



(RESEARCH ARTICLE)



Symptomatology of star anise poisoning in pediatric patients

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Abstract

Traditionally, Star Anise has been used as an antispasmodic in the form of home infusions for the treatment of newborn colic. The objective of this study was to identify the most frequent symptoms of intoxication due to the administration of star anise infusion in pediatric patients. A literature search was performed to identify published reports regarding star anise poisoning in the MEDLINE, PubMed, and Google Scholar databases. 137 cases of star anise intoxication were detected for the period 2014-2019 in which it was found that star anise intoxication has neurotoxic, hepatotoxic, gastrointestinal toxicity and inducer of hypersensitivity reactions.

Keywords: Intoxication; Star Anise; Pediatric

1. Introduction

The *Illicium verum* is a shrub belonging to the Illiciaceae family, it is native to the southwest of China, it is also called French anise, Chinese badian, Chinese anise and star anise. ¹ It can reach 5 meters in height, its leaves are spearhead-shaped, its flowers are yellowish-green with 15 to 20 spiral-shaped petals, the fruits are reddish-brown in color that are formed between six to eleven follicles. They have a pointed end, are found around a central petiole, resembling a star, inside there is an ovoid seed. ^{2,3} There are references to star anise since 1127 BC, when it was used in China as a masticatory and religious perfume. ⁴ Traditionally, Star Anise has been used as an antispasmodic in the form of home infusions for the treatment of newborn colic, as well as postpartum uterine contractions in women who are breastfeeding. It is also used to relieve colds and bronchiolitis as an expectorant; as a flavor and odor corrector in the pharmaceutical, food and liquor industries. ⁵ The essence, precisely because of its high anethole content, at high doses can be toxic, causing seizures, central nervous system depression, coma, respiratory depression and even death. ² Occasionally, cases of hepatotoxicity and hypersensitivity to anethole, as well as contact dermatitis have been reported. ⁶⁻¹⁰ Since ancient times, the knowledge about this plant spread throughout Europe and Asia, as well as its use for therapeutic purposes. Dioscorides already records it from the 1st century AD, in his great work *De Materia Medica*, a treatise on plants with therapeutic uses. Within the humoralist conception - in force until the 19th century - anise is granted a calorific and desiccative virtue that facilitates breathing, in addition to considering it analgesic, resolutive, diuretic, solvent and in infusion, good to quench thirst. ¹¹ During the 19th century, the seed was used in medicine with characteristics: carminative, stomachic and aperitif, and therefore it warms a little, encourages vital forces and helps digestion when a weak stomach precedes, in this sense, it facilitates the digestion of milk in children, as well as expectoration of mucous matters in wet asthma. ¹² Currently in our country, a preparation of leaves and seeds in tea is recommended to remove abdominal pain, eliminate intestinal gas and improve digestion and appetite. ¹³

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2. Material and methods

A literature search was performed to identify published reports regarding star anise poisoning in the MEDLINE / PubMed database: the articles were validated as they included information pertinent to the pathophysiology, diagnosis, treatment, and prevention of poisoning by star anise, as well as the presentation of clinical cases that allowed for the analysis of the more and less frequent adverse reactions, in addition to the therapeutic measures used. Google search engines and Google Scholar were also used, due to their less complexity, greater coverage and greater speed, in the search for articles on star anise poisoning, whose scientific reports are limited or scarce. In the automated bibliographic search strategy, in MEDLINE / PubMed, for the period 2014-2019, with the term "Illicium verum" 39 results were reached, of which 2 were taken; With the term "Illicium verum poisoning" 3 results were achieved. In the Google Scholar search engine, the phrases used were: "pediatric star anise intoxication" "star anise intoxication in children" "star anise intoxication". 3 long articles were obtained on the subject, while in the Google search engine 2 articles were located in the 2008-2019 interval.

3. Results and discussion

According to the literature review, it was found that star anise intoxication has neurotoxic, hepatotoxic, gastrointestinal toxicity and inducer of hypersensitivity reactions (Table 1). In total, 137 cases of star anise intoxication were reviewed in an age range from 19 days to 6 years of age.

Neurological symptoms occurred in 77 patients (56.20%), gastrointestinal symptoms in 79 patients (58.39%), hepatotoxic damage occurred in 23 cases which showed abnormal elevations of transaminases which had an average remission time of 1 to 2 months (16.78%) and hypersensitivity reactions also occurred, but only in 3 cases of those reviewed (2.18%).

