ABSTRACT
Perioperative hypertension is a largely unnoticed major public health problem frequently encountered in clinical practice. Despite the large number of studies, which have demonstrated an increased perioperative morbidity and mortality in hypertensive patients, there remains a lack of consensus guidelines regarding the perioperative management of hypertension creating a major challenge for the physicians, anesthetists and surgeons. This issue mandates discussion and this paper reviews the accepted ideas in the general practice and the supporting various studies in regard to the preoperative evaluation, risk stratification and therapeutic management of perioperative hypertension.

INTRODUCTION
Hypertension, defined as blood pressure readings greater than 140/90 mmHg is one of the most common chronic medical condition affecting 1 billion individuals worldwide with the incidence increasing with age. In 2000, 26.4% of the world adult population had hypertension with 26.6% men and 26.1% women. The projected score of 29.2% in 2025 is probably underestimated considering the rapid change in lifestyle and a concurrent increase in the risk of hypertension.1 Survey over the past one to two decades has found the prevalence in increasing trend in the developing countries. Epidemiological studies from India has shown that hypertension prevalence has stabilized in urban population to about 25-30% but has increased in rural population from 15 to 25%.2 Treatment of hypertension is essential as it is a well known risk factor for chronic adverse debilities such as cardiovascular diseases, renal diseases and stroke. As the duration and severity of hypertension increases there is a proportionate increase in the degree of end-organ damage and morbidity and mortality.

PERIOPERATIVE HYPERTENSION
Hypertension is a major clinical problem in the management of patients undergoing surgery. Frequent cancellation and postponement of planned surgery due to poor control of hypertension is a major public health problem which largely goes unnoticed. Numerous studies have demonstrated an increase in perioperative morbidity and mortality with chronic hypertension but there is a lack of literature and nationally accepted guidelines creating a major challenge for the physicians and anesthetists in the preoperative evaluation and management of patients with hypertension.

Perioperative refers to the time of hospitalization directly related to a surgical procedure and includes the preoperative, intraoperative and postoperative (ie, 3 or 4 days post) periods.3 Perioperative rise in blood pressure occurs in 25% of patients undergoing surgery4,5 increasing the complications and mortality following a wide range of surgical procedures. Both normotensive or pre-existing hypertensive patients are likely to develop elevated blood pressure and tachycardia during induction of anesthesia in surgery.7 Hypertension was found to be the second most common risk factor for surgical morbidity by The National Veterans Administration Surgical Risk Study in 83,000 patients8 further confirmed by various other studies.

A meta-analysis of 30 observational studies and extensive literature review by Howell et al. reported an odds ratio of 1.35 (95% CI 1.17-1.56) times higher perioperative cardiac complications in hypertensive patients compared to normotensives.9 Prys-Roberts et al. and Goldman and Caldera et al. have demonstrated an increase in arrhythmias and postoperative myocardial ischemia in hypertensive patients in the early 1970s.4,5 Aronson and colleagues have demonstrated a 30% increase in adverse outcome risk in patients with Isolated systolic hypertension undergoing cardiac surgery.10 Fontes et al. demonstrated increased pulse pressure as an independent risk factor associated with increased incidence of postoperative neurological complications and cardiac failure.11 Perioperative hypertension may occur during airway instrumentation and induction of anesthesia, intraoperatively or in the early postoperative period secondary to sympathetic stimulation due to pain, hypothermia, hypoxia, bladder distension and/or volume overload either due to intraoperative excessive fluid therapy or postoperative mobilization of fluid from the extravascular space. The incidence of postoperative hypertension varies from 4% to 30% following cardiac or noncardiac surgery.12 Hypertensive events are common with carotid or abdominal aortic surgery, peripheral vascular surgery and intraperitoneal or intrathoracic surgeries.4 Hypertensive patients are also prone for hypotension resulting in myocardial or cerebral ischemia due to reduced systemic vascular resistance soon after induction of anesthesia or significant fluid depletion during surgery due to their labile hemodynamics.13 This has led the anesthetists to adopt few techniques to achieve a more stable hemodynamics which includes invasive arterial pressure monitoring with titrated or prophylactic vasopressors, monitoring depth of anesthesia and
optimisation of stroke volume with intravascular fluid therapy.

