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Review on Pharmacology of Atropine, Clinical Use and Toxicity

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Extracts of the deadly nightshade plant, Atropa belladonna, contain a naturally occurring amine, Atropine, which is isolated from Atropa belladonna and other nightshade plants (Solanaceae). The plants are used for making a wide range of drugs. Drug absorption via the mucosal membrane of the stomach is extremely low because the acid gastric contents. Atropine is a prescription pharmaceutical used to treat the symptoms of decreased heart rate (bradycardia). Atropine is also used to suppress salivation and bronchial secretions before to surgery. Atropine can be used on its own or in combination with other drugs. Anticholinergic, Antispasmodic Agents are the class of medications that include Atropine. Toxic side effects include ventricular fibrillation (VF), as well as hypotension (hyperventilation), convulsions (delirium), hallucinations (delirium), convulsions (delirium), delirium (delirium), and excitation (excitation) in the elderly. Except in levels often used for preanesthetic treatment, atropine is generally contraindicated in individuals with glaucoma, pyloric stenosis, or prostatic hypertrophy. In this review the history and pharmacolog of atropine will be discussed in details. In addition to medical uses of this drug and contraindications.

Keywords: Atropine; Therapeutic; Toxicity; Uses.

Atropine source and history

Source

Extracts of the deadly nightshade plant, Atropa belladonna, contain a naturally occurring amine, Atropine, which is isolated from Atropa belladonna and other nightshade plants (Solanaceae). These plants produce secondary metabolites, which are used as a wide range of drugs Deadly nightshade gets its genus name from Atropos, one of the three Fates in Greek mythology who predetermined how a person died. Many Solanaceae plants contain atropine, which is a psychoactive substance. There are four primary sources of Datura: Datura inoxia (Atropa belladonna), Datura metel (Datura stramonium), and Datura metel (Datura inoxia) [1]. Members of the genera Brugmansia and Hyoscyamus are also potential sources. Tropine and hydrochloric acid can be used to manufacture atropine by reacting tropine with tropic acid. L-Phenylalanine is used to synthesize atropine, which is then converted to phenyl-lactic acid via a transamination step [2]. A P450 enzyme initiates the radical rearrangement of phenyl-lactic acid and tropine to generate littorine, which subsequently undergoes the radical rearrangement of tropine and littorine [3].

The aldehyde is reduced to a primary alcohol by a dehydrogenase, resulting in hyoscamine, which is subsequently racemized to produce atropine.

History

Solanaceae plants produce the naturally occurring muscarinic antagonists atropine and scopolamine. Physicians have traditionally utilized belladonna preparations, which were known to the ancient Hindus [4, 5]. Linnaeus named the deadly nightshade plant Atropa belladonna after Atropos, the oldest of the three Fates who breaks the thread of life, because it was commonly used to produce a mysterious and often lengthy poisoning during Roman and Medieval times [6]. Because of the widespread belief that Italian ladies once used this preparation to artificially widen their pupils, the moniker belladonna has stuck ever since [7, 8]. Also discovered in Datura stramonium is Atropine (d,l-hyoscyamine) (Jamestown or jimson weed) [8, 9]. Hyoscyamus niger contains the majority of the world's supply of scopolamine (l-hyoscine) (henbane). Asthma sufferers in India have taken the smoke inhaled from burning jimson weed root and leaves [10]. Following this custom, British colonists began using belladonna alkaloids in their medicines in the early 1800s [11]. Cleopatra employed Egyptian henbane atropine extracts to dilate her pupils in the last century B.C. to make her more attractive [12]. Atropa belladonna berries were employed by Renaissance women to expand the pupils of their eyes for cosmetic purposes. In the late nineteenth and early twentieth centuries in Paris, this technique was briefly revived [12. 13,14]. Friedlieb Ferdinand Runge, a German chemist, examined the mydriatic effects of atropine among others (1795-1867). Heinrich F. G. Mein (1799-1864), a German pharmacist, was born in 1831 and died in 1964 [15]. Atropine crystals were successfully prepared. In 1901, German chemist Richard Willstätter created the first synthetic version of the compound. It was discovered by Bezold and Bloebaum (1867) and Heidenhain (1872) that atropine prevented salivary secretion when the chorda tympani was stimulated [17]. Belladonna alkaloids and a wide range of synthetic muscarinic receptor antagonists have both been synthesized in part to affect GI or bladder activities without inducing dry mouth or pupillary dilatation [18].

