MALIGNANT HYPERTENSION THERAPY

Dani Feldman
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HYPERTENSION- DEFINITION

- BLOOD PRESSURE IS A CONTIONOUS VARIABLE

- THE DEFINITION OF HYPERTENSION HAS BEEN ADVOCATED AS A GUIDELINE FOR TREATMENT

- THE DEFINITION IS BASED ON THE ESTIMATED LEVEL OF BLOOD PRESSURE ABOVE WHICH THE BENEFIT OF THE PHARMACALOGIC THERAPY IN REDUCING C.V RISK EXCEEDS THE RISK AND INCONVENIENCE OF THERAPY

BLOOD PRESSURE – CLASSIFICATION (for adults >= 18 years old)

CATEGORY	SYS. PRESSURE (mmHg)	DIAS. PRESSURE (mmHg)
OPTIMAL	<120	<80
NORMAL	<130	<85
HIGH NORMAL(PRE HT):	130-139	85-89
HYPERTENSION		
STAGE 1 (MILD)	140-159	90-99
STAGE 2 (MODERATE)	160-179	100-109
STAGE 3 (SEVERE)	>=180	>=110

HYPERTENSION ETIOLOGY

PRIMARY/ESSENTIAL(90%):

- GENETIC
- MEN
- ALCOHOL
- OBESITY
- PHYSICAL INACTIVITY
- INCREASED SALT INTAKE
- BLACK

HYPERTENSION ETIOLOGY (CONT.)

SECONDERY (10%):

-*RENOVASCULAR DISEASE*

-*RENAL PARANCHYMAL DISEASE*

-*ENDOCRINE*: CUSHING,THYROID, PHEOCHROMOCYTOMA, HYPERALDOSTERONISM, HYPERPARATHYRODISM

-*HEMATOLOGIC*: POLYCYTHEMIA

-*COARCTATION OF THE AORTA*

-CARCINOID SYNDROM

-*NEUROGENIC DISOEDR:* I.C.P, BRAIN TUMORS, ENCEPHALITIS, POLYNEURITIS….

-*DRUG INDUCED*: OCP'S, LICORICE, COCAINE, SYMPATHOMIMETICS, MAO- INHIBITORS, CYCLOSPORIN…

HYPERTENSION - EPIDEMIOLOGY

- PREVALENCE WORLD WIDE = 1 BILLION

- PREVALENCE IS HIGHER IN DEVELOPED COUNTRIES (OBESITY, LIFE SPAN, DIATERY HABITS…)
(MOST COMMON CAUSE OF PREVENTABLE DEATH IN DEVELOPED COUNTRIES)

-PREVALENCE IS INCREASING RAPIDLY IN DEVELOPING COUNTRIES

-TOTAL DEATH OF 7 MILLION PER YEAR

-RACE: African Americans have a higher incidence of hypertensive emergencies than Caucasians.

-SEX: Males are at greater risk of hypertensive emergencies than females.

-AGE: Most commonly in middle-aged people.Peak age:40-50yrs.

HYPERTENSION SYNDROMS

SYSTOLIC B.P>230 mmHg
DIASTOLIC B.P>130 mmHg

SEVERAL SYNDROMS:

- HT URGENCY: the BP is a potential risk but has not yet caused acute end-organ damage. These patients require BP control over several days to weeks.

- HT EMERGENCY: severe hypertension with acute impairment of an organ system (e.g., central nervous system [CNS], cardiovascular, renal). In these conditions, the blood pressure (BP) should be lowered aggressively over minutes to hours.Presence

1. ACCELERATED HT: recent significant increase over baseline blood pressure that is associated with target organ damage. This is usually vascular damage on fundoscopic examination, such as flame-shaped hemorrhages or soft exudates (GRADE 3) , but without papilledema.

2. MALIGNANT HT: high b.p with pappiledema (GRADE 4)

MALIGNANT HYPERTENSION

- HYPERTENSIVE EMERGENCY!!!
- LEADING TO AN ACUTE END ORGAN DAMAGE
- LESS THAN 1% OF HT PATIENTS DEVELOP THE MALIGNANT PHASE
- AVARAGE AGE OF DIAGNOSIS IS 40
- MEN>WOMEN

HYPERTENSION CRISIS- RETINA

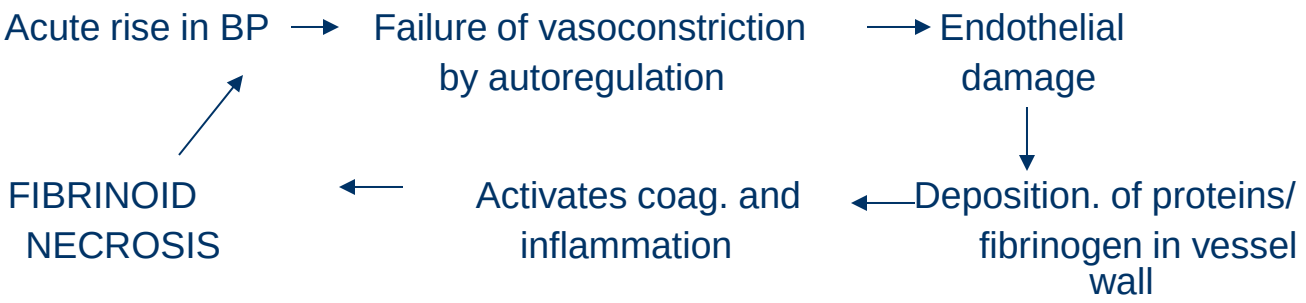
Retinal hemmorhages (grade 3)- ACCELERATED HT