**MANAGEMENT OF ANESTHESIA FOR HYPERTENSIVE PATIENTS**

**Preoperative evaluation**
- Adequacy of blood pressure control
- Review of antihypertensive drugs patient is receiving
- Continuation of the antihypertensive drugs
- Evidence of end-organ damage

**Induction and maintenance of anesthesia**
- Anticipation of hypotension to anesthetic drugs
- Limit duration of direct laryngoscopy
- Balanced anesthesia to blunt hypertensive responses
- Invasive hemodynamic monitors
- Monitoring for myocardial ischemia

**Postoperative management**
- Anticipation of periods of systemic hypertension
- Continuous monitoring of end-organ function

**PREOPERATIVE HYPERTENSION & EVALUATION**

Diastolic blood pressure more than 110 mmHg is suggested as a preoperative marker of perioperative cardiac complications in patients with chronic hypertension.\(^5\) Browner et al reported an increased odds ratio for postoperative death to 3.8 times in preoperative hypertensives who underwent noncardiac surgery\(^{14}\). Forrest et al. showed an association of perioperative bradycardia, tachycardia and hypertension with perioperative hypertension.\(^{15}\) Mangano et al. and Wolfsthal et al. have demonstrated that controlled preoperative hypertension are comparatively associated with lower risk of intraoperative BP elevations.\(^{16,17}\)

Following points are to be considered in preoperative evaluation of hypertensive patients

1. Newly diagnosed or known hypertensive?
2. Whether Primary or secondary hypertension?
3. White coat hypertension or sustained hypertension?
4. Severity of hypertension and end organ damage?
5. What Antihypertensive Drug therapy the patient is on?

The preoperative assessment provides an opportunity to identify longstanding undiagnosed hypertensive patients as hypertension per se is generally asymptomatic in most patients. Diastolic hypertension \(<110\) mmHg is not considered as a contraindication for postponement of surgery. Observations suggest that stage 1 & 2 hypertension without evidence of end organ damage is not an independent risk factor for perioperative cardiovascular complications, hence patients may go for surgery without delay. However, surgery may be postponed for patients with stage 3 hypertension (SPB \(>180\) and/or DBP \(>110\) mmHg) until the blood pressure is adequately controlled. Isolated systolic hypertension (SPB \(>140\) mmHg; DBP \(<90\) mmHg) common in elderly is an independent risk factor for postoperative Silent myocardial infarction (SMI) as shown by Howell et al.\(^8\)

With the above-discussed recommendations applicable for elective surgery, if clinical conditions necessitate for emergency surgery, the patient may be taken for surgery with adequately controlled blood pressure using the short-acting parenteral antihypertensive therapy.

Patients with secondary hypertension require further diagnostic evaluation by the suggested approach methods prior to elective surgery to rule out renal, endocrine or other causes according to the age.

White coat hypertension, defined as an office/preoperative blood pressure \(>140/90\) mmHg with an average daytime reading \(<135/85\) mmHg is a frequent misconception which occurs due to stress induced sympathetic stimulation.\(^{18}\) Yet treatment is justified since an association with increased incidence of SMI is observed.\(^{19}\)

A review of patient’s antihypertensive medications is necessary for specific considerations with each group. Anti-hypertensive therapy is generally continued up until the day of surgery.

Angiotensin converting enzyme inhibitors (ACEI) and angiotensin II receptor blockers (ARBs) are notable exceptions because they blunt the compensatory activation of renin-angiotensin-aldosterone system during surgery resulting in prolonged hypotension, hence recommended to hold them the day before surgery.\(^{20,21}\)

Chronic diuretic therapy requires special attention to arrhythmia because of hypokalemia and intraoperative hypovolemia, hence avoided on the day of surgery.

Abrupt withdrawal of beta blockers and clonidine may cause rebound hypertension with adverse perioperative events which may be prevented and continued perioperatively by supplementing with parenteral therapy or clonidine patch. Clonidine reduces the risk of myocardial ischemia by providing hemodynamic stability and reducing sympathoadrenal activity. Patients with hypertension and coronary heart disease should continue with beta blockers as it is associated with favorable outcome in perioperative myocardial ischemia and reduced risk of death after coronary artery bypass surgery.\(^{22}\) \(\beta\)-blockers also provide hemodynamic stability and interactions are well tolerated with both regional and general anesthesia.

Goldman cardiac risk index was the first original cardiac risk index developed by Goldman et al. in 1977 for cardiac risk stratification for non-cardiac surgery. Later in 1999, Lee et al. published a revised cardiac risk index (RCRI) using six independent variables which is easier to use and more accurate and extensively validated (Table 1).\(^{23}\)

**INTRAOPERATIVE HYPERTENSION**

Acute intraoperative blood pressure elevations of \(>20\)%,
more likely in chronic hypertensives are considered a hypertensive emergency. Intraoperative hypertensive events are more common in vascular surgeries. Perioperative hypertension management in patients undergoing cardiac surgery represents a unique pathophysiological situation characterized by peripheral vasoconstriction and reduced baroreceptor sensitivity. The presence of pre-existing left ventricular dysfunction or coronary heart disease is a risk factor for myocardial ischemia or heart failure.

**ACUTE POSTOPERATIVE HYPERTENSION (APH)**

APH is defined as significant elevation of blood pressure in the immediate postoperative period. Although no standardized definition exists to define APH, an increase of SBP by >20% or DBP >110 mm Hg are considered to be indicative of treatment in non-cardiac surgery and BP >140/90 mmHg or a mean arterial pressure >105 mmHg for treatment with meticulous BP control in cardiac surgery patients. APH is more commonly encountered with cardiothoracic, vascular, head and neck and neurosurgical procedures. APH usually occurs in the initial 20 minutes of postoperative period and may last up to 4 hours. Untreated postoperative hypertension is associated with an increased risk of cardiovascular, neurologic or surgical site complication. The ECLIPSE trial study has demonstrated a significant association of 30-day mortality with SBP variability outside a range of 75 – 135 mmHg intraoperatively and 85 – 145 mmHg pre and postoperatively. Rose et al. found that higher risk of APH is associated with patients presenting with intraoperative hypertension, excessive pain or inadequate ventilation.

Blood pressure in APH should be decreased gradually over 30 – 60 mins by not more than 25% or to a target value <180/110 mmHg. Prior to start of treatment, attention should be given to the reversible causes as mentioned earlier, assessment of volume status and appropriate analgesia and sedation. Postoperative rebound hypertension due to the withdrawal of patient’s longterm hypertensive regimen can be prevented by substituting with long-acting preparations on the morning of the day of surgery. Parenteral therapy is advocated for patients unfit for oral intake and/or with end organ damage.

**PHARMACOTHERAPY**

A drug which is rapid in action, predictable and easily titrated, convenient, safe and inexpensive forms an ideal agent for treatment of hypertensive emergencies. Varieties of drugs with distinct advantages and disadvantages are available, their selection being dependent on the patient’s clinical picture. The commonly used drugs are listed in Table 2.

**LABETALOL**

A combined selective α1 and nonselective β-adrenergic receptor blocker, administered either as IV bolus or continuous infusion has been used for pregnancy-induced hypertension crisis. Labetalol reduces the systemic vascular resistance without compromising the peripheral and visceral blood flow. Heart rate is either maintained or slightly reduced due to its β-blocking effect but the cardiac output is maintained in contrary to the pure β-adrenergic blocking agents which decrease it. Labetalol is safe and effective for APH following cardiovascular, intracranial and general surgeries with reported 85-100% response rates. Labetalol is avoided and caution to be exercised in patients with severe sinus bradycardia, asthma, heart blocks greater than first degree and heart failure.

