American College of Cardiology/American Heart Association (ACC/AHA) lowered hypertension thresholds through their new guidelines published in November 2017. They defined the new limits of hypertension as levels at or above 130/80 mmHg for healthy adults (1). But some physicians especially Family Physicians did not accept the new categorization under the concern of increased prescription costs, treatment discordances, anxiety and complications with elderly patients (2). In 2018 European Society of Cardiology (ESC) published their current guidelines for hypertension. According this guideline, blood pressure (BP) levels at or above 140/90 mmHg were described as hypertension for normal adults (3).

In 2019 according to Turkish Hypertension Consensus Report, hypertension is defined as a systolic/diastolic blood pressure at or above 140/90 mmHg for healthy adults (4). Likewise the guideline for diagnosis and treatment of hypertension published by Turkish Society of Endocrinology and Metabolism in 2018 described hypertension for adults as systolic/diastolic blood pressure at or above 140/90 mmHg by repetitive measurements (5). The new hypertension categories is defined at table 1 (4,5).

In ACC/AHA guide, BP over 180/120 mmHg is named “hypertensive crises” but it did not describe clearly and in details the managing of this situation (1). There are also definitions like “malign hypertension”, “asymptomatic hypertension”, “hypertensive crises”, “hypertensive emergency” or “urgency” (5,7,8). Usually these terms are used instead of each other by emergency doctors.

Table 1: Classification of Blood Pressure

<table>
<thead>
<tr>
<th>Category</th>
<th>SKB (mmHg)</th>
<th>DKB (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;120 and</td>
<td>&lt;80</td>
</tr>
<tr>
<td>Elevated</td>
<td>120–139 and/or 80–89</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>≥140 and/or ≥90</td>
<td></td>
</tr>
<tr>
<td>Stage 1</td>
<td>140–159 and/or 90–99</td>
<td></td>
</tr>
<tr>
<td>Stage 2</td>
<td>≥160 and/or ≥100</td>
<td></td>
</tr>
</tbody>
</table>

In ACC/AHA guide, BP over 180/120 mmHg is named “hypertensive crises” but it did not describe clearly and in details the managing of this situation (1). There are also definitions like “malign hypertension”, “asymptomatic hypertension”, “hypertensive crises”, “hypertensive emergency” or “urgency” (5,7,8). Usually these terms are used instead of each other by emergency doctors.

In 2017, the hypertensive patient number was 14.3 million in Turkey and 8 million of them were women while 6.3 million were men. The rate of need for antihypertensive medication among these patients which are 40 years old or over, is 48% for men and, 63.5% for women. But the rate of regular drug use among these patients is just 63% for men, and 74% for women. The incidence of prehypertension in the middle-ages (48 ± 12 years) was 32.8% (as 130-139 / 80-89mmHg) and the rate of hypertension development in this group was twice as high as normotensive ones. Therewithal only 48% of the patients the blood pressure could kept under control (6).

ABSTRACT
“Hypertensive emergency” is a life threatening condition that caused by acute increase of blood pressure usually ≥180/120 mmHg leading end-organ damage. In the Emergency Department appropriate management of “Hypertensive Emergencies” is crucial for preventing death or irreversible disability.

ÖZET
“Hipertansif Acil Durum” ani ve hızlı şekilde tansiyonun genelde ≥180/120 mmHg seviyesine yükselmesi yüzden end-organ hasarı oluşmasıdır. Acil serviste “Hipertansif Acillerin” düzgün yönetimi ölüm ve kalıcı sakatlığı önlemek için çok önemlidir.

Key Words:
Hypertension, Emergency, Hypertensive emergency.

Anahtar Kelimeler:
Hipertansiyon, Acil, Hipertansif acil durum.
Hypertensive emergency is a severe high blood pressure (BP) condition (≥180/120 mmHg) without end-organ damage. This is also called “asymptomatic hypertension” (8). In this situation emergency physicians must differentiate if the rise of BP is acute or chronic, and lower the tension level appropriately for preventing end-organ damage (7).

INITIAL EVALUATION
The patient must be carefully evaluated in a short time. The previous history and especially previously used drugs, if it has any, must absolutely be examined (9). The evaluation of the patient can be handled under three titles: History, Physical examination, and Laboratory evaluation (10-13). The physical examination must be evaluated through laboratory tests. The targeted goal in the evaluation is to differentiate between hypertensive urgency and emergency (11). Whether there is end organ damage or not, may provide us with clues about whether the case is hypertensive urgency or an emergency. Hypertensive emergency is a severe high blood pressure characterized by end-organ damage, while hypertensive urgency does not include organ damage (14-16). When these two conditions are compared to each other, a hypertensive emergency is observed to be a more severe and deadly setting (17).

HISTORY
By keeping the time as short as possible, the physician must focus on the crucial points in the patient’s history. The previous history of the patient (preexisting hypertension, regular antihypertensive use) and drugs must be questioned in detail because monoaminooxidase (MAO) inhibitors and narcotics such as amphetamine, phencyclidine, and cocaine can cause hypertensive attacks/crisis (11,15). Another significant point is that the administration of drugs with MAO inhibitor combined with food including tyramine increases the side effects of these drugs (18). The neurological symptoms, such as headache and confusion mostly point hypertensive encephalopathy, while focal neurological findings such as lateral findings are more in favor of cerebrovascular incidents. Symptoms such as dyspnea, cough, and fatigue must not be ignored in the cardiovascular examination, because these kinds of symptoms are the guide for the determination of disorders that can result in myocardial infarction or angina (19). Don’t forget that sometimes hypertension can be a result rather than a cause so patient admitted to emergency department with a pressure at or higher than 180/120 mmHg must be also evaluated for history of acute head injury, trauma, ischemic stroke and pregnancy (for preeclampsia, risk of eclampsia) (8). Detailed sign or symptoms of target-organ damage and probable causes are described at table 2 (8) and incidence of end-organ damage for hypertensive emergencies is defined at table 3 (7).

PHYSICAL EXAMINATION
The neurological, renal and funduscopic examination, are the key steps that need to be carried out by physicians, and BP levels of each extremity should be checked carefully. The most important finding in favor of the hypertensive crisis is the acute changes in blood pressure (10). Because, any severe clinical condition or target-organ damage may not appear unless long-term systolic blood pressure (SBP) is higher than 200 mmHg and diastolic blood pressure (DBP) is higher than 150 mmHg (20).

LABORATORY EVALUATION
For the identification of the at-risk target organ/s (eg, heart, brain, aorta or kidneys) laboratory tests can guide us. Hemogram, biochemistry (eg, creatinine, electrolytes, cardiac biomarkers, Pro-BNP), and urine analysis (microscopic hematuria for acute renal failure, proteinuria for chronic rena failure), electrocardiogram (ECG), chest radiography, and computed tomography (CT) are helpful for evaluating the patient (7,9,10,15). Chest radiography can be used to indicate acute cardiac failure (14). It is beneficial for determining pulmonary edema (10). Contrast-enhanced thorax CT and magnetic resonance imaging (MRI) scans are used in exclusion of especially aorta dissection. Although transesophageal echocardiography (TEE) is a perfect method to show aorta dissection, but we cannot use it without bringing blood pressure to ideal levels. Also, transthoracic echocardiography might be used to find many problems of the heart and distinguish them (21). Brain CT or MRI can show intracranial hemorrhage, ischemic stroke and brain edema (8). ECG shows ischemia, hypertrophy and arrhythmias of the heart. The creatinin level is used for calculation of glomerular filtration rate to identify acute kidney failure (22).

INITIAL MANAGEMENT
There is no need to admit an asymptomatic patient to the hospital, unless he or she has significant clinical findings pointing end-organ damage because of elevated BP (usually ≥180/120 mmHg). In this setting this is a “hypertensive emergency” so the patient must be monitored at the Emergency Department or intensive care unit for a while with intravenous (IV) treatment (5,7,8). Monitoring and follow up can change depending on the condition of the patient (22). In case of elevated BP (≥180/120 mmHg) without end-organ damage signs
or symptoms it is a “hypertensive urgency”. So blood pressure must be gradually decreased under 180/120 mmHg by oral treatment and we can discharge the patient with recommendations of follow-up, and outpatient control (7).

When a hypertensive patient is examined, a differentiation must be made between accelerated hypertension and malignant hypertension. They are different although both are characterized by severe hypertensive symptoms (23). The common point in both, whether accelerated hypertension or malignant hypertension, is the fact that high blood pressure is observed with hemorrhage and exudate (24). Although they have many common points, papilledema is observed in malignant hypertension but not in accelerated hypertension (9,11,12,15). Papilledema is found in grade 4 hypertension. Therefore, malignant hypertension is grade 4 hypertension (12).

Table 2: Sign or Symptoms of Target-Organ Damage and Probable Diagnosis

<table>
<thead>
<tr>
<th>Sign Or Symptoms Of Target-Organ Damage</th>
<th>Probable Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea and vomiting, dizziness, headache</td>
<td>increased intracranial pressure, intracranial hemorrhage</td>
</tr>
<tr>
<td>Generalized neurologic symptoms (agitation, delirium, stupor, seizures, or visual disturbances)</td>
<td>hypertensive encephalopathy, intracranial hemorrhage</td>
</tr>
<tr>
<td>Focal neurologic symptoms</td>
<td>hemorrhagic stroke</td>
</tr>
<tr>
<td>Chest discomfort or pain</td>
<td>myocardial ischemia or aortic dissection</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>pulmonary edema</td>
</tr>
<tr>
<td>Acute, severe back pain</td>
<td>aortic dissection</td>
</tr>
<tr>
<td>Fresh flame hemorrhages, exudates (cotton-wool spots), or papilledema (grade III or IV hypertensive retinopathy)</td>
<td>hypertensive encephalopathy (rarely)</td>
</tr>
</tbody>
</table>

Table 3: Incidence of Hypertensive Emergencies according to end-organ damage,

<table>
<thead>
<tr>
<th>Damaged End-Organ</th>
<th>Diagnosis</th>
<th>Incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>Acute Heart Failure</td>
<td>14-37</td>
</tr>
<tr>
<td></td>
<td>Acute Coronary Syndrome</td>
<td>11-12</td>
</tr>
<tr>
<td>Brain</td>
<td>Acute Ischemic Stroke</td>
<td>37-45</td>
</tr>
<tr>
<td></td>
<td>Spontaneous Intracranial Hemorrhage</td>
<td>6-25</td>
</tr>
<tr>
<td></td>
<td>Hypertensive Encephalopathy</td>
<td>5-23</td>
</tr>
<tr>
<td>Kidney</td>
<td>Acute Renal Failure Risk</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>Acute Renal Failure</td>
<td>8</td>
</tr>
<tr>
<td>Vasculary</td>
<td>Eclampsia</td>
<td>1-2</td>
</tr>
<tr>
<td>Other</td>
<td>Eclampsia</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Acute Hypertensive Retinopathy</td>
<td>1</td>
</tr>
</tbody>
</table>