Pharmacology of Atropine

An alkaloid found in the bark of the belladonna plant known as Atropine is a racemic combination of equal amounts of the d and l isomers of the belladonna alkaloid hyoscyamine. As an anticholinergic or parasympathetic (parasympatholytic) medication, Atropine is widely used [19, 20, 21]. Antimuscarinic agents, on the other hand, block the acetylcholine and other choline esters' muscarine-like effects [7]. Asystole can be prevented by administering atropine at the correct dosage [22]. Using choline esters, anticholinesterase medicines or other parasympathomimetic pharmaceuticals, as well as stimulation of the vagus nerve, the drug prevents or abolishes bradycardia or asystole [23]. Atropine may also reduce the severity of a partial heart block if vagal activity is a contributing cause [24]. Atropine in clinical doses counteracts choline ester-induced dilation of the peripheral vessels and sudden drop in blood pressure [25]. The blood vessels and blood pressure do not respond dramatically or uniformly to the administration of atropine alone.

The aromatic acid tropic acid and the complex chemical base tropine combine to form the organic ester atropine. Just like atropine, tropine is converted into the base known as scopine by the addition of an oxygen bridge (the oxygen bridge is between the carbon atoms highlighted) [26]. Asymmetrical and thus sterioisomeric, the molecule has two radicals linked to the third carbon atom [27]. There is a reasonable expectation that atropine, which is made up of a racemic mixture of 1 (-) and D (+) hyoscyamines, will be less effective than 1 (-) hyoscine. The active base in 1 mg of atropine sulphate is 833 pg, while that in 1 mg of hyoscine hydrobromide is only 692 pg, but clinically, in 0.6 mg of the racemic atropine, the active base is 250 and that in 0.4 mg is 277

When it comes to complicated molecules like atropine, the shape is just one factor that needs to be taken into account [27]. Recent work employing X-ray diffraction of the crystal structure has established that hyoscine has an extended chain with what was previously assumed to be a "S" shape for atropine [28]. Since the aromatic ring is important for activity, it has long been assumed that the nitrogen group is the specific active component, which is electrostatically linked to the anionic site of the receptor protein [29]. The third carbon atom, where the aromatic ring originates, also serves as an additional active site for the molecule [30].

The distance between these two locations and the acetylcholine molecule is identical. The antagonist atropine or hyoscine differs from the agonist acetylcholine in that it has a more intricate molecular attachment and an extra hydroxyl group than the agonist [31]. However, it appears the nitrogen group is the uniquely active component and links the anionic site of receptor protein via electrostatic forces, which has been realized for some time that aromatic ring is important for activity [32]. An additional active site (allosteric) can be found in the third carbon atom from which the aromatic ring is formed. The acetylcholine molecule has two locations with a comparable distance apart [33]. An extra hydroxyl group, as well as a more intricate molecular attachment, distinguishes the antagonist atropine from the agonist acetylcholine [34]. Both the nitrogen group and the aromatic ring are located on the same chain in atropine.

Hyoscine, atropine, and muscarinic sites in the parasympathetic and sympathetic neural systems that govern sweat glands are all inhibited by these three drugs [35]. Agonists bond according to the law of simple mass action, whereas antagonists appear to function in a more complicated manner [36]. If these medicines are taken in high doses, they can impact other cholinergic locations, such as the neuromuscular junction, which can lead to muscle spasms.

Fate of atropine in the body

Drug absorption via the mucosal membrane of the stomach is extremely low because the acid gastric contents (mean pH = 2.5) virtually fully ionise the medications, resulting in poor absorption [37]. There is a difference in the pKa values for atropine and hyoscine. Atropine is more efficient when administered intramuscularly than orally in adults, with a ratio of 1.86:1; in children and newborns, the ratio is closer to 3:1.

Before recently, atropine's metabolism and elimination were studied mostly through animal studies, which were stymied by inaccuracies in established methods of analysis like the Vitali reaction [38]. Paper chromatography has been utilized recently in human studies to distinguish between the most experimental animals and humans. The plasma half-life of atropine is 2.5 hours, and up to 50% of the medication is bound to plasma proteins in the circulation. 32 Throughout the first 8 hours, up to 80% of a tagged dose is found in the urine, and this percentage rises to 94 percent during the first 24 hours [39]. 3 percent of the CI4 is retrieved in the feces as carbon dioxide, indicating a rather low level of metabolic activity.

Medical uses of Atropine

As an antidote for cholinergic medication overdose or mushroom poisoning, Atropine is a prescription pharmaceutical used to treat the symptoms of decreased heart rate (bradycardia). Atropine is also used to suppress salivation and bronchial secretions before to surgery [40]. Atropine can be used on its own or in combination with other drugs. Anticholinergic, Antispasmodic Agents are the class of medications that include Atropine [41].

Each patient at danger of poisoning by a nerve agent or organophosphate insecticide should have three (3) Atropine autoinjectors on hand: one (1) for mild symptoms and two (2) more for severe ones [42]. Atropine should only be given to individuals who are showing signs of organophosphorus poisoning and whose exposure has been confirmed or is suspected. Autoinjectors of Atropine are designed to treat insecticide and nerve agent muscarinic symptoms immediately upon appearance of symptoms; quick medical attention should be sought [43]. Because it can cause ventricular fibrillation and seizures when administered in the context of hypoxia, atropine is best avoided until cyanosis is fully resolved before it can be safely utilized. People who have received enough training in the diagnoses and management of nerve agent or pesticide intoxication should be able to use the Atropine autoinjector, however caregivers or self-administration can be utilized if a trained provider isn't nearby [44]. For a minimum 48 to 72 hours after treatment, all patients should be closely monitored. A benzodiazepine or other anticonvulsant medication may be necessary if seizure is indicated in the unconscious person due to the poison's effects, which may make overt jerking difficult to detect [45]. A cholinesterase reactivator like pralidoxime chloride may be useful in organophosphorus nerve agent and insecticide poisonings [23]. The mid-lateral thigh is the preferred location for the injection. The Atropine autoinjector can be used to administer the drug even when the wearer is dressed in garments [11]. In addition, make sure there are no pockets around the injection site

[46]. If the injection site does not have a lot of fat, it should be administered in the mid-lateral thigh if the leg is bundled up before to the injection.

Medical uses of Atropine in the eyes

Topical atropine is a cycloplegic and a mydriatic, both of which temporarily block the accommodation reflex [47]. In contrast to tropicamide, a faster-acting cholinergic antagonist, and phenylephrine, a -adrenergic agonist, which are recommended as an ocular examination aid, atropine degrades slowly and normally wears off in 7 to 14 days [48]. To put it another way, when occlusion isn't an option for patients with refractive or accommodative amblyopia, atropine might be used to temporarily blur vision in the good eye. Both occlusion and atropine penalization have been shown to improve vision just as well. Antimuscarinic topical treatment can delay the progression of myopia in youngsters, but it can also cause papillae and follicles to become inflamed, making it difficult to see clearly [49]. While higher doses of atropine are more likely to cause negative effects, all amounts appear to be effective [50]. Due to fewer adverse effects and less rebound deterioration after atropine is withdrawn, the lower 0.01 percent dose is often suggested.

Medical uses of Atropine in the heart

Symptomatic or unstable bradycardia can be treated with injections of atropine. Due to a lack of evidence, Atropine was withdrawn from the worldwide resuscitation guidelines in 2010 for the treatment of cardiac arrest linked with asystole and PEA. One to three milligrams of intravenous methylprednisolone (0.5 to 1 mg) may be administered intravenously for patients with symptomatic bradycardia [3]. Third degree heart block with a strong Purkinje or AV-nodal escape rhythm can also be treated with Atropine, as can second degree heart block Mobitz type 1 (Wenckebach block). Second-degree heart block Mobitz type 2 and third-degree heart block with a low Purkinje arwhat is frequently ineffective with this method [43]. Evidence does not support the use of atropine in an attempt to thwart a low heart rate during intubation of youngsters.

Side effects of Atropine

Toxic side effects include ventricular fibrillation (VF), as well as hypotension (hyperventilation), convulsions (delirium), hallucinations (delirium), convulsions (delirium), delirium (delirium), and excitation (excitation) in the elderly [34]. Atropine's ability to pass the blood–brain barrier is responsible for the latter effects. A number of people have experimented with the drug's hallucinatory characteristics in order to get high, despite the dangers and discomfort of doing so. To put it another way, Atropine is toxic in large amounts.

Antidiarrheal opioid medicines like diphenoxylate or difenoxin, in which the atropine secretion-reducing effects can also help the antidiarrheal benefits, sometimes have atropine added to them, which may make them more addictive. To put it another way, as an emergency medication for bradycardia, atropine can elicit paradoxical heart rate reduction when administered at very low dosages (i.e. 0.5 mg), likely as a consequence of central activity in the central nervous system [29]. Atropine's paradoxical bradycardia impact at low doses may be due to a blockade of inhibitory presynaptic muscarinic autoreceptors, which inhibits the parasympathetic response, according to one hypothesis.

Ten to twenty milligrams of Atropine per person is enough to cause a person to lose consciousness. It has a probit slope of 1.8 and an LD50 of 453 mg per person (by mouth). Pilocarpine or physostigmine can be used as an antidote to atropine. To put it another way, "hot as a hare, blind as a bat, dry as bone, scarlet as a beet, and mad as a hatter" is a classic way to remember the physiologic effects of an atropine overdose.

As a result of the decreased sweating, blurred vision, decreased lacrimation, and vasodilation, these relationships represent the unique alterations to warm, dry skin and the central nervous system's effects on muscarinic receptors type 4 and 5 [9]. Anticholinergic toxidrome is the medical term for this constellation of symptoms, which can also be brought on by other anticholinergic medications, like hyoscine hydrobromide (scopolamine), diphenhydramine, phenothiazine antipsychotics, and benztropine.

Contraindication of atropine

Except in levels often used for preanesthetic treatment, atropine is generally contraindicated in individuals with glaucoma, pyloric stenosis, or prostatic hypertrophy [19]. All people over the age of 40 should use Atropine Sulfate Injection, USP with caution.

CONCLUSION

For the treatment of nerve agent poisoning and sluggish heart rate as well as for reducing saliva production during surgery, Atropine is a tropane alkaloid and anticholinergic drug. It is usually administered intravenously or intramuscularly. Eye drops for the treatment of uveitis and mild amblyopia are also available. Once the intravenous solution is administered, it might last anywhere from 30 minutes to an hour. For some poisonings, it may be necessary to administer a large amount. A dry mouth, wide pupils, urine retention, constipation, and a rapid heart rate are all common adverse effects. People with angle-closure glaucoma should avoid using it. Despite the lack of evidence that it causes birth abnormalities, this has not been thoroughly investigated. During breastfeeding, it's most likely safe. As an anticholinergic, it inhibits the parasympathetic nervous system, a sort of antimuscarinic (anticholinergic). Natural sources of atropine include deadly nightshade (belladonna), Jimson weed, and mandrake (also known as the nightshade family). It was discovered in 1833, and is on the WHO's Essential Medicines list. As a generic drug, it is easily accessible. All people over the age of 40 should use Atropine Sulfate Injection, with caution.

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