**ESMOLOL**

An ultra-short acting cardioselective β-adrenergic blocker with no vasodilatory action, an ideal agent for hypertensive patients with tachycardia and increased cardiac output is especially useful in severe postoperative hypertension. Because of its RBC dependent metabolism, it has the advantage of safety in renal or hepatic dysfunction but anemia may prolong its half-life and hypertensive action. Esmolol is contraindicated in patients already on β-blockers, with bradycardia and decompensated heart failure according to American College of Cardiology (ACC) /American Heart Association (AHA) guidelines as it may compromise myocardial function and to be used with caution in chronic obstructive pulmonary disease due to bronchospasm.

**ENALAPRILAT**

An ACE inhibitor administered as IV bolus with demonstrated efficacy in hypertensive patients with congestive heart failure and prevention of worsening renal function in diabetic and non-diabetic nephropathy. Advantages include lack of reflex tachycardia and effect on intracranial pressure, reported to be effective in patients undergoing craniotomy. Difficulties in dose titration due to delayed onset and peak with long duration of action makes enalaprilat a poor choice for use in hypertensive emergency, yet used for management of postoperative hypertension in combination with easily titrable fast acting drugs such as labetalol or nicardipine.
Table 2: Summary of Commonly Used Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Class</th>
<th>Dose</th>
<th>Onset &amp; Duration of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labetalol</td>
<td>Combined α+β-blocker</td>
<td>Loading dose-20mg followed by 20-80mg incremental dose every 10mins. Alternatively, infusion 1-2mg/min after initial loading dose until hypotensive effect</td>
<td>Onset 2-5mins; reaches peak at 5-15mins, lasts up to 4hours; elimination half-life 5.5hours</td>
</tr>
<tr>
<td>Esmolol</td>
<td>B-blocker</td>
<td>Loading dose 500-1000µg/kg in 1min, then infusion starting at 50µg/kg/min increasing up to 300µg/kg/min as required</td>
<td>Rapid onset 60secs; short duration of action 10-20mins</td>
</tr>
<tr>
<td>Enalaprilat</td>
<td>ACE inhibitor</td>
<td>1.25mg over 5mins every 6hours increased by 1.25mg at 12-24hours to a maximum 5mg every 6hours</td>
<td>Variable response, slow onset &amp; long duration of action, titration difficult</td>
</tr>
<tr>
<td>Fenoldopam</td>
<td>Peripheral Dopamine-1(DA) receptor agonist</td>
<td>Starting dose 0.1µg/kg/min, increasing by 0.05-0.1µg/kg/min up to a maximum 1.6µg/kg/min</td>
<td>Onset within 5mins, maximal response by 15mins, duration of action 30-60mins, elimination half-life 5mins</td>
</tr>
<tr>
<td>Hydralazine</td>
<td>Direct-acting arteriolar vasodilator</td>
<td>IV bolus: 10-20mg every 1-4 hours as required IV infusion: Loading dose 0.1mg/kg followed by continuous infusion 1.5-5µg/kg/min</td>
<td>Onset 5-15mins, circulating half-life3hours, fall in BP may last up to 12hours</td>
</tr>
<tr>
<td>Nicardipine</td>
<td>Dihydropyridine CCB – 2nd generation</td>
<td>5mg/hr, incrementing by 2.5mg/hr every 5-15mins not to exceed 15mg/hr</td>
<td>Onset 5-15mins, duration of action 4-6hours</td>
</tr>
<tr>
<td>Clevidipine</td>
<td>Dihydropyridine CCB – 3rd generation</td>
<td>Starting infusion at 1-2mg/hr, dose can be doubled every 90secs. As blood pressure approaches goal increase dose by less than doubling and increase time adjustments every 5-10mins</td>
<td>Half-life 2mins, duration of action 5-15mins</td>
</tr>
<tr>
<td>Nitroglycerin</td>
<td>Arterial &amp; venous dilator</td>
<td>Starting infusion at 5µg/min, increased by 5µg/min every 3-5mins up to 20µg/min</td>
<td>Onset 2-5mins, duration of action 10-20mins</td>
</tr>
<tr>
<td>Nitroprusside</td>
<td>Arterial &amp; venous dilator</td>
<td>Initial infusion 0.25-0.3µg/kg/min, increase by 0.5µg/kg/min every 1-2mins to achieve desired results</td>
<td>Rapid onset in seconds, duration of action 1-2mins, plasma half-life 3-4mins</td>
</tr>
</tbody>
</table>