Table 1 Symptoms and signs present in pediatric patients with star anise poisoning

Symptoms or signs	Number of cases	Percentage
Gastrointestinal	79	58.39%
Neurological	77	56.20%
Hepatotoxic damage	23	16.78%
Hypersensitivity reactions	3	2.18%

The most frequent neurological symptoms (Table 2) were: Lethargy in 31 cases, irritability in 77 cases, hyperreflexia in 15 cases, nystagmus in 44 cases, seizures in 25 cases, spasticity in 33 cases, and fever in 3 cases.

Table 2 Neurological symptoms in pediatric patients with star anise poisoning

Neurological symptom	Number of cases	Percentage
Lethargy	31	22.62%
Irritability	77	56.20%
Hyperreflexia	15	10.94%
Nystagmus	44	32.11%
Convulsions	25	18.24%
Spasticity	33	24.08%
Fever	3	2.18%

Regarding the gastrointestinal symptoms (Table 3) that prevailed were: vomiting in 80 of the cases, abdominal distention in 74 cases and only 3 patients presented liquid stools.

Table 3 Gastrointestinal symptoms in pediatric patients with star anise poisoning

Gastrointestinal symptom	Number of cases	Percentage
Vomiting	80	58.39%
Abdominal distention	74	54.01%
Liquid stools	3	2.18%

The time of onset of symptoms and signs of star anise intoxication was variable for each patient and with a very large temporal dispersion; There were cases with onset of symptoms from a few hours (1-2 hours) to several days (5-14 days). The reasons for the use of star anise infusion (Graph 1) in most cases are not specified (64.23%), but in 32 cases it was for the treatment of infant colic (23.35%), 9 of the cases to treat irritability (6.56%), and in 8 of the cases to treat vomiting (5.83%).

Star anise is traditionally used in infusions as a home remedy mainly to promote the expulsion of gases, reduce flatulence and colic in infants.^{1,2,5} The commercial forms of star anise present a great variety, from the product packaged in individual bags to the sale in bulk.⁴ The infusions are prepared by adding 1 gram to a cup of boiling water (200 ml) which is equivalent to 2-3 stars per cup, let it rest for five minutes and then filter, it should be consumed at the moment and the maximum dose recommended is 2 grams per day.^{3,5}

The pharmacological principle of star anise is made up of the whole fruits, the seeds or the essential oil extracted from the fruits. The components are: monoterpenes: anethole (80-90%) and estragole, terpenic carbides (phelandrene, limonene, dipentene), flavonoids, tannins, organic acids (quinic, psychic), coumarins, triterpenes and sesquiterpenic lactones known as veranisatins A, B and C. Due to its high content of anethole and estragole, the essential oil is neurotoxic, which is why most patients present mainly irritability, nystagmus and lethargy.^{2,3,5,6} Hepatotoxic damage is reflected in the elevation of transaminases, in addition to the fact that anethole has an antispasmodic effect on intestinal and bronchial smooth muscle.⁷ Among other actions, it has an estrogen agonist and galactagogue effect, stimulating appetite. The verasatins, especially A and B, have a tropism for neurons, producing seizures and lethal toxicity.³

On the other hand, the adulteration or contamination of star anise by the species *Illisium anisatum* known as “Japanese star anise”, can cause even more serious adverse effects, since its fruits contain anisatins and neoanisatins which are known as the most lethal toxins from the plant world for its non-competitive antagonist activity of gamma aminobutyric acid (GABA) receptors. Therefore, the lack of function of this inhibitory mechanism leads to an excess of excitatory neuronal impulses and consequently to seizures, which can be fatal.^{3,4,9}

The neurotoxic symptoms usually remit between 24 to 48 hours after ingestion. The most frequent according to the bibliographic review are: irritability, nystagmus, spasticity, lethargy and seizures.^{6,8}

Many are the factors that can contribute to the hepatotoxicity of star anise are attributed mainly to the toxic effect of its substances, and to the contamination of plants by chemicals or heavy metals. However, in the case of natural products, its identification as a cause of hepatotoxicity is relatively recent, which makes it a problem that is scarcely considered and investigated. Hepatocellular injury is reflected in the isolated increase in transaminases twice the limit of normality.⁹

Currently no antidote for this intoxication is known, so the treatment that was indicated in most cases was symptomatic, for example, with benzodