. *Stroke* 2009;40:2251-6.
- Reith J, Jorgensen HS, Pedersen PM, Nakayama H, Raaschou HO, Jeppesen LL, *et al.* Body temperature in acute stroke: Relation to stroke severity, infarct size, mortality, and outcome. *Lancet* 1996;347:422-5.
- Yenari MA, Hemmen TM. Therapeutic hypothermia for brain ischemia: Where have we come and where do we go? *Stroke* 2010;41:S72-4.
- Williams LS, Rotich J, Qi R, Fineberg N, Espay A, Bruno A, *et al.* Effects of admission hyperglycemia on mortality and costs in acute ischemic stroke. *Neurology* 2002;59:67-71.
- Capes SE, Hunt D, Malmberg K, Pathak P, Gerstein HC. Stress hyperglycemia and prognosis of stroke in non-diabetic and diabetic patients: A systematic overview. *Stroke* 2001;32:2426-32.
- Gray CS, Hildreth AJ, Sandercock PA, O'Connell JE, Johnston DE, Carlidge NE, *et al.* GIST Trialists Collaboration.

- Glucose-potassium-insulin infusions in the management of post-stroke hyperglycemia: The UK Glucose Insulin in Stroke Trial (GIST-UK). *Lancet Neurol* 2007;6:397-406.
23. McCormick MT, Muir KW, Gray CS, Walters MR. Management of hyperglycemia in acute stroke. How, when, and for whom? *Stroke* 2008;39:2177-85.
 24. Kruyt ND, Biessels GJ, Devries JH, Roos YB. Hyperglycemia in acute ischemic stroke: Pathophysiology and clinical management. *Nat Rev Neurol* 2010;6:145-55.
 25. Bhalla A, Sankaralingam S, Dundas R, Swaminathan R, Wolfe CD, Rudd AG. Influence of raised plasma osmolality on clinical outcome after acute stroke. *Stroke* 2000;31:2043-8.
 26. Rodrigues B, Staffl, Fortunato G, McCullough LD. Hyponatremia in the Prognosis of Acute Ischemic Stroke. *J Stroke Cerebrovasc Dis* 2013; pii: S1052-3057(13)00277-2. doi: 10.1016/j.jstrokecerebrovasdis.2013.07.011. [Epub ahead of print]
 27. Helbok R, Kurtz P, Schmidt JM, Stuart RM, Fernandez L, Malhotra R, *et al.* Effect of mannitol on brain metabolism and tissue oxygenation in severe hemorrhagic stroke. *J Neurol Neurosurg Psychiatry* 2011;82:378-83.
 28. Schwarz S, Schwab S, Bertram M, Aschoff A, Hacke W. Effects of hypertonic saline hydroxyethyl starch solution and mannitol in patients with increased intracranial pressure after stroke. *Stroke* 1998;29:1550-5.
 29. Toung TJ, Chang Y, Lin J, Bharadwaj A. Increases in lung and brain water following experimental stroke: Effect of mannitol and hypertonic saline. *Crit Care Med* 2005;33:203-8.
 30. Farquhar WB, Paul EE, Prettyman AV, Stillabower MA. Blood pressure and hemodynamic responses to an acute sodium load in humans. *J Appl Physiol* (1985) 2005;99:1545-51.
 31. CLOTS Trials Collaboration. Dennis M, Sandercock PA, Reid J, Graham C, Murray G, Venables G, *et al.* Effectiveness of thigh-length graduated compression stockings to reduce the risk of deep vein thrombosis after stroke (CLOTS trial 1): A multicentre randomized controlled trial. *Lancet* 2009;373:1958-65.
 32. CLOTS (Clots in Legs or sTockings after Stroke) Trial Collaboration. Thigh-length versus below-knee stockings for deep venous thrombosis prophylaxis after stroke: A randomized trial. *Ann Intern Med* 2010;153:553-62.
 33. Kikuchi K, Kawahara KI, Miura N, Ito T, Morimoto Y, Tancharoen S, *et al.* Secondary prevention of stroke: Pleiotropic effects of optimal oral pharmacotherapy. *Exp Ther Med* 2012;4:3-7.
 34. Higgins P, Macfarlane PW, Dawson J, McInnes GT, Langhorne P, Lees KR. Noninvasive cardiac event monitoring to detect atrial fibrillation after ischemic stroke: A randomized, controlled trial. *Stroke* 2013;44:2525-31.
 35. Idicula TT, Waje-Andreassen U, Brogger J, Naess H, Lundstadsveen MT, Thomassen L. The effect of physiologic derangement in patients with stroke treated with thrombolysis. *J Stroke Cerebrovasc Dis* 2008;17:141-6.
 36. Cavallini A, Micieli G, Marcheselli S, Quaglini S. Role of monitoring in management of acute ischemic stroke patients. *Stroke* 2003;34:2599-603.
 37. Aaron S, Alexander M, Maya T, Mathew V, Goyal M. Treatment of acute ischemic stroke: awareness among general practitioners. *Neurol India* 2010;58:441-2.
 38. Srivastva MV. Mechanical thrombectomy for acute ischemic stroke: The road thus far. *Neurol India* 2012;60:395-9.
 39. Sharma SR, Sharma N. Hyperacute thrombolysis with recombinant tissue plasminogen activator of acute ischemic stroke: Feasibility and effectivity from an Indian perspective. *Ann Indian Acad Neurol* 2008;11:221-4.

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- If the reference is correct for its bibliographic elements and punctuations, it will be shown as CORRECT and a link to the correct article in PubMed will be given.
- If any of the bibliographic elements are missing, incorrect or extra (such as issue number), it will be shown as INCORRECT and link to possible articles in PubMed will be given.