General anesthesia 2

IV drug : Dexmedetomidine

- highly selective A2 adrenergic agonist >>if patient receive clonidine therapy will decrease anesthetic requirements .
- Action of dexmedetomidine

1- hypnotic effects : via action in locus Ceruleus >>stimulate A2 >>reduces central sympathetic output >>increase firing of inhibitory neurons (facilitated inhibition) → in CNS
2- Analgesic effect : at level of spinal cord modulates release of substance P
3- Sedative effect : activate endogenous sleep pathway (promote normal sleep mechanism)

Therapeutic uses :

1- short term sedation of intubation & ventilation in a ICU setting
2- adjunct to general anesthesia
3- decrease doses needed for inhaled and injected anesthesia

Adverse effects :

1- not common tolerance & dependence but may happen
2- moderate decrease in heart rate , systemic vascular resistance , blood pressure in repeated infusion
3- unopposed vagal stimulation >>heart block , sever bradycardia , asystole (worsens effect)

major adverse effects of dexmedetomidine

Inhaled anesthesia

1. Volatile anesthetics: halothane, enflurane, isoflurane, desflurane, sevoflurane. → Contains halogens. Cl, F...
2. Gaseous anesthetics: nitrous oxide, xenon.

Pharmacokinetics of inhaled anesthesia :

1-more anesthetic effect depends on concentration of drugs in CNS and this consentration depends on :
A- uptake and distribution of inhaled anesthesia (IA) : HIgh con. In inspired lead to spread to alveoli then from alveoli to blood then from blood to brain
B - elimination of IA from brain not from body : revers events of uptake
2-IA are relatively insoluble in blood & brain >> rapid onset & fast elimination than soluble
3- washout of (nitrous oxide , desflurance , sevoflurance they are less soluble) rapid >>rapid recovery compared with halothane & isoflurane (more soluble)
4-major route of elimination from the body by lungs
5- contribution of hepatic metabolism :
Oxidative metabolism by CYP2E1 of halothane >>trifluoroacetic acid and release of chloride and bromide ions.
Under low O2 tension halothane metabolized to chlorotrifluoroethyl free radical >>halothane hepatitis.
6-isoflurane & desflurane are least metabolized of fluorianated a
7-The metabolism of methoxyflurane (70%) results in elevation of renal fluoride levels → nephrotoxicity.
8- nitrous oxide can mtabolized by bacteria in GIT
9-Sevoflurane is degraded by contact with the carbon dioxide absorbent soda lime in anesthesia machines yielding a vinyl ether which can cause renal damage if high concentrations are absorbed.

"Less Soluble → faster onset of Action."
"More soluble → Shorter Onset of Action."

→ degraded Not metabolized.

Pharmacodynamics of IA :

1-primarily halogenated inhalational agents target GABA receptor chloride channel directly active or facilitated as sedative
2-IA also target glycine receptors >> inhibitory neurotransmission in spinal cord & brain stem
3-Nitrous oxid & ketamin they only general anesthetics do not act on gaba & glycine , they act on NMDA glutamate receptor.
4- ALL anesthetic agent (IV & INHALED) have action on GABA & GLYCINE
5- Inhalational agents >>nicotinic acetylcholine receptors are inhibited >>analgesia & amnesia
6- certain IA >>hyperpolarization by activation of K channel
7- interaction with specific nerve >> modification of ion currents
8-IA >>presynaptic inhibition of neurotransmitter release in hippocampus >> amnesia

Organ system effects of IA :

– : decrease.
+ : increase.

1- cardiovascular
A. Halothane&enflurane : reduce CO THEN ABP.
B. Isoflurane & desflurane & sevofluran : Vascular dilation > reduce ABP
C.HALOTHANE: direct stimulate vagal Then bradycardia
D. Desfluran & isoflurane : increase Heart rate
E. All depress myocardial function Including nitrous oxide
F. Halothane & lesser extent isoflurane Ventricular arrhythmias

2- respiratory
A. All except nitrous reduce. tidal volume >>increase RR
B.all volatile >respiratory depressant >reduce response to CO2 >increase PaCO2.
c.respiratory depressant overcome by assisted vortex controlled ventilation ↓ can't be prevented if it's happened...
D.IA depress mucociliary > pool mucus >atelectasis>postoperative. respiratory infection .
E. All volatile have Some degree of bronchodilating action
F. Airway irritation in desflurane

3- brain
A. (-) metabolic rate of brain
B. + cerebral Blood flow by (-) cerebrovascular resistance
Nitrous the least likely to + CBF
C.increase ICP Reduced by hyperventilation before given Volatile

4-on kidney.
A. (-) GFR & Urine flow
B. Impair autoregulation of RBF

5- on liver
A. (-) portal blood flow

6-on uterine smooth muscle
A. Nitrous has little effect
B. Halogenated anesthesia are potent muscle relaxants (not given during delivery)

Toxicity of IA :

1- Hepatotoxicity :
A. Previous expositor to halothane >> potentially life threatening
B.it is rare C. Obese patient most susceptible

Mechanism of hepatotxicity :
A. Initiation of immune-mediated responses by reactive metabolites
- Serum of patients with halothane hepatitis contain a variety of autoantibodies against hepatic proteins.
- Trifluoroacetylated proteins in the liver could be formed in hepatocytes during halothane biotransformation.
- Even patient do not have hepatitis have autoantibodies in sera after halothane anesthesia

2. Nephrotoxicity :

- **long exposure to methoxyflurane & enflurane >> formation fluoride ions by renal enzyme B-lyase > change renal concentrating ability & may be proximal tubular necrosis**

3- malignant hyperthermia :

Autosomal dominant disorder of skeletal muscle in general anesthesia with volatile + succinylcholine (important)

- **rapid onset of tachycardia & hypertension , sever muscle rigidity , hyperthermia, hyperkalemial , acidosis (important)**

it's rare but important cause of morbidity or mortality

Dantrolene reduce malignant hyperthermia

Note → Malignant means Rapid elevation of temp.

4- prolonged exposure to nitrous >> (-) methionine synthase activity >>megaloblastic anemia in inadequately ventilated operating room personnel.

 # nitrous has analgesic & amnesia

↳ NO , No Anesthetic effect.

Done by : Ibrahim alfadel

IA : inhaled anesthesia

ICP : intra cranial Pressure

RR : respiratory rate

CBF : cerebral blood flow

CO : cardiac output

ABP : arterial blood Pressure .