Pappiledema (grade 4)- MALIGNANT HT

MALIGNANT HYPERTENSION-PATHOPHYSIOLOGY

BP =PVR*CO(SV*HR)

Rate at which MAP rises more important than absolute rise



- RAAS plays an important role in initiating and perpetuating BP rise by causing vasoconstriction and fluid retention.

- THIS CYCLE MUST BE STOPPED IN ORDER TO PREVENT FURTHER VASCULAR INJURY AND TISSUE ISCHEMIA!

MALIGNANT HYPERTENSION- ACUTE END ORGAN DAMAGE- CNS

1. Neurological –

-normal: increase in BP → cerebral arterioles vasoconstrict → cerebral blood flow (CBF) remains constant

-hypertensive emergency: loss of autoregulation ability (decomp.) → dialation of cerebral vessel exsessive cerebral blood flow+ leakage from cappilaries

RESAULT:

Hypertensive encephalopathy- 3RD MOST COMMON (16.3%)

Cerebral vascular accident/cerebral infarction – MOST COMMON (24.5%)

Subarachnoid hemorrhage

Intracranial hemorrhage -

Retinopathy Keith-Wagner- GRADES 3 AND 4.

Eclampsia

MALIGNANT HYPERTENSION- ACUTE END ORGAN DAMAGE- CNS

2. Cardiovascular

- Myocardial ischemia/infarction – 4TH (12%).

- Acute left ventricular dysfunction

- Acute pulmonary edema – 2ND MOST COMMON (22.5%)

Aortic dissection -

3.RENAL

ARTERIOSCLEROSIS, FIBRINOID NECROSIS ⟶ overall impairment of renal protective autoregulation mechanisms!

RESAULT:

- Worsening renal function - **Acute renal failure/insufficiency** (BP ↑)
- Hematuria + red blood cell (RBC) cast formation
- Proteinuria.

4. Microangiopathic hemolytic anemia

MALIGNANT HYPERTENSION-CLINICAL SYMPTOMS

C.V:
palpitations, arrhythmias, chest pain, dyspnea, pul. Edema.

BRAIN:
headaches, nausea, vomiting, blindness, seizures, coma

KIDNEY:
oliguria, hematuria, proteinuria, electrolyte imbalance, uremia, azothemia

EYE:
flashes, scotoma

GENERAL:
sweating, pallor, flushes, tinnitus, epitaxis, fear of death

MALIGNANT HYPERTENSION-THERAPY - general

- HOSPITALIZATION
- RELAXATION (NON STRESSED ENV.)
SCREEN FOR END ORGAN DAMAGE

INITIAL AIMS:

1. CORRECTION OF MEDICAL COMPLICATION
2. REDUCTION OF MAP BY 20-25% IN THE 1ST HOUR
3. REDUCTION OF DIASTOLIC PRESSURE TO 1\3 OVER MINUTES TO HOURS HOURS=110 mmHg (BUT NOT BELOW <95 mmHg – IN ORDER NOT TO CAUSE CEREBRAL HYPOPERFUSION)

BP should be reduced

- immediately-
- gradually

(Specifically)

DRUGS should be used i.v

MALIGNANT HYPERTENSION THERAPY – IV DRUGS

Drug	Route	Starting Dose	Time Course of Action			Oral Preparation Available
			Onset	Peak	Duration	
IMMEDIATE ONSET						
Nitroprusside	Continuous IV	0.25 μg/kg per min	<1 min	1–2 min	2–5 min	No
Nitroglycerin	Continuous IV	5 μg/min	1–5 min	2–6 min	3–10 min	No
Diazoxide	IV bolus	50 mg q5–10min up to 600 mg	1–5 min	2–4 min	4–12 h	No
Fenoldopam	Continuous IV	0.1–0.3 μg/kg per min	<5 min	5–10 min	30 min	No
Esmolol	Continuous IV	250–500 μg/min × 1 min; then 50–100 μg/kg per min × 4 min	1–2 min	2–3 min	10–20 min	No
DELAYED ONSET						
Enalaprilat	IV	1.25 mg q6h	10–15 min	3–4 h	6–24 h	Yes
Hydralazine	IV, IM	5–10 mg q20min × 3	10–20 min	20–40 min	4–12 h	Yes
Labetalol	IV	20–80 mg q10min up to 300 mg	5 min	20–30 min	3–6 h	Yes
Nicardipine	IV	5–15 mg/h	5–10 min	20–40 min	1–4 h	Yes

MALIGNANT HYPERTENSION THERAPY – IV DRUGS cont.