There is not a consensus on which medication to administer first in the control of hypertension emergencies and urgencies (5). In a hypertensive emergency, the medications change according to the affected organ (25). In case of hypertensive emergency, the aim is not decrease rapidly the BP to normal level. The mean arterial pressure (SBP + 2 (DBP/3) must be lowered about 10 to 20% within the first 30-60 minutes and then a further 5-15% during the next 23 hours (5,8). Following reaching targeted BP levels oral antihypertensive treatment. But if the patient’s emergent condition is combined with aorta dissection, then this duration must be shorter and targeted pressure level must be normotensive levels (SBP 100-120 mmHg in 20 minutes) (5,7,8,14,26). In case of severe preeclampsia/eclampsia or crises of pheochromocytoma the SBP should be decreased under 160 mmHg (7). If the patient has an acute ischemic stroke we should not lower the BP unless it is ≥220/120 mmHg (5,8). Besides...
if thrombolytic therapy is planned for the patient the targeted BP must be \( \geq 185/110 \) mmHg (5,8). In the management of hypertensive emergency (the idea agreed upon Europe and America), a decrease of 25% in the first hour can be accepted as rational. Again, the treatment must be performed as intravenously (5,25,27). If these changes are more than 25%, then auto regulatory mechanisms can be damaged and after a certain level, this can cause hypoperfusion, shock, and ischemia (15). The targeted goal in a hypertensive emergency (in the cases like pulmonary edema, hypertensive encephalopathy…) is 160/100-110 mmHg within 2-6 hours and of course, the patient must be brought to this level after the stabilization in the first hour (25). In the management of intracerebral hemorrhage the targeted BP levels are variable (8). In hypertensive urgency, on the other hand, the situation must be controlled using oral medicines in the first 24-48 hours, and again rapidly decreased blood pressure levels spoils perfusion and cause ischemia and infarction (20). Recommended target in general hypertension treatments is different. If the patient is 60 or over, the targeted level is lower than 150-90 mmHg and if 60 or under, it is lower than 140-90 mmHg. This advice is for the individuals between the ages of 29-60. For 15-29 years old people there are not enough randomized controlled studies so these advices are not valid (28). Many cases such as pregnancy, obesity, old age, and diabetes are associated with the hypertensive crisis. For this reason, the relationship between the hypertensive crises with such cases must be carefully studied (12). Similarly, a hypertensive crisis can be associated with many cases: subarachnoid hemorrhage, hypertensive intraparenchymal hematoma, acute ischemic stroke, hypertensive encephalopathy, intracranial hemorrhage, eclampsia, pheochromocytoma, unstable angina and acute left ventricular failure (9). The First choice medications for some conditions are described below (Table 4) (7,8).

**TREATMENT**

A-Calculator Channel Blockers

Calcium channel blockers can be a good option in the treatment of hypertensive cases because they have the ability to extend both smooth muscles and veins. In spite of this, they must be administered carefully in patients with congestive heart failure because they can give rise to severe adverse-effects such as AV Block and bradycardia (29).

1-Clevidipine

Clevidipine is a third generation dihydropyridine class calcium channel blocker metabolized by red blood cells, which has no adverse effect on the kidney and liver.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>First Choice for treatment</th>
<th>Attention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic Dissection</td>
<td>Esmolol / Labetalol</td>
<td>Decrease rapidly the SBP ( \geq 120 ) mmHg</td>
</tr>
<tr>
<td>Acute Pulmonary Edema</td>
<td>Clevidipin, Nitroprussid Nitroglicerin</td>
<td>Beta blockers are contraindicated</td>
</tr>
<tr>
<td>Acute Coronary Syndrome</td>
<td>Esmolol*, Labetalol, Nikardipin, Nitroglicerin*</td>
<td>Application of Nitrates together with PDE-5 inhibitors may induce deep hypotension. In case of mid-severe left ventricular failure with pulmonary edema, bradycardia (&lt;60/min.), hypotension, poor peripheral circulation, 2, or 3. Degree cardiac bloc and bronchospasm Beta blockers are contraindicated</td>
</tr>
<tr>
<td>Acute Renal Failure</td>
<td>Clevidipin, Fenoldopam, Nikardipin</td>
<td>In the need of rapid BP decrease, ACE inhibitors, ARBs, renin inhibitors and nitroprusside are contraindicated</td>
</tr>
<tr>
<td>Eclampsia/Preeclampsia</td>
<td>Hidralozin, Labetolol, Nikardipin</td>
<td>In the need of rapid BP decrease</td>
</tr>
<tr>
<td>Acute symphatic Discharge /Catecholamine discharge / (Feocromasitoma)</td>
<td>Clevidipin, Nikardipin, Fentolamin</td>
<td>In the need of rapid BP decrease</td>
</tr>
</tbody>
</table>

*Preferable for Acute Coronary Syndromes*
Nicardipine plays an important role in myocardial oxygenation because of its two properties as increasing stroke volume and coronary blood flow. Nicardipine is given in intravenous way so as to decrease blood pressure in both cardiac and cerebral ischemia (38). It's 100 times more soluble in water than Nifedipine so intravenous way is advised (39).

