

Nicotine

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General

The most widely abused drugs of modern times. (5)
Nicotine is a naturally occurring alkaloid found in plant family of solanaceous which includes the tobacco plant. (12)
Source of Nicotine:
Cigarettes, Cigars, snuff (moist and dry), chewing tobacco, and in some countries insecticide(1)
Past few years nicotine replacement products (gum, patch, nasal spray, inhalation MDI) also have become a source of nicotine.(1)
Nicotine or methylpyridylpyrrolidine (5)
water soluble alkaloid (5)
Pure nicotine solution is initially clear but turns brown on contact with air. (5)
Concentration of nicotine in tobacco products from lowest to highest is chewing tobacco, cigar, oral snuff, pipe, followed by cigarette as the highest. (7)
Nicotine is tested to not be genotoxic. (12)

Absorption

Inhalation
Dermal
Ingestion
One cigarette can contain 8-20 mg of nicotine with 0.05-2.5mg absorbed.(1)
One cigar contains up to 40 mg of nicotine(1)
Rapidly absorbed through skin, alveoli, mucous membrane and gastrointestinal mucosa(1)
Induces early vomiting by stimulation of the chemo-receptor trigger zone. (5)
Directly stimulates the nicotinic subset of central and peripheral acetylcholine receptors. (5)
Effects on the GI tract are due largely to parasympathetic stimulation. The combined activation of parasympathetic ganglia and cholinergic nerve ending results in increase tone and motor activity of bowel, nausea and vomiting and occasionally diarrhea.(8)

Distribution

Serum and urine level of nicotine are available but limited value in acute setting(1)
Toxicology testing of neonate's first urine has been reported to be positive when the mother smokes

Metabolism

Nicotine is hydroxylated at the 5' position yielding an unstable intermediate, 5'-hydroxynicotine which exists in equilibrium with $\Delta^{1,(5)}$ iminium ion.(4)
The 5'-hydroxylation of nicotine is catalyzed by cytochrom P450 2A6 with some contribution of P450 2B6 and D6.(4)
The 5'-hydroxynicotine is oxidized by aldehyde oxidase to continine. (4) =>continine-Gluc, trans-3'-hydroxycontinine and trans-3'-hydroxycontinine-Gluc
Liver P450 2A6 participates in making aminoketone which is a NNK precursor (3)
Lung and kidney specific enzyme similar to P450 2A6 (3)
70-80% Nicotine =>continine=>variety of other compounds (4)

20-30% Nicotine is metabolized to ketoacid and hydroxy acid which are partially derived from continine (3) with major source being from nicotine-Gluc and several other minor metabolites (4) Ketoacids are derived through 2'-hydroxylation of nicotine =>2'-hydroxynicotine which spontaneously yields $\Delta^{1(2)}$ iminium ion and 4-(methlyamino)-1-(3-pyridyl)-1-butanone (aminoketone also known as pseudooxynicotine). (4)

Aminoketone could ultimately be converted to keto acids and keto aldehyde.(4)

Aminoketone is the direct precursor to the tobacco-specific lung carcinogen 4-(methlynitrosamino)-1-(3-pyridyl)-1-butanone (NNK) which could be formed from aminoketones by simple nitrosation. (4)

Aminoketone is nitrosated through an intrinsic rate constant pathway. (4)

The pH maximum for nitrosation of secondary amines is 3-4, which means that these reactions could readily occur in the stomach. However nirtosation occurs in neutral pH under variety of other conditions. (4)

Nicotine patches do not have elevated concentration of NNK. (3)

Nicotine accelerated the release of dopamine in the CNS(2)

Continine can be measured in the plasma, urine, saliva, cervical mucus and hair. (6)

Saliva measurements are usually done (6)

Passive smoker continine levels < 5 ng/ml, with heavy exposure leading to values at times to > 10 ng/ml.(6)

Levels of continine in regular smokers are usually greater than 100 ng/ml. (6)

Level between 10-100 ng/ml are indicative of infrequent active smoking or smoking with low nicotine intake.(6)

Exposure to nicotine through other routes than inhalation could result in lower continine levels as in chewing nicotine gum, using smokeless tobacco or snuff dipping.; however chewing tobacco results in saliva continine concentrations similar to active smokers. (6)

Elimination

Urine

Urine acidification will increase excretion of nicotine in urine but in order to acidify urine one needs to acidify blood and that is not indicated in an acutely ill person.(1)

Stool

Excretion of nicotine was highest in cigarette smoke followed by pipe smokers, smokeless tobacco and cigar smokers. (7)

Continine excretion was highest in pipe smokers followed by cigarette smokers, smokeless tobacco and cigar smokers. (7)

Nicotine elimination half life averages 11.2 hours and continine 19.5 hours based on urine concentration. (7) Plasma concentrations for nicotine usually range in the 2-3 hour range. The explanation being that nicotine is slowly released from high affinity tissue binding sites, whereas, continine is less avidly taken up by tissue.(7)

Eliminated through the breast milk to child. (9,10)

Intoxication

SLUDGE

Salivation, Lacrimation, Urination, Defecation, Gastrointestinal upset, Emesis from stimulatoin of parasympathetic nicotine receptors sites, similar to patients poisoned by organophosphates (1)

Mild symptoms may include nausea, abdominal cramps, and tremor (1)

Initial signs of cholinergic excess may be followed by neuromuscular paralysis with involvement of the respiratory muscles (1)

When high dose of nicotine are taken =>ganglionic blockade develops => receptors become refractory to acetylcholine stimulation, as if curare was present => CNS depression and neuromuscular paralysis may develop(1)

The most common nicotine ingestions seen in ED involve those of cigarettes by children. (5)

DD of nicotine poisoning: include xenobiotics that can produce signs of cholinergic excess and others that cause rapid CNS depression and respiratory arrest (1)
Organophosphate
Meningitis
Stroke
Intracranial hemorrhage
Children with unexplained seizures

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