**FENOLDOPAM**

A unique peripheral vasodilator by its peripheral dopamine-1 receptor agonism is used for management of perioperative hypertension patients with or at risk of renal dysfunction. It causes renal artery vasodilation and activation of dopamine receptors in the proximal and distal tubules thereby promoting natriuresis and diuresis. Disadvantages include reflex tachycardia, dose-dependent increase in intraocular and intracranial pressures and rebound hypertension after stopping the infusion.

**HYDRALAZINE**

A direct-acting arteriolar vasodilator affecting diastolic more than systolic blood pressure with its advantage and disadvantage profile similar to fenoldopam is often used as a first-line agent in pregnancy-induced hypertension. A recent meta-analysis has suggested the possibility of its association with increased maternofetal complications due to reflex tachycardia and increased myocardial demand in at-risk patients. Hydralazine is best avoided for hypertensive crisis management because of its difficulty in titration due to its prolonged and unpredictable antihypertensive effects. Hydralazine is also avoided in patients with dissecting aneurysm.
NICARDIPINE
A short-acting second generation dihydropyridine calcium channel blocker (CCB) produces selective coronary and cerebral vasodilatation, thus reduces the risk of ischemia and beneficial in patients with coronary artery disease and systolic failure. The American Heart Association/American Stroke Association guidelines also recommend nicardipine for treatment of ischemic stroke with diastolic pressure >120 mmHg or systolic pressure >220 mmHg.

CLEVIDIPINE
An ultrashort-acting third generation dihydropyridine CCB reduces afterload by selective arterial vasodilatation without affecting cardiac filling pressures or causing reflex tachycardia. Clevidipine increases coronary blood flow with consequent increase in stroke volume and cardiac output thus maintaining renal and splanchnic blood flow and protects against ischemia/reperfusion injury in animal model of myocardial ischemia by direct coronary vasodilatory effect. The ECLIPSE trial has demonstrated significantly lower mortality rate with clevidipine in comparison to nitroprusside group in perioperative treatment of hypertension.

NITROGLYCERIN
A direct vasodilator of peripheral capacitance and resistance vessels, also acts as an antianginal by coronary artery dilatation and increased blood supply to ischemic regions of the myocardium. Disadvantages include reflex tachycardia and hypotension frequently exacerbated with volume depletion and undesirable effects in patients with compromised cerebral and renal perfusion. Nitroglycerin is not considered as primary therapy in hypertension emergencies or urgencies but used as a suitable adjunctive therapy.

SODIUM NITROPRUSSIDE
With similar mechanism of action to nitroglycerin, nitroprusside is often considered a drug of choice in hypertensive emergencies with documented efficacy in perioperative settings. A significant reduction in coronary perfusion pressure may occur in patients with coronary heart disease. Due to its untoward effect of decreased cerebral perfusion and increased intracranial pressure, nitroprusside is avoided in patients with hypertensive encephalopathy or a cerebrovascular accident. Cyanide accumulation adds to the adversities of nitroprusside.

CONCLUSION
Perioperative management of hypertension in patients undergoing surgery has been a longstanding problem. With wide range of antihypertensives and clinical experiences, there is no unanimity regarding the management of these patients. Therefore, it is essential to develop a consensus guidelines regarding the perioperative management of hypertension. It includes appropriate patient selection, preoperative evaluation of the patient including the assessment of end-organ damage, appropriate therapeutic goals and drug selection for the intraoperative and postoperative hypertension management.

REFERENCES
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