Predisposing Factors and Management of Hemodynamic Depression Following Carotid Artery Stenting

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Abstract

Carotid artery stenting (CAS) involves dilatation of carotid bulb which can trigger a series of neuronal responses resulting in hemodynamic depression that might influence the outcome of the procedure. This is a frequent but underdiagnosed complication of CAS. Although it is mild, transient and self-limiting in majority of cases, it can result in significant morbidity and mortality if persistent. Neurologists should be aware of the predisposing factors and management of this common complication. In patients who present with stroke following carotid stenting, neurologists should be aware of hypoperfusion secondary to hemodynamic depression as a cause of stroke apart from the stent thrombosis and occlusion.

Keywords: Carotid, depression, hemodynamic, stenting

Introduction

Carotid artery stenting (CAS) is an alternative treatment to carotid endarterectomy (CEA) in selected patients with carotid artery stenosis. Its use is increasing since it is less invasive, produces less discomfort and is associated with reduced length of hospital stay. CAS may, however, be associated with complications like periprocedural stroke, myocardial infarction and death. The use of embolic protection devices has significantly reduced the incidence of periprocedural stroke. A frequent but underdiagnosed periprocedural complication of CAS is hemodynamic depression (HD). CAS involves dilatation of carotid bulb which can trigger a series of neuronal responses resulting in HD that might influence the outcome of the procedure.

Definition of HD

Although there is significant heterogeneity between definitions used among clinical studies, hemodynamic depression following carotid angioplasty and stenting is commonly defined as an absolute or a proportional decrease in systolic blood pressure (SBP) and heart rate (HR). The lower cut off for SBP and HR is usually taken as 90 mm Hg and 60 beats/min respectively. Alternatively, an absolute fall in SBP more than 30 mm Hg and decrease in HR more than 20 beats/min regardless of the need for vasopressor support, atropine, or a pacemaker is also considered as HD.[1] HD is considered to be persistent if there is a fall in SBP for more than 1 hour or if hypotension mandates use of continuous vasopressor administration.[2]

Frequency

Hemodynamic depression which includes hypotension and bradycardia is a well-recognised physiologic response following carotid angioplasty and stenting. The incidence of this vasodepressor reaction ranges between 5 and 76%, whereas the incidence of persistent hypotension ranges between 11 and 35%.[3-9] Variation in incidence across the studies can be largely explained because of the differences in definition, inclusion criteria and procedural technique. In a meta-analysis of 27 randomised trials with over 4000 patients, the pooled estimate for hypotension was 12.1%, 19.2% for persistent hypotension, 12.2% for bradycardia, and 12.5% for both hypotension and bradycardia.[10]

Pathogenesis

In the normal state, baroreceptors located in the carotid bulb via the medullary vasomotor nuclei mediate changes in blood pressure and heart rate to maintain a hemodynamic steady state and adequate cerebral perfusion. During CAS, stimulation of these baroreceptors because of the distension of carotid bulb by the catheter results in reflex inhibition of sympathetic output (loss of tone in peripheral vasculature) and increased parasympathetic output (increased vagal activity) leading to hypotension and bradycardia.[11]

Risk factors

Though catheter mediated dilatation of the baroreceptors in the carotid sinus is the main stimulus behind the hemodynamic

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depression, the frequency of its occurrence is not uniform across studies. Apart from the clinical characteristics, complexity of the procedure and type of stent may play a role in development of hemodynamic instability. Previous studies evaluated the risk factors that might increase the chance of its occurrence.[12-19] There is a close relationship between HD caused by CAS and baroreceptor function. Increasing age impairs this reflex function which increases the risk of hemodynamic instability.[10] Plaque involving the carotid bifurcation increases the risk due to the presence of high concentration of baroreceptors. Also presence of calcified or ulcerated plaque increases the risk of hemodynamic instability following CAS.[20] Compared to self-expandable stents, use of balloon-expandable stents is associated with increased risk of persistent hypotension.[21] Also use of nitinol stents is associated with higher risk of HD as compared to Wall stents, likely due to increased carotid sinus stimulation.[22] Although few studies showed decreased risk with smoking and Diabetes mellitus due to impaired reflexes, further studies failed to show this effect.[10,23,24] History of prior CEA is associated with reduced risk of HD, likely due to decrease in the number of baroreceptors and scar formation following CEA.[10] Apart from these, contralateral carotid occlusion and simultaneous bilateral carotid stenting also increase the risk of HD following CAS [Table 1].[10,25]

Complications of HD

Many previous studies evaluated the impact of HD on complications associated with CAS. Although HD is considered to be mild and self-limiting in majority of the cases, these studies showed high incidence of neurological and cardiovascular ischemic events among patients in the HD group. These ischemic events may be related to several pathophysiological changes associated with impairment of baroreceptor reflex – increased platelet aggregability, coronary vasoconstriction and impaired cerebrovascular autoregulation.[26,27] HD especially when it is persistent increases the incidence of these events. In a retrospective study by Lin *et al*.,[28] persistent HD was associated with increased risk of neurological complications (OR 2.67, 95% CI 1.38–6.32, $P = 0.01$) and non-neurologic clinical adverse events (OR 3.25, 95% CI 1.58–7.52, $P = 0.02$). Gupta *et al*.[24] reported that persistent HD increases the risk of major adverse clinical events (OR 3.05, $P < 0.02$) and stroke (OR 3.34 $P < 0.03$). In another study by Lian *et al*.,[19] presence of persistent HD was significantly associated with increased rates of angina pectoris, TIA and stroke ($p = 0.001$). Altinbas *et al*. showed that occurrence of HD is associated with more than three times higher number of new ischemic brain lesions on diffusion weighted imaging.[29]

Table 1: Predisposing factors

Clinical features	Elderly age, Diabetes mellitus, smoking, H/o prior CEA, C/L carotid occlusion, prior MI, EF <25%
Plaque characteristics	Carotid bulb, ulcerated or calcified plaque
Type of stent	Balloon expandable stents, Nitinol stents

Management

Hemodynamic depression following carotid stenting although considered benign has been linked to higher incidence of neurovascular complications in a number of previous studies. It results in significant morbidity and mortality. A high degree of anticipation, close monitoring of vital parameters and prompt initiation of management can prevent the hazardous consequences. However, the ideal treatment of CAS-related hypotension and bradycardia remains a subject of debate. There are no controlled trials and guidelines available for the management of HD. Here we try to summarise the available evidence from the previous studies.

General principles

Blood pressure, heart rate and neurological status should be closely monitored following the procedure. Strict bed rest should be maintained in all patients at least until the next morning. In hypertensives, oral antihypertensive drugs should not be resumed except in those patients who had significant hypertension or those who are at risk for hyperperfusion syndrome and intracerebral haemorrhage. Hemodynamic depression is unlikely to occur in post-operative period in the absence of intra-operative hypotension and bradycardia. On the contrary, presence of intraprocedural hypotension (OR 14.6) and intraprocedural bradycardia (OR 12) strongly predicts postoperative hypotension and bradycardia respectively.[7] HD is associated with adverse clinical outcomes if not treated. Hence early recognition and prompt pharmacologic treatment should be considered. Wherever possible, admission into ICU must be considered. Any patient found to be having hypotension should be started on intravenous crystalloids. If the hypotension is refractory to fluid resuscitation, vasopressors should be started immediately.

