

NAME	BARBITURATES	PROPOFOL	KETAMINE
	THIOPENTAL    METHOHEXITOL		
<b>STRUCTURE</b>	DERIVATIVE OF BARITURIC ACID UREA + MALONIC ACID BASIC STRUCTURE SIDE CHAINS AND SUBSTITUTIONS DENOTE ACTIVITY AND SIDE EFFECTS SULFA- INCREASED LIPID SOL. CH <sub>3</sub> - SHORT ACTING BUT CONVULSANT PROPERTIES BRANCH CHAIN- ANTICONVUL.	ALKYLPHENOL 2,6,-DIISOPROPYLPHENOL Mw 178	PHENCYCLIDINE DERIV. RACEMIC MIXTURE S-MORE ANALGESIA RAPID METABOLISM FEWER EMERGENCE REACTIONS M.W. 238
<b>PREPARATION</b>	DRUG +ANHYDROUS SODIUM CARBONATE    pH 10-11 ANTIMICROBIAL PROPERTY STABLE ONE WEEK IN FRIDGE IF MIX WITH ACIDIC DRUGS PRECIPITATE IN IV IE. SUCCINYLCOLINE, PANC, VEC, ATRAC, ALFENT, SUF, MIDAZOLAM	1% SOL'N IN 10% SOYBEAN OIL 2.25 %GLYCEROL 1.2% EGG PHOSPHATIDE  GOOD BACTERIAL MEDIUM EDTA METABISULFITE DILUTE WITH DSW	CHLOROBUTANOL AS SOLVENT- NEUROTOXIC THEREFORE AVOID INTRATHECAL OR EPIDURAL
<b>MECHANISM</b>	INTERACT WITH GABA A ENHANCE ACTION OF GABA MIMIC GABA AT ANESTH CONC. HYPERPOLARIZE POSTSYNAPTIC MEMBRANE INCREASE CL CONDUCTION INHIBIT SYNAPTIC TRANSMISSION OF GLUTAMATE AND ACh	ACT AT B1 SUBUNIT OF GABA NMDA RECEPTOR NOT ANTIANALGESIC	NMDA RECEPTORS TO PRODUCE ANESTHESIA OPIOD RECEPTORS Mu, Delta, Kappa MUSCARINIC ANTAG DELERIUM, BRONCHODIL SNS ACTION
<b>PHARMKIN</b>	VOL. D(l/kg) 2.5+/-1.0 2.2+/-0.7 CL(ml/min/kg) 3.4+/-0.5 10.9+/-10 ELIM 1/2(hrs.) 11.6+/-6 3.9+/-2.1 80% PROTEIN pH CHANGES AFFECT IONIZAT. ACIDOSIS INCREASED EFFECT	3.4-4.5 30-60 0.5-1.5 GLUCORONIDATION - INACTIVE SOME EXTRAHEPATIC	2.5-3.5 16-18 2-3hrs TO NORKETAMINE( 20-30% ACTIVITY) TO HYDROXY- NORKET

