Adverse Effect Of Honey On Infants: Infant Intestinal Toxemia Botulism, A Neuroparalytic Disease

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Abstract - **Worldwide appreciated insect derived natural product honey is well known not only for its nutritional value but also for its traditional uses in clinical field from wound healing to cancer treatment. Honey is extensively used to treat cough of baby. It has flavonoids and polyphenols which are two main bioactive substances, acts as antioxidants. Besides so many beneficial effects, regular giving honey to infants exerts some ill effects also. Honey is ideal for children and adults, but it has adverse effects on babies mostly because they are at risk of infant botulism. Infant botulism can occur any time in the first twelve months, but it is most common in the first six months. Honey may contain a spore of a bacterium, Clostridium botulinum. It is a gram positive, anaerobic, spore forming bacteria, responsible for a disease called botulism. It occurs when infants eat honey, which contains spores of C. botulinum which germinate, colonize, and produce neurotoxin in the infant's intestinal tract. It is a serious illness that affects the nervous system and finally causes muscle weakness and paralysis. Botulism in infants include constipation, loss of appetite, weakness, breathing trouble, an altered cry and a striking loss of head control.**

keywords - **Honey, antimicrobial agent, Clostridium botulinum, Infant botulism.**

1. INTRODUCTION

Honey is a sweet, viscous natural food product which is enriched in different important nutritional components. Honey is produced by the bees by regurgitation, enzymatic activity and evaporation of floral nectar. It is used by human since ancient period. Honey has some cosmetic and therapeutic values also. It contains high concentration of fructose and that's why in old days it was used as natural sweetener. Nowadays in different research and studies it is observed that honey is a potent antimicrobial, anti-diabetic, anti-inflammatory agent and it has high antioxidant property. As honey has so many beneficial effects on human health, it is an automatic choice for the parents to give honey as food to give their children. Honey can easily use in topical treatment and also wound dressing process (Oskouei et al., 2017). But in some recent research, it is revealed that due to the presence of spores of *Clostridium botulinum* and it can cause health damage of an infant by producing a neurotoxin. Other clostridial bacteria, like *C. butyricum* and *C. baratii* can also produce the toxin leading to signs and symptoms of botulism. Though rare, the illness is potentially fatal (S. Mohanty et al., 2001). Other than honey *Clostridium botulinum* normally live in soil or dust and then become airborne where they are breathed in and swallowed by the infants. The bacteria can present on surfaces like carpets and floors and also can contaminate honey. Infant botulism tends to affect babies between the ages of 2 and 6 months but has been reported in infants as young as 54 h and as late as 1 year (C. O. Abdulla et al., 2012). Infantile botulism was first described separately in 1976 by Midura and Arnon and by Pickett et al. Colonization of the intestine by neurotoxigenic clostridia, with consequent production of botulinum toxin in the intestine, leads to intestinal toxemia botulism. When this occurs in an infant, it is referred to as infant botulism, whereas in adults or children over 1 year of age, it is intestinal colonization botulism (R. A. Harris et al., 2020). As per WHO, infant botulism occurs when infants ingest *C. botulinum* spores, which germinate into bacteria that colonize in the gut and release toxins. Symptoms of infant botulism include generalized weakness and hypotonia, lethargy, constipation, difficulty feeding, and cranial nerve palsies (M. J. Khouri et al., 2018). General treatment of Infant botulism is with an antitoxin called botulism immune globulin intravenous (BIGIV) and babies with botulism treated with BIGIV recover sooner.

2. CHEMICAL COMPOSITIONS OF NATURAL HONEY

Honey is rich in different types of nutrients. Natural honey contains amino acid, vitamins and enzymes but the primary and main compounds are sugar, water, minerals presence in the honey. There is also present hydrogen peroxide, phenolic compounds, bee defensin-1 and 1,2- dicarbonyls which are responsible for the antimicrobial activity of honey (Nolan et al., 2019). Sugar amount in honey dry matter is 95-99%. Carbohydrates include fructose (32.56 to 38.2%) and glucose (28.54 to 31.3%) are present in honey which represents 85-95% of total sugar. Some disaccharides such as sucrose, nigerose, maltose, maltotriose, panose, isomaltose, melezitose etc. also present in honey. There are 4 to 5% fructooligosaccharides present in honey which serve as probiotics agents.

Another compound is water. Honey is acidic because there is present 0.57% organic acid. Gluconic acid present in honey which is a bye product of enzymatic digestion of glucose and produce hydrogen peroxide. This organic acid is responsible for

the acidic nature of honey and also contributes a characteristic taste of honey. The presence of the carbohydrates and water are responsible for increase of osmotic pressure and high pH of honey.