Choice of vasopressor

There are no specific guidelines or RCTs suggesting favourability of one vasopressor over the other. But according to the published reports, Dopamine has been the most commonly used vasopressor in the management of these patients likely because of its ability to treat bradycardia as well as hypotension. However, in a study by Nandalur *et al*., use of selective alpha agonist (Noradrenaline/Phenylephrine) was significantly associated with shorter drug infusion time, shorter length of stay and fewer major adverse events as compared to dopamine.[30]

Role of atropine

The need for treatment of intraoperative bradycardia during CAS remains a subject of debate. Cayne *et al*. studied the role of prophylactic administration of atropine prior to balloon inflation or stent deployment in patients planned for carotid stenting.[31] In this study, there was significantly reduced incidence of intraoperative bradycardia and cardiac morbidity in patients receiving prophylactic atropine. In

another study by Leisch *et al*., only 5% of patients developed HD after routine administration of atropine.[3] However, many authors recommend against routine administration of atropine because of the accompanying tachycardia. Tachycardia may increase cardiac oxygen demand and may result in an increased incidence of myocardial infarction. Hence, atropine administration is usually considered only when bradycardia occurs. However, it is to be noted that cardiac complications occur in only 0.5% of patients after atropine administration and it may be reasonable to administer atropine in this population.[32]

Role of pacemaker

Carotid artery stenting induced bradycardia is a common condition and occurs as a reflex response due to the stimulation of sinus baroreceptors. Role of transvenous cardiac pacemakers has been investigated previously.[33,34] In these studies, pacemakers have been shown to alleviate symptoms but did not eliminate the occurrence of hypotension in this population. However there are no controlled studies available to support this strategy.

Other pharmacological options

Tsutsumi *et al*. studied the effects of two different types of antiplatelet medications, cilostazol and thienopyridine drugs. In this study, use of cilostazol was associated with reduced incidence of hemodynamic instability compared to thienopyridines.[35] Midodrine, an alpha-1 agonist, has been approved by FDA for the treatment of symptomatic orthostatic hypotension. A study by Sharma *et al*. showed oral midodrine as a safe and effective alternative to intravenous vasopressors in the management of hypotension associated with CAS.[36] Another potential therapeutic option include transcutaneous instillation of lignocaine in the region of carotid sinus. This has been effectively used in CEA patients.[37]

Non-availability of controlled trials make all these treatments investigational.

Optimal period for observation

Previously, postprocedural monitoring of patients following CAS consisted of close observation for initial 24 to 48 hours in intensive care units before considering transfer to general ward and subsequent discharge. However, advances in endovascular techniques, increase in experience of interventionists and an increased desire for cost containment led to increased use of CAS being performed as an outpatient procedure.[38] However, there are no clear consensus on what the optimal observation period should be. Previous studies showed that hemodynamic instability occurs most commonly within the first six hours following carotid stenting and usually resolves within 8-10 hours. Delayed onset HD is rare and almost always associated with intra-procedural HD. It has been observed that new onset HD beyond six hours of stenting was present in only 8% (hypotension) and 15% (bradycardia). Also absence of HD during the first six hours carries a negative predictive value of 97% (hypotension) and 93% (bradycardia) for new onset HD beyond six hours.[17] This justifies a postprocedural monitoring of minimum 12 hours. However, majority of these studies are from the western literature. We often see post carotid hypotension and bradycardia as a significant condition in majority of our people lasting up to 48 hours requiring inotropes in our institute. Outpatient CAS may be associated with delayed complications and patient may not be able to recognize the problem leading to a delay in hospital contact and may present with ischemic event during the first few days after the procedure. Hence, we suggest that patients should be closely monitored for orthostatic hypotension and bradycardia during the first 24 hours. Only those patients without orthostatic hypotension and were otherwise doing well should be considered for discharge. Patients having orthostatic hypotension should be observed for another 24 hours or more until the orthostasis is resolved. This can prevent the morbidity and mortality associated with hemodynamic depression.

Conclusion

Hemodynamic depression following carotid stenting is a common complication following carotid stenting. Although it is mild, transient and self-limiting in majority of cases, it can result in significant morbidity and mortality if persistent. Neurologists should be aware of the predisposing factors and management of this common complication. In patients who present with stroke following carotid stenting, neurologists should be aware of hypoperfusion secondary to hemodynamic depression as a cause of stroke apart from the stent thrombosis and occlusion.

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Conflicts of interest

There are no conflicts of interest.

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