BARBITURATES http://www.rxmed.com/

Amobarbital

Butabarbital

Pentobarbital

Phenobarbital

Secobarbital

Anticonvulsant - Sedative-Hypnotic

Pharmacology: Barbiturates are nonselective central nervous system (CNS) depressants, capable of producing all degrees of depression from mild sedation and hypnosis to general anaesthesia, deep coma and death. The extent of CNS depression varies with the route of administration, dose and pharmacokinetic characteristics of the particular barbiturate. Patient specific factors such as age, physical or emotional state and the concomitant use of other drugs will also affect response.

The mechanism of action of barbiturates is not completely known. They may act by enhancing and/or mimicking the synaptic action of gamma-aminobutyric acid (GABA), an inhibitory neurotransmitter. The sedative-hypnotic action of barbiturates may be due to an inhibition of conduction in the reticular formation resulting in a decrease in the number of impulses reaching the cerebral cortex.

Anticonvulsant activity may result from a reduction in CNS synaptic transmission and an increase in the threshold for electrical stimulation of the motor cortex. Phenobarbital is the only barbiturate with anticonvulsant activity at subhypnotic doses.

The therapeutic index of barbiturates is narrow. Amounts needed to relieve anxiety and those causing general CNS depression are not greatly different. Therefore, the use of barbiturates as anxiolytics is almost always accompanied by some degree of impairment of cognitive function. Supratherapeutic doses lead to marked impairment of mental and motor faculties i.e. distortion of judgment, clouding of perception, slurring of speech and ataxia. In some patients however, (especially children and the elderly), drowsiness may be paradoxically preceded by transient euphoria, elation, excitement and confusion.

Pharmacokinetics: See Table I. After oral administration, absorption is usually rapid and relatively complete. The sodium salts undergo rapid dissolution and are absorbed more quickly than their corresponding free acids. The rate of absorption is increased when the barbiturate is formulated as a liquid, when the stomach is empty and when alcohol is ingested concurrently. The onset of action following rectal administration is similar to that following oral administration. After i.v. administration, the onset of action is immediate for amobarbital and pentobarbital and within 5 minutes for phenobarbital. The onset of action *following i.m. administration* is slightly faster than when the drugs are administered orally or rectally.

Once absorbed the barbiturates are rapidly distributed to all tissues and fluids. High concentrations appear in the brain, liver and kidneys. Secobarbital has the highest degree of lipid solubility and thus the fastest distribution, phenobarbital is the least lipid soluble and has the slowest distribution. Barbiturates readily cross the placenta and are excreted into breast milk. If administered i.v., fetal blood concentrations are approximately equal to maternal serum concentration; if administered orally fetal concentrations are less than maternal levels.

Barbiturates are slowly metabolized and/or conjugated in the liver and then excreted renally. Amobarbital, butabarbital, pentobarbital and secobarbital are almost completely metabolized. Due to its lower lipid solubility, phenobarbital is not metabolized as extensively and almost 25% is excreted unchanged in the urine. Metabolic elimination is influenced by age (being slower in the elderly and infants), chronic liver disease and other drugs.