<b>PHARMDYN</b>	INDIVIDUAL VARIATION HYPOVOLEMIA MORE TO BRAIN AND LESS REDISTRIBUTION AWAY LEAN BODY MASS DECREASED WITH AGE, AGE INCREASED VOL.D IN KIDS NEED MORE DECREASED IN ELDERLY 25-30% RENAL FAILURE INCREASED VOL. BUT DECREASE PROTEIN. SAME IN LIVER DISEASE	SAME PRINCIPLES NOT IN PREG NOT UNDER 3 ELDERLEY - CONCENTRA- TION DEPENDENT SENSIT- IVITY CPB - INCREASE VOLUME OF DISTRIBUTION - SAME CHILDREN	S-KETAMINE ANTIAPOPTOTIC
<b>DOSE</b>	ADULT 2.5-4.5 mg/kg CHILD 5-6 mg/kg ELDERLY 30% reduction IF PREMED. IE 5 ugm/ kg FENT REDUCE 40%  METHOHEX 1.5mg/kg = 4.0mg/kg THIO	DOSE ED95 ADULT 2-2.5 mg/kg < 2 YEARS 3.0mg/kg ELDER 1-2 SEDATION 25-100 ugm /kg/min ICU HYPERLIPEMIA. VT NOT PEDS	INDUCTION 0.5-2 mg/kg IV 4-6 mg/kg IM MAINTENANCE 0.5-1 mg/kg prnq 15 min 15-45ugm/kg/min(70% n2o) 30-90 ugm/kg/min SEDATION 0.2-0.8 mg/kg 2-4 mg IM ANALGESIA 0.25 mg/kg
<b>CNS</b>	SUBANESTHETIC DOSE HYPERALGESIC DOSE RELATED EEG SUPPRESSION FLAT EEG AT 4mg/kg/hr DECREASE CMRO2 PARALLEL DECREASE CBF, ICP METHOHEXITOL INCREASE SEIZURE RISK DECREASE SSEP AT FLAT EEG BUT MAINTAINED IOP DECREASE FOR 2 MINUTES 40% DOES NOT DECREASE BASAL METABOLIC FUNCTION IN CNS	SIMILAR TO BARBS □ DEPENDENT DECREASE IN BIS 63 50% UNCON 51 95% UNCON DECREASE ICP 30% AND DECREASE CBF 10% NORMAL RESPONSE TO CO2 AND AUTOREGULATION WHEN INCREASE ICP DECREASE 30-50% AND DECREASE CBF BUT CMRO2 36%	FUNCTIONAL DISORGANI- SATION THALAMONEOCORTICAL PROJECTION SYSTEM DECREASE FUNCTION IN ASSOCIATION AREAS OF CORTEX AND THALAMUS PROFOUND ANAGESIA BUT MANY REFLEXES INTACT CORNEAL, COUGH, SWALLOW BUT MAY NOT BE PROTECTIVE

OVERALL PROTECTIVE  
 IN HYPOXIC INJURY  
 BRAIN STEM ER NO CHANGE  
 AUDITORY ABRUPT DECRE.  
 RARE POSTOP SEIZURE  
 RISK 1/50000  
 USUALLY OK IN EPILEPSY  
 TOLERANCE/ADDICTION

IOP DECREASE 30-40%  
 EVEN BETTER WITH  
 SECOND SMALL DOSE

SUPPRESS NMDA  
 DECREASE ACh  
 INCREASE DOPAMINE  
 INCREASE PLEASURE,  
 ADDICTION  
 DECREASE SEROTONIN  
 DECREASE EMESIS

30 SEC ONSET  
 MAX AT 1 MIN  
 PUPILS DILATE  
 LACRIMATION  
 SALIVATION  
 NYSTAGMUS  
 AWAKE  
 LIMB MOVEMENTS  
 AWAKE 10-15 MIN  
 FULL ORIENTATION 15-30  
 INCREASE CMRO2  
 CBF, ICP  
 CO2 RESPONSE MAINTAIN  
 IF VENTILATE CAN  
 DECREASE ICP  
 INCREASE IOP

RESP

APNEA  
 DECREASE RESPONSE TO  
 HPOXEMIA AND HYPERCAPNIA  
 RELATIVE INCREASE IN LARYNGEAL  
 REFLEXES TO PROPOFOL  
 DECREASED MUCOCILIARY  
 CHANGE  
 SAFE IN ASTHMA  
 NO BRONCHODILATION

SIMILAR TO BARBS  
 APNEA 25-30%  
 OFTEN > 30 SEC.  
 RATE DECREASE 2 MIN  
 MIN VOL. 4 MIN  
 DECREASE CO2 RESPONSE  
 AT 100ugm/kg/min  
 APPROX 50-60%  
 EQUAL TO 1 MAC  
 HALOTHANE BUT LITTLE  
 FURTHER CHANGE EVEN  
 IF DOUBLE INFUSION RATE  
 BRONCHODILATION  
 - MUSCARINIC RECEPTORS  
 - VAGAL INHIBITION  
 -METABISULFATE CANCELS  
 BRONCHODILATION