3-Nifedipine

Nifedipine is a medicine which directly affects coronary vessels but whose hypotensive effect cannot be directly controlled and therefore which is not suggested to be given to the patients especially to the elderly whose blood pressure is uncontrolled. It has two forms; oral and sublingual (19). Its effects begin after 5-10 minutes and last up to 6-8 hours. After 30-60 minutes, it reaches maximum efficacy (40). Nifedipine can disrupt cerebral and renal blood flow in the case of uncontrolled blood pressure and can cause myocardial ischemia; what’s more, such cases can result in death (41-44). It is not advised in patients who have severe hypertension. It is of risk in respect of hearth block like nicardipine and verapamil, which are among other calcium channel blockers (45).

B-ACE Inhibitors

Ace inhibitors show their effect blocking the Angiotensin Converting Enzyme and undertake important roles in managing malignant hypertension and must not be used by pregnant women because it can cause severe damage to the fetus in the 2nd and 3rd months of pregnancy. Besides, it must be used carefully in patients with bilateral artery stenosis. It has some rare adverse effects such as dry cough, rash, and taste problems. Another point not to be forgotten is the fact that it must absolutely be taken before the meals because absorption level increases when it is taken with meals (29).

1-Enalaprilat

When enalaprilat and captopril are compared, Enalaprilat has intravenous forms (15,19). That’s why enalaprilat is more popular in Hypertensive Emergency (15). One advantage of it over Captopril is the fact that it does not elevate intracranial pressure and not cause reflex tachycardia. The half-life of Enalaprilat, whose effect starts at the 15th minute and last 11 hours. Starting with 1.25 mg dosage it must be fortified as time goes on. Fortification dosages start with 1.25 mg and must be maximum 5 mg in a period of 12-24 hours (14). Enalaprilat, just like clonidine, is used in hypertensive urgency because it is effective for long periods and is poorly titratable (46).

2-Captopril

Captopril can be used as sublingual or oral. Because sublingual captopril has a rapid impact, it is used mostly in the cases where high blood pressure is characterized by an end-organ damage. On the other hand, this form is unfavorable and can cause allergic reactions in the body.
Although the oral form doesn’t have such disadvantages, it has a much slower impact than sublingual form. For this reason, sublingual form should be used in an emergency (47).

C-Beta and Alpha Blockers

1-Esmolol

Esmolol is a kind of cardio selective beta blocker that takes effect in a short time and is used in order to decrease blood pressure and systolic pressure. When esmolol is given as a bolus, its effect generally peaks in 6 or 10 minutes and also its half-life is 8 minutes (48). The total effect time of esmolol whose first effect can be seen in some minutes varies from 10 and 20 minutes. Its infusion dose starts from 50 µg/kg /min and it reaches up to 300 µg /kg/min (16). Not only does esmolol decrease blood pressure but also it blocks the stimulation of epinephrine and norepinephrine. For all these reasons, Esmolol can cause dizziness, dysrhythmias, congestive heart failure, bronchoconstriction and gastric pain (29). Its metabolism is done by erythrocytes in the blood and this explains the question of why it doesn’t damage the liver and the kidney (40).

2-Labetalol

Labetalol’s oral and parenteral forms can be found and its parental form can be given as a bolus or infusion. It decreases the blood pressure rapidly (16). Labetalol blocks alpha1 receptors and beta receptors. It blocks beta receptors 7 times more than alfa receptors (49). The effect of Labetalol, which can be used for many patients, starts in 5 or 10 minutes. Its effect continues from 3 hours up to 6 hours. One must be careful with using it on the patients who have diseases such as bronchospasm, congestive heart failure, or a serious bradycardia (48). In order to understand which one was more effective than the other one on the blood pressure in 30 minutes, CLUE trials of Labetalol and nicardipine were applied to 226 patients and at the end of these trials, it could be understood that labetalol was not as effective as nicardipine to reach the wished target of SBP (50).

3-Fentolamin

Fentolamin is a non-selective alpha receptor antagonist (5,8). It is used as IV bolus of 5-15 mg. and could be repeated if necessary in every 10-15 minutes as IV bolus (5,8). It should be used for the treatment of hypertensive emergencies associated with catecholamine discharge like feocromatisoma, MAO inhibitors’ interactions with drugs or foods, cocaine toxicity, amphetamine overdose or clonidine withdrawal (5,8).

D-Direct Acting Vasodilators

1-Fenoldopam

Fenoldopam is an agent which shows its vasodilatation making ability on periphery and which makes vasodilatation on kidneys (51-53). It is ten times more selective than other dopamine agonists because it is specific for Dopamin 1 receptors (19). As far as renal functions are concerned, Fenoldopam can be one of the drugs which are suggested to be given in hypertensive emergency (54). The early dose of this drug is 0.1 µg/kg/min, whose metabolism occurs rapidly without using CYP 450 enzymes and the effect of this drug continues from 30 up to 60 minutes. It peaks in ten minutes and its half-life time is 5 minutes (55). Whether its renal functions are normal or not, Fenoldopam increases clearance of creatin, flow rates of urine and sodium excretion (19). It never causes cyanide poisoning like Nitroprusside but it may have such side-effects as headache, dizziness, flushing and high-intraocular pressure (19).

2-Nitroprusside

Nitroprusside is a medicine used with intravenous infusions in many hypertensive emergency cases. When nitroprusside is used, it can bring about undesirable cases such as cyanide toxicity (29). Although Cyanide toxicity is a rare case, it is risky because it can cause renal failure (56). In the treatment of Cyanide toxicity, Hydroxocobalamine is used (19). Nitroprusside is a vasodilator which has vasodilatation effect both in arteries and veins (19). It effects begins within minutes following IV infusion and initial dose is 0,25-0,5 mcg/kg/dk (max dose is 8-10 mcg/kg/dk) (5). It has some disadvantages like luminous sensitivity and intraarterial monitoring requirement. One of its dose-dependent effect is increasing intracranial pressure. It is risky in terms of possibility to see coronary steal syndrome (20). For all these reasons, it can be an alternative medicine in patients whose kidneys and liver work adequately (19).

3-Nitroglycerin

Nitroglycerin causes vasodilatation by acting on veins more than it does on arteries. Arterial vasodilatation takes place only when high dosages are reached. The duration action of this medicine is 3-5 minutes and effect start at the 2nd -5th minutes. It is suggested to start with 5µg/kg/min. This dosage is increased every 3-5 minutes by 5µg/kg/min. There is no dosage limitation although hypotension risk increases with the dosages over 200 µg/kg/min (5,12). Its effect mechanism lowers the preload and cardiac output. By this means, it lowers the blood pressure. Yet, this disrupt the nourishment of brain and kidneys. Two adverse effects such as hypotension and reflex tachycardia can be observed. However, it can be used as a supplementary drug to another one in small dosages in the case that hypertensive emergency is together with acute coronary syndrome or acute pulmonary edema (13).

4-Hydralazine

Hydralazine shows its effect on arteries directly, and it is one of the medicine to be preferred with pregnant patients in respect of lowering blood pressure, primarily
HYPERTENSIVE CRISES WITH CHILDREN

It should be regarded not to reduce the blood pressure rapidly within the control of hypertensive emergency experienced with children and adolescents, because a rapid blood pressure reduction may cause hypoperfusion in vital organs (58). If the hypertensive disorders experienced by children and adults shall be analyzed in terms of end organ damage, it can be particularly analyzed in terms of left ventricle hypertrophy.

Echocardiography may be applied in order to determine the availability of left ventricle hypertrophy (59). For the control of emergency, it's more helpful to use intravenous drugs by infusion. Labetalol and sodium nitroprusside may be used for this purpose. Oral drugs are preferable for the control of hypertensive urgency (58).

HYPERTENSIVE CRISSES DURING PREGNANCY

Hypertension observed in pregnant women may be examined under different titles. Among these, particularly preeclampsia and eclampsia should be considered since they are urgent. Preeclampsia is a hypertensive type accompanied with proteinuria and if it's also accompanied with mental fog, it's called eclampsia. Preeclampsia has a significant mortality rate among infants younger than 34 months and mothers (60).

REFERENCES