Hypertensive emergencies are life-threatening conditions because their course is complicated with acute target organ damage. They can be presented with neurological, renal, cardiovascular, microangiopathic hemolytic anemia, and obstetric complications. These patients present with a mean arterial pressure >140 mm Hg and grade III to IV retinopathy. After diagnosis, they require the immediate reduction of Blood Pressure (BP) in less than 1 hour, using intravenous drugs administered at an intensive care unit. In these critical conditions BP should be reduced about 10% during the first hour and another 15% gradually over 2-3 more hours to prevent cerebral hypoperfusion. The exception to this management strategy is aortic dissection, for which the target is systolic BP <120 mm Hg after 20 minutes.

Once the patient is stabilized that happens after 6-12 hours of parenteral therapy, oral antihypertensive therapy can usually be instituted. Hypertensive urgencies are severe elevations of BP without evidences of acute and progressive dysfunction of target organs. They demand adequate control of BP within 24 hours to several days using orally administered agents.

Key Words: Hypertension, Treatment, Hypertensive emergencies.
Critically elevated BP without evidences of acute and progressive dysfunction of target organs are called hypertensive urgencies\(^1,8\). They demand adequate control of BP within 24 hours to several days using orally administered agents in a closely monitored outpatient setting. The purpose of this review is to describe rational approach and appropriate therapy of hypertensive emergencies.

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**Table 1. Hypertensive Emergencies Causes**

**Abbreviations:** MDMA: 3,4 methylene dioxymethamphetamine, SSRI, Selective Serotonine Re-uptake Inhibitors; ACEI, angiotensin-converting
Medical history directed to the chief complaint should include previous treatments (antihypertensive agents and adherence), illicit drugs use (cocaine and others); cardiovascular manifestations (heart failure, angina, aortic dissection), neurologic symptoms (headache, blurring vision, changes in mental status, nausea, vomiting, weakness, renal symptoms as hematuria and, oliguria). Other medical problems as thyroid diseases, Cushing syndrome, systemic lupus, systemic sclerosis, abdominal pain, dyspnea. In premenopausal women, last menstruation date must be interrogated.

Physical exploration should be directed mainly to cardiovascular and neurological systems. Measurement of BP must be performed in both arms to detect any significant differences, peripheral pulse exploration for absence or delay which suggest aortic dissection, fundoscopy (searching for soft exudates, hemorrhages and, papilledema), cardiac and lung auscultation (S3, rales), assessment of mental status, and focal or lateralizing neurologic signs that are infrequent in hypertensive encephalopathy and usually suggest some other cerebrovascular disease (hemorrhage, embolism, or atherosclerotic thrombosis). Laboratory studies and EKG should be performed immediately after presentation and may provide crucial clues to underlying conditions. Imaging will be performed according the presumptive diagnosis of the primary cause of the hypertensive emergencies.

The distinction between hypertensive emergencies and urgencies are often ambiguous. It appears to be better considering in all patients to institute immediate antihypertensive treatment, leaving the decision on the agent and the route of administration to clinical criteria and available resources.

The first consideration in BP management in the setting of a life threatening condition is that BP pressure level is not the most critical factor in determining the existence of a hypertensive emergency. Prehospital treatment may include furosemide when there is clear evidences of volume expansion as in heart failure, or acute nephritis. However, use of loop diuretics may worsen hypertension that is secondary to increased renin production by causing further volume contraction.

Nitrates and oxygen administration may be used in conditions where they are indicated. In hypertensive emergencies sublingual or oral nifedipine is absolutely contraindicated because produces a nonpredictable reduction of BP accompanied by heart and brain ischemia.

Clonidine is also contraindicated because it is a strong sedative and causes hypertensive rebound when it is discontinued. After hospital admission the hypertensive emergency has to be managed choosing according the etiology among the parenteral drugs enlisted in Table 2.

The main objective is to reverse end-organ damage that is accomplished reducing mean arterial pressure by up to 25 % over minutes to few hours. Once the patient's situation has stabilized, the patient may be switched to an oral medication and the physician should discuss with the patient long term follow up plans.

The following are the drugs of choice in hypertensive emergencies treatment.
Sodium Nitroprusside
It is a first-choice agent for the majority of hypertensive emergencies\textsuperscript{10,11}. This agent is a potent arterial and venous vasodilator with a rapid rate (within seconds of beginning an infusion) of action, a very short duration of effect, and easily titrable. It is administered as an I.V. infusion, with intra-arterial line BP monitoring. It reduces preload, afterload and oxygen myocardial requirements. Because it is light-sensitive, container and tubing must be light-resistant. Sodium nitroprusside dose can be carefully adjusted for a controlled reduction of BP. Its main indications are hypertensive emergencies complicated with hypertensive encephalopathy, heart failure, aortic dissection, and adrenergic crises. The most important adverse effect of sodium nitroprusside is thiocyanate intoxication that may occur when this agent is administered for more than 48-72 hours, particularly in patients with renal or liver dysfunction.

Thiocyanate intoxication presents with nausea, vomiting, tinnitus, muscle cramps, hyperreflexia, disorientation and psychosis\textsuperscript{12}. Treatment of cyanide toxicity includes hydroxycobalamin and sodium thiosulfate infusions, and in chronic renal failure dialysis may be indicated. Nitroprusside in high doses may increase intracranial pressure what could limit its usefulness in patients with central nervous system complications. Extravasation can cause local tissue necrosis.

Nitroglycerin
It is a powerful venodilator that reduces preload, increases coronary blood flow through collateral coronary vessels dilation, suppresses coronary vasospasm and decreases cardiac oxygen demands. Higher doses are required to produce arteriolar vasodilatation. Nitroglycerin is the best agent in hypertensive emergencies that are complicated with ischemic heart disease and, after coronary bypass\textsuperscript{10,12}. It has been demonstrated nitroglycerin

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Onset of Action</th>
<th>Duration of Action</th>
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<tr>
<td>Sodium Nitroprusside</td>
<td>0.25 – 10 μg/kg/min as I.V. Infusion. Maximal dose for 10 min only</td>
<td>Seconds-2 min after beginning of Infusion</td>
<td>1-3 min.</td>
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<tr>
<td>Nitroglycerin</td>
<td>5-100 μg/min. As I.V. Infusion</td>
<td>2-5 min</td>
<td>5-10 min</td>
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<td>Fenoldopam</td>
<td>0.1-0.3 μg/kg/min. As I.V. Infusion</td>
<td>5-15 min</td>
<td>30 min-4 hr</td>
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<td>Enalaprilat</td>
<td>0.625- 1.25 mg as I.V in bolus during 5 min and (preferably) Infusion</td>
<td>15 min-4 hr</td>
<td>6 hr</td>
</tr>
<tr>
<td>Nicardipine</td>
<td>5-15 mg/hr. As I.V. Infusion</td>
<td>1-5 min.</td>
<td>15-120 min.</td>
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<tr>
<td>Hydralazine</td>
<td>10-20 mg. as I.V. Bolus or I.M.; repeat every 4-6 hr. (maximum dose: 40 mg)</td>
<td>10-20 min.</td>
<td>3-8 hr</td>
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</table>
tolerance when administering continuously during 24-48 hours. Glass containers must be used because polyvinyl chloride containers and tubing may absorb it in unpredictable manner. This agent is contraindicated in cerebral hemorrhage because it may increase intracranial pressure, and in closed-angle-glaucoma.

**Nicardipine**

It is a dihydropiridine type calcium antagonist with intermediate beginning and duration of effects and prolonged half-life, that has been used for the control of perioperative hypertension in cardiac surgery patients. Nicardipine also reduces cerebral ischemia. Its adverse effects include reflex tachycardia, headache, nausea, and vomiting. This agent potentiates curare effects and has interaction with inhalant anesthetics. Nicardipine contraindications are heart block, acute myocardial infarction, and renal failure 2,7.