MINIMAL EFFECT ON RESP.  
 DRIVE  
 APNEA AT HIGH DOSES  
CHILDREN MAY BE MORE  
SENSITIVE  
 BRONCHODILATOR BY  
 SNS AND DIRECT EFFECT  
 INCREASE SALIVATION  
 ? AIRWAY SAFETY

ATTENUATES HPV

**CVS**

<p>VENODILATION AND PERIPHERAL POOLING DECREASE PRELOAD          DECREASE CONTRACTILITY          GREATER THAN PROP, MID, KET, ETOM          LESS THAN INHALATIONAL          DECREASE NO SYNTHETASE          DECREASE INFLUX TRANSAR-COLEMMAL          CALCIUM          INCREASE HR, MVO2          NO CHANGE SVR, CATECHOL SENSITIVITY</p>	<p>DECREASE BP 25-40%          CI,SVI,SVR          RIGHT AND LEFT HEART          DECREASE PRELOAD AND AFTERLOAD          DECREASE BARORECEPTOR          NO CHANGE AV OR CONDUCT          NO CHANGE HR (INHIBITS BRONCHORECEPTOR)          INFUSION LESS EFFECTS          GLOBAL DEMAND BALANCE          SUPPRESS ATRIAL TACHY          AVOID IN EP. STUDIES</p>	<p>INCREASE HR, BP,CI,MVO2          SECOND DOSE MAY NOT RESPOND OF OPPOSITE EFFECT DUE TO CATECHOL DEPLETION          IF INCREASE PVR MAY INCREASE RELATIVE TO SVR          CENTRAL AND SYNPATHO-ADRENAL AXIS          BLUNTED BY BENZOS          INHALED, OPIATES ETC</p>
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**NMR**

NO CHANGE	NO CHANGE	INCREASED NMB
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**MH**

OK	OK	OK BUT CONFUSING
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**ALLERGY**

<p>1/30000 BOTH ANAPHLACTOID AND AXIS          STEVENS -JOHNSON SYNDROME</p>	<p>ANAPHYLACTOID DRUG AND EMULSION          ATOPY          CROSS SENSITIVE TO COSMETICS</p>	RARE
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**ENDOCRINE**

<p>SLIGHT INCREASE CORTISOL, GLUCOSE           PORPHYRIA ABSOLUTE CONTRIND, IN ACUTE INTERMITTENT AND VARIEGATE          ( INTERFERE WITH AMINO LEVULINIC ACID SYNTHETASE)</p>	NONE	<p>SEE ABOVE          AVOID IN HYPERTHYROID</p>
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<b>MISC</b>	MINIMAL HISTAMINE DECREASE RENAL FLOW DECREASE NEUTOPHIL FUNCTION	AS EFFECTIVE AS NALOXONE FOR PRURITIS NO CHANGE HEPATIC OR FIBRINOLYTIC FUNCTION SUPPORTS GROWTH OF E.COLI, PSEUDOMONAS	INHIBITS CENTRAL SENSITIZA- TION - DECREASES ANALGESIC PERIOP EPIDURAL USE 0.5 - 1.0 MG/KG AVOID IN SCHIZOPHRENIA+ WHEN OTHER CAUSES OF DELERIUM
<b>RECOVERY</b>	11-20 % N+V THROMBOSIS AND PHLEBITIS IF INTRARTERIAL SEVERE SPASM. TREAT WITH IV LIDO AND STELLATE EPIDURAL... DILUTE AND BUPIVICAINE TO PRECIPITATE  DRIVING 8 HRS ABN SLEEP 12 HRS	MAKES YOU BABE IN EYES OF PATIENT ANTIEMETIC PAIN ON INJECTION LIDO, FENT,METOCLOPROM INTRAART HURTS BUT NO SPASM MYOCLONUS POSTURING PROPOFOL INFUSION SYNDROME - 5 MG/KG/HR OR > 48 HRS. - CARDIOMYOPATHY, ACIDOSIS LIPEMIA ETC. - CARNITINE DEFICIENCY BLOCKS UPTAKE OF FATTY ACIDS INTO MITO.	EMERGENCE DELERIUM LESS COMMON IN CHILDREN AND WITH REPEATED USE BLOCKED BY BENZOS MISINTERPRETATION OF AUDITORY AND VISUAL STIMULI LOSS OF PERCEPTION OF GRAVITY GREATER IN FEMALE, HIGHER DOSE, ATROPINE PERSONALITY DISORDER, DROPERIDOL