2 MAIN CLASSES OF DRUGS:

1.Vasodilators:

Nitroprusside
Nitroglycerine
Nicardipine
Hydralazine
Enalapril
Fenoldopam

2. Adrenergic inhibitors

Labetalol (a+b blocker)
Esmolol (b-1 selective blocker)
Phentolamine (a1 blocker)

MALIGNANT HYPERTENSION-THERAPY – SPECIFIC DRUGS

1. NITROPRUSSIDE :

- 1ST CHOICE FOR HT CRISIS!
- ONSET 30 SEC FOR FEW MIN

VEINS + ARTERIES

DECREASE PRELOAD = USED IN ACUTE MI!

SIDE EFFECT: THIOCYANIDE TOXICITY, METHEMOLOBINEMIA, HYPOTHYRODISM

2. NITROGLYCERIN:

- Coronary vasodilator
- Direct venodilator (variable arterial effects)

SIDE EFFECT: headaches and tachycardia ,Methemoglobinemia

3. LABETALOL:

Combined alpha & beta blocker

Beta blockade blunts reflex tachycardia from alpha blockade

Myocardial depression

Caution in patients with reactive airway disease

MALIGNANT HYPERTENSION-THERAPY – SPECIFIC DRUGS

4. FENOLDOPAM : (DOPAMIN AGONIST)

Short acting (30 MIN)

Rapid elimination upon discontinuation

No dosing adjustment for pre-existing renal or hepatic impairment

Increases renal blood flow and maintains GFR

5. HYDRALAZINE (oral):

- Strict arteriole vasodialator

-3rd \ 4th option in HT crisis.

MALIGNANT HYPERTENSION THERAPY: SPECIFIC RECOMMENDATION FOR DIFFERENT CLINICAL FORMS (exmamples)

1. Hypertensive encephalopathy

Preferred medications **:**

Labetalol

Nicardipine

Esmolol

Medications to avoid **:**

Nitroprusside (was used in the past- caused ICP↑)

Hydralazine

Treatment guidelines: **Reduce mean arterial pressure (MAP) 25% over 8 hours.**

MALIGNANT HYPERTENSION THERAPY: SPECIFIC RECOMMENDATION FOR DIFFERENT CLINICAL FORMS (exmamples)

2. Aortic dissection –

Immediate redn. In BP and mainly shear stress (change in BP with change in time) is essential to limit the extension of damage as surgery is being considered.

Preferred medications

Labetalol

Nicardipine

Nitroprusside (with beta-blocker)

Esmolol

Morphine sulfate

Medications to avoid

Avoid beta-blockers if there is aortic valvular regurgitation or suspected cardiac tamponade, HYDRALAZINE (increase shear stress)

Treatment guidelines: **Maintain SBP <110 mm Hg, unless signs of end-organ hypoperfusion are present.**

+Narcotic analgesics

TIME TO ACHIEVE: 20 MINUTES!!!!!

MALIGNANT HYPERTENSION THERAPY: SPECIFIC RECOMMENDATION FOR DIFFERENT CLINICAL FORMS (exmamples)

3. Preeclampsia/eclampsia

Preferred medications

Hydralazine

Labetalol

Nifedipine

Medications to avoid

Nitroprusside

Angiotensin-converting enzyme inhibitors

Esmolol

Treatment guidelines: **In women with eclampsia or preeclampsia, SBP should be <160 mm Hg and DBP <110 mm Hg in the prepartum and intrapartum periods. If the platelet count is <100,000 cells mm3 BP should be maintained below 150/100 mm Hg. Patients with eclampsia or preeclampsia should also be treated with IV magnesium sulfate to avoid seizures**

MALIGNANT HYPERTENSION THERAPY: SPECIFIC RECOMMENDATION FOR DIFFERENT CLINICAL FORMS (exmamples)

4. CARDIAC CRISIS
L.V FAILURE AND PUL. EDEMA

Preferred medications
Nitroglycerin
Enalaprilat
Nitroprusside

Treatment guidelines: **Treatment with vasodilators (in addition to diuretics) for SBP ≥140 mm Hg. IV or sublingual nitroglycerin is the preferred agent**

BP CONTROL IS SECONDARY to the primary problem - *open the infarct related artery and treat pain, diurese and oxygenate those in pulmonary edema*

MALIGNANT HYPERTENSION THERAPY: SPECIFIC RECOMMENDATION FOR DIFFERENT CLINICAL FORMS (exmamples)

4. RENAL INSUFFICENCY:

Goal is to prevent further renal damage by maintaining adequate blood flow**.**

Preferred medications:

Nitroprusside

MALIGNANT HYPERTENSION-PROGNOSIS

Median survival duration:144 months

for all patients presenting to ED with hypertensive emergency.

5 yr survival rate :74%.

THANK YOU FOR YOUR ATTENTION