**Fenoldopam**

It is a selective agonist of dopaminergic-1 receptors, which produces arterial vasodilatation, increasing renal blood flow and natriuresis what is beneficial in patients with renal failure 12. This agent has a rapid onset of action and ease of BP titration. Fenoldopam must be used as I.V. infusion and not in bolus; the increments must not exceed 0.1 μg/kg/min at 20 min intervals, and total dose has not to be higher than 1.7 μg/kg/min. It does not cause rebound hypertension that allows its discontinuation either tapered or abruptly. The efficacy of fenoldopam is similar to nitroprusside but it has the advantage of not requiring a line for intra-arterial BP monitoring.

However, it is expensive and not readily available. Its main indications are severe hypertension with renal failure and, acute heart failure. This agent is contraindicated in glaucoma. Side-effects include headache, flushing, dizziness, tachycardia or bradycardia, hypokalemia, and local phlebitis.

**Labetalol**

It is a non-selective beta- and alpha1- blocker (in the ratio of 3-7:1) with a rapid onset of action, sustained effect and low toxicity 12,14. It reduces peripheral vascular resistance without reflex increasing of systolic volume. Labetalol administration does not require intra-arterial BP monitoring. Its main indications are hypertensive encephalopathy and, adrenergic crises. This agent is contraindicated in heart failure, heart block, and chronic obstructive pulmonary diseases (COPD).

**Esmolol**

It is an ultra-rapid and short acting beta-1 selective blocker with no intrinsic sympathomimetic activity that was approved by FDA only for perioperatives hypertensive emergencies. Esmolol administration requires a line for intra-arterial BP monitoring. It may produce thrombophlebitis and, extravasation of this agent results in local necrosis. It is contraindicated in cocaine toxicity when using alone, heart failure, COPD/asthma and, heart AV blokade.

**Enalaprilat**

It is the only ACE inhibitor available for parenteral use and may be useful in treating hypertensive emergencies in patients with heart failure. However, it may cause a precipitous reduction in BP in those patients who are hypovolemic (patients with heart failure, hyponatremia, those on high dose diuretic therapy, renal dyalysis). Enalaprilat may produce hyperkalemia, and angioedema. It is contraindicated in pregnancy.

**Hydralazine**

It is a direct arterial vasodilator. It has also the property of improving uterine blood flow. Adverse effects include significant reflex sympathetic stimulation, sodium and water retention, flushing, headache and increase of intracranial pressure. It is indicated only in pre-eclampsia and eclampsia and, contraindicated in patients with coronary atherosclerosis 1,2,4-9.

**Phentolamine**

It is a competitive, non-selective alpha-blocker, that is the drug-of-choice only for adrenergic crises (drug-induced or secondary to a pheochromocytoma). After administering a bolus I.V. injection of 5-10 mg BP decreases within several minutes 6-8.

**Criteria for Agent Selection**

Because there are no available comparisons of the long-term outcome after the use of various agents, the choice of treatment is based on rapidity of action, ease of administration, and possible side effects 5.

**Management of Specific Hypertensive Emergencies**

In general, BP should be reduced about 10% during the first hour and another 15% gradually over 2-3 more hours. The exception is aortic dissection, for which the target is systolic BP <120 mm Hg after 20 minutes. In the elderly it should be used lower doses of drugs and the objective is to reduce BP less than in the youngest. As many patients with hypertensive emergencies have a volume de-
pletion resulting from pressure-induced natriuresis use of loop-diuretics should be avoided initially unless there is clear evidence of volume overload (as occurs in heart failure). Because the same reason, potent vasodilators like nitroprusside may cause a sudden decrease of BP below a safe target level. Oral antihypertensive therapy can usually be instituted after 6-12 hours of parenteral therapy. 