<b>SUMMARY</b>	<b>CEREBRAL EFFECTS</b>	<b>RESPIRATORY EFFECTS</b>	<b>CARDIOVASCULAR</b>
<b>THIOPENTAL</b>	POS	NEG	NEG
<b>METHOHEX</b>	POS	NEG	NEG
<b>ETOMIDATE</b>	POS	NEUT	POS
<b>PROPOFOL</b>	POS	NEG	NEG
<b>KETAMINE</b>	NEG	POS	NEG
<b>DIAZEPAM</b>	POS	NEUT	NEUT

**MIDOZOLAM**

POS

NEUT

NEUT



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## ETOMIDATE

CARBOXYLATED IMIDAZOLE  
WATER SOLUBLE AT  
PHYSIOLOGIC pH  
ONLY DEXTRO ISOMER IS  
ACTIVE

0.2% SOL'N  
35% PROPYLENE GLYCOL  
pH 6.9--PAINFUL  
LITTLE RISK OF PRECIP.

GABA ?  
REVERSED BY GABA  
ANTAGONISTS

INACTIVE METAB. KIDNEY ELIM.  
2.2-4.5  
10--20  
2--5  
75% PROTEIN BINDING  
RAPID ONSET 30 SECS

SAME PRINCIPLE AS BARB

INDUCTION

0.2-0.6 mg/kg

MAINTENANCE

10ugm/kg/min with opiate

SED/ANALGESIA

5-8ugm/kg/min

RECTAL

CHILD 6.5mg/kg

4 MINUTE ONSET

NO ANALGESIA

DECREASE CMRO<sub>2</sub> 45%

NO CHANGE MAP

BENEFICIAL INCREASE

O<sub>2</sub> SUPPLY

DECREASE ICP 50%

LASTS THRU INTUBATION

AUTOREG OK

HYPERVENT TO FURTHER

REDUCE ICP

IOP DECREASE 30-60%

FOR 5 MINUTES

CAN INDUCE GRAND MAL

SEIZURES IN SUSCEPTIBLE

HIGH INCIDENCE MYOCLON  
DECREASE AUD EVOKED  
NO EFFECT MOTOR EVOKED

MAPPING OF ELEPTOGENIC  
FOL 1

MINIMAL EFFECT ON  
VENTILATION  
NO HISTAMINE RELEASE  
LESS DECREASE OF  
VENTILATORY DRIVE

LITTLE OR NO CHANGE  
IN VALVE DISEASE 50%  
DECREASE IN MYOCARDIAL  
BLOOD FLOW  
AND O2 DEMAND  
MINIMAL EFFECT ON QT  
NEED OPIATE TO BLUNT  
SNS FROM INTUBATION

INCREASE NMB

OK

RARE, PROPYLENE GLYCOL  
TOXICITY--HYPEROSMOLAR

DOSE DEPENDENT INHIBIT  
OF 11beta HYDROXYLASE  
INCREASED CORTISOL  
PRECURSORS AND ACTH  
DECREASE MINERALCORT  
SUPPLEMENT WITH VIT C  
MAY MITIGATE EFFECT  
FOR SINGLE USE +/-  
SHORT INFUSION NO ISSUE  
1) NO KNOWN NEGATIVE

OUTCOME 2)USUALLY LOW NORMAL 3)IN HIGH STRESS SURG. RESPONSE OK
VITAMIN C RESTORES CORTISOL LEVELS TO NORMAL
AVOID IN PATIENTS PRONE TO NAUSEA AND VOMITTING

<b>RECOVERY</b>
POS POS NEG VERY POS SLIGHT NEG POS

POS



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