Mineral is another important component which is present in honey and it's concentration in honey ranges from 0.1 to 1.0%. The major mineral component is potassium. There also present sodium, sulphur, calcium, phosphorus, magnesium etc. Some nitrogenous compounds are also present in honey like vitamin C, B1 complex like nicotinic acid, B6, pathogenic acid and riboflavin.

Various enzymes like invertase, diastase, amylase, oxidase, catalase etc. present in honey. But the main enzyme is diastase and glucose oxidase. Become they play a very important role in the fermentation process of honey. Hydrogen peroxide along with gluconic acid produce from glucose by the help of the enzyme glucose oxidase (Oskouei et al., 2012).

Because of the high pH value of honey only some spore forming and ten species non spore forming micro organisms can survive in the honey without any growth. It is only the spore forming microorganisms that can survive in honey at low temperature. The spore count remained the same 4 months after. *Bacillus cereus, Clostridium perfringes* and *Clostridium botulinum* spores were inoculated into honey and stored at 25°C. The *Clostridium botulinum* population did not change over a year at 4°C (Olaitan et al., 2007).

Figure 1: Honey bees and honey comb

Figure 2: Pure honey

3. GOOD EFFECTS OF HONEY ON INFANTS

Honey is very useful in infant's nutrition. Honey provides instant relief from cold, flue, and cough. If honey is used for at least seven days after dinner on infants who is suffering cold, cough, the infants recover soon without any use of antibiotics. So honey has a power to reduce the use of antibiotics. Honey is a store house of multivitamins, minerals, essential amino acids and flavonoids. Honey has antifungal properties which lead to faster healing of wounds. Infants can tolerate honey better than sucrose. For this reason infants gain better weight and better blood inflammation.

Honey can increase the haemoglobin contain in blood and that's why an infant get better skin colour. When infants fed by honey they had no digestive problems and they are suffering less frequently from Diarrhoea.

When a baby on a diet of mixture of milk and honey, showed the regular weight gain (Bongdanov et al., 2009). Zaid et al., (2010) concluded that "honey could be an alternative hormone replacement therapy". Beside this honey showed physiological effects on radiation mitosis patients and on hepatitis A patients.

4. ADVERSE EFFECTS OF HONEY ON INFANTS: INFANT BOTULISM

Although honey has so many good effects it is not safe to give honey regularly to the infants below one year age. Honey can cause serious infant botulism if it contains *Clostridium botulinum* spores. After entering in the intestine of baby, bacteria can grow and replicate to produce botulinum toxin. It can be found in the soil, water, and air with a lethal toxin dosage of only 1mcg/kg that would be invisible to the naked eye. Infant botulism, a disease that results in a blockade of voluntary motor and autonomic functions, was first recognized in the United States in the late 1970s. Since then, more than 1000 cases in this country have been reported to the Centres for Disease Control and Prevention (CDC) (G. Maria et al., 2012). It is the most common type botulism infection predominates 70% of all new cases of botulism annually. In USA, there are about 100 cases of infant botulism reported every year. Among them about 20% are linked to the consumption of raw honey. Other sources of infantile botulism include consumption of powdered milk, natural sweeteners, corn syrup, and medicinal herbs (L. Ngoc et al., 2020).

Epidemiology

The infant botulism begins after *Clostridium botulinum* bacterial spores grow in a baby's gastrointestinal tract. It typically occurs in babies between the ages of 2 months and 8 months. If infant botulism is related to food, such as honey, problems generally begin within 18 to 36 hours after the toxin enters the baby's body. If a baby below one year ingests the spores of *C.*

botulinum, there is a high chance of production of botulinum neurotoxin after germination of spore within his/her digestive system as that part lacks the protective gastrointestinal bacterial flora.

Depending upon the route of exposure, botulism can be classified into six forms. The three most common types of botulism are food borne botulism, wound botulism and infant botulism. Foodborne botulism happens due to ingestion of pre-formed toxin in food. Wound botulism develops when *C. botulinum* gets into a wound and grows, resulting in toxin production in situ. Infant botulism occurs when *C. botulinum* forms colony in infant intestinal tract, and colonization of the intestinal tract of adults or children over 1 year of age causes intestinal toxemia botulism (J. Sobel, 2005). Eight toxins have been identified, A to H; A, B, E, and F have been associated with different human disease (E. Weisenberg, 2019). Among cases of infant botulism, approximately half are caused by toxin type A and half by toxin type B with occasional cases caused by toxin types C, E, F and G (R. Schechter et al., 1999). Ab, Ba and Bf botulinum toxins can also cause infantile botulism.