**Hypertensive Encephalopathy**
The main goal of treatment is to decrease Mean Arterial Pressure (MAP) in 20% of Diastolic Blood Pressure (DBP) to 100-110 mm Hg in the first hour. In general, the drug of choice is sodium nitroprusside. Nevertheless, sometimes it may reduce cerebral blood flow in areas with a fixed arterial narrowing and produce cerebral steal phenomenon and focal ischemia. It has been proposed that labetalol or nicardipine could be a better choice, because they are less likely to decrease cerebral blood flow. Failure in improving neurologic symptoms suggests a stroke. Cerebral blood flow autoregulation is disrupted in the setting of acute brain ischemia. This is the result of a failure in the responsiveness of cerebrovascular resistance to changes in the cerebral perfusion pressure. When BP is suddenly reduced in these conditions cerebral blood flow may be strongly decreased and neurologic deficits may be worsen. There is consensus in that BP must not be reduced in ischemic stroke patients unless they are candidates for thrombolytics.

When thrombolytics are planned to be administered in an ischemic stroke BP must be > 180/105 mm Hg. If this is the case, when BP is >220/120 it would be acceptable to gradually reduce it in 24-48 hours. When DBP is >140 mm Hg sodium nitroprusside should be administered in order to decrease DBP 10-15 % in 12-24 hours. There are no evidences that hypertension increases intracerebral hemorrhage or the risk of a new hemorrhage. Vasospasm and reduction of brain perfusion are common in adjacent areas to an intracerebral hematoma and, as well as in ischemic stroke the sudden reduction of MAP may aggravate brain ischemia. Hypertension appears to be a secondary phenomenon and BP may spontaneously decrease in a few hours.

**Heart Failure**
When the patient has pulmonary edema, nitroglycerin or nitroprusside are the drugs of choice, and the target is to reduce BP to normal or near-normal levels. When there signs of fluid retention (pulmonary edema, peripheral edema) furosemide may be added.

**Coronary Insufficiency**
Nitroglycerin is the drug of choice and should be rapidly titrated to effect. One alternative to I.V. route is to administer 1.25 mg of isosorbide dinitrate aerosol upon arrival. If BP does not decrease with nitroglycerin it should be added nitroprusside. Nevertheless, adverse reactions of nitroprusside may include baroreflex activation, causing tachycardia and, coronary steal phenomenon with ischemic worsening in areas with fixed coronary stenosis. Other agents that can be used when there is no concomitant heart failure are beta-blockers.

**Aortic Dissection**
When affecting the proximal ascending aorta comprise surgical emergencies and carry poor prognosis. Medical therapy in that context aims mainly to stabilize the patients as much as possible before transfer to the operating room when surgery is feasible. When localized distal to the left subclavian artery, such aneurysms may be treated with thoracic endovascular aortic repair. Beta-blockade must be established previously to begin nitroprusside infusion. An alternative agent is labetalol that may be used as the only treatment because it has beta- and alpha-blocking effects. Heart rate must be maintained between 60-80 beats/min.

**Adrenergic Crises**
The drug of choice is phentolamine; another option is the association of sodium nitroprusside and a beta-blocker. It has to be taken into account that beta-blockers can exacerbate hypertension in patients with adrenergic crises and thus, should not be used until adequate alpha-receptor blockade is achieved. Labetalol is relatively contraindicated because it produces more beta than alpha blocking effects, allowing a paradoxical increase of BP caused by the absence of opposition to the alpha effect of catecholamines (or cocaine, amphetamines, or tianeptine in those receiving MAO inhibitors).

**Pre-eclampsia**
This condition either mild or severe, is managed best with a policy of delivery at or beyond 37 and 34 weeks’ gestation, respectively. Even though no single antihypertensive has been proven to be better than another, hydralazine is probably the initial intravenous agent of choice. The aim is to decrease DBP to 80-100 mm Hg. Severe pre-ecl-
lampsia should be treated with magnesium to prevent progression to eclampsia. It must be recalled that nitroprusside is relatively contraindicated in pregnancy.

**Hypertensive Emergencies in The Perioperative Setting**

The drugs of choice are esmolol, nitroglycerin (after coronary bypass surgery), nicardipine, nitroprusside and, fenoldopam.

**References**