Many risk factors have been associated with infant botulism. They include age of the babies and ingestion of honey and ingestion of corn syrup. As bees moving from one plant to another to accumulate spores along with pollen, honey frequently contains *C. botulinum* spores and acts as the source in about 15% of infant botulism cases. The source of *C. botulinum* spores in remainder of cases is not known properly, but is presumed to be soil or dust (O. Sonnabend et al., 1981). Botulinum toxin resists destruction by proteolytic enzyme, it remains effective when ingested. It acts like curare, affecting principally the end plates of nerves and specifically the myoneural junctions of the motor apparatus.

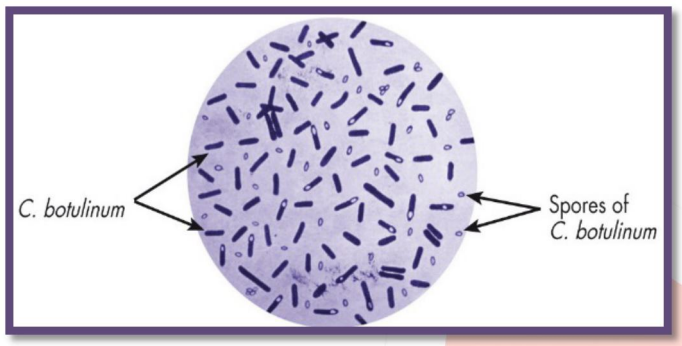

Figure 3: *Clostridium Botulinum* spores.

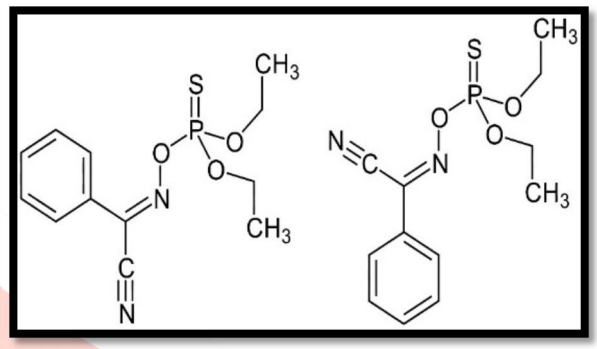

Figure 4: Structure of Botulinum toxin.

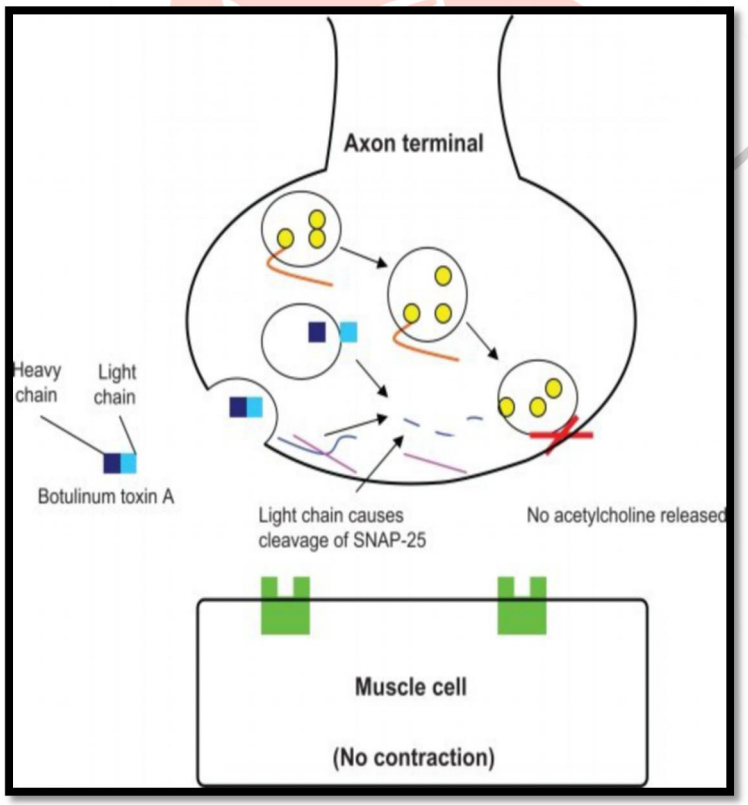

Figure 5: Mechanism of action of Botulinum toxin.

Pathophysiology

Bacterial spores can germinate and grow in specific conditions. These mature bacteria then secrete the toxin which quickly spreads into the bloodstream and binds to nerves. Botulism develops when those nerves no longer work. Conditions that allow spores to germinate include lack of oxygen, low acidity, sugar or salt, cooking temperatures that are too low and storage temperatures that are too warm. Botulinum toxin (BoNT) is known as one of the most dangerous substances. Botulinum toxins are synthesized as a single polypeptide chain having molecular weight of 150 kDa. Comparison between botulinum toxin and tetanus toxin genes suggests that the BoNT employ similar mechanism of action and both of them are probably

derived from a common ancestor. BoNT is produced in the large intestine then it is absorbed and carried by blood stream. BoNT binds to peripheral cholinergic nerve endings cleaves key intracellular proteins necessary for acetylcholine release resulting in flaccid paralysis. This neurotoxin blocks the presynaptic release of acetylcholine across the neuromuscular junction, leading to a toxic neuropathy. The toxin binds to membrane receptors of the synaptic vesicles and degrades the synaptobrevin, a protein associated with the synaptic vesicle, thus causing paralysis and respiratory failure. BoNT not only affects the peripheral nervous system, causing diffuse paralysis, but also the autonomous nervous system, inducing vegetative disturbances which decrease the vital prognosis (A. Gentil et al., 2008).

Symptoms of infant botulism

The incubation period for infantile botulism can range from 3 to 30 days after exposure to the spores. The clinical presentation can vary from mild hypotonia to severe bulbar paralysis, and may cause sudden infant death (M. Nevas et al., 2005). Constipation followed by lethargy is often the first sign. The other typical symptoms include listlessness, poor feeding, ptosis, dysphagia, floppy movements due to muscle weakness and loss of head control, visual problems, dry mouth and generalised weakness. Botulism can lead to paralysis lasting for days and weeks, and in some cases to respiratory failure. Fever is usually absent. *C. botulinum* in infants includes weak cry, irritability, drooling, drooping eyelids, difficulty sucking or feeding and paralysis. Disturbance of the infant gut flora is thought to be providing a suitable environment for any spores present to germinate, colonize and produce toxin. For most cases of infantile botulism, the source of spores is never identified and it is assumed that they are swallowed from the environment. However, honey is a dietary reservoir of *C. botulinum* spores for which there is both microbiological and epidemiological evidence (S. S. Arnon et al., 2004). A relation between infant botulism and sudden infant death syndrome (SIDS) came to light when a similarity was observed between the sudden respiratory arrest of an infant with botulism and SIDS.

Figure 6A: Sign of acute muscular hypotonia, a common sign of infant botulism.

Figure 6B: After the occurrence of the disease, the girl could not sit independently and had no control on her head.

Figure 6C: Floppiness is accompanied by ptosis, feeding problems and excessive drooling

Figure 6A, 6B, 6C: Six months old baby girl with infant botulism in Slovenia at University Children's Hospital in Ljubljana (Source: Anja Radsel et al., 2013).

Worldwide outbreak of Infant botulism

The worldwide incidence of infant botulism is rare, the majority of cases are diagnosed in the United States (N. Cox & R. Hinkle, 2002). Every year in USA, about 100 cases of infant botulism are reported among them 20% is linked with raw honey consumption (N. L.Van Horn & M. Street, 2020). Researchers suggested that *C. botulinum* spores may be present in soil near construction and agricultural sites. The yearly number of infant botulism cases now exceeds the number of foodborne and wound botulism combined (R. Chaudhry et al., 1998). The United States, Argentina, Australia, Canada, Italy, and Japan, in this order, reported the largest number of cases. Most countries have not yet reported cases of infant botulism. This limited reporting of the disease to date contrasts with the known global occurrence of *Clostridium botulinum* spores in soils and dust and suggests that infant botulism may be under-recognized, underreported, or both (R. Koepke et al., 2008). Infant botulism has been reported from countries on all the inhabited continents except Africa.

Infant Botulism cases in India

In India, uses of honey were referred in different ancient literature like Rig Veda, Upanishads, Ramayana, Mahabharata and Jataka Kathas. At that time honey used against the poison of snakes, scorpions, and other insects and played an important role in many rites and ceremonies. For more than 5000 years, Indians have been continually using honey in ayurvedic medicine. In today's India, when a baby was born, he/she was supposed to be fed with a drop of honey. But there are very limited reporting of botulism cases and not a single reported case of infant botulism in India till date. Few cattle botulism (S. Jegaveera Pandian et al., 2015), foodborne botulism (Arora Amit et al., 2014), (Chaudhury Rama & Benu Dhawan, 1998) and botulism related cases (Chaudhury Rama, 2011) were reported.

5. CONCLUSION

It is clear that honey can be used to treat many diseases, but honey should not be recommended to any child below one year age as there is a high chance of presence of spores of *C. botulinum* which can cause infant botulism, a severe paralytic disease. Botulism is not spread from person to person. In order to reduce the risk of infantile botulism, public health measures need to be taken such as educating parents, community health visitors, midwives etc against feeding honey to infants. Exposed individuals should be kept under surveillance and treated with antitoxin when botulism symptoms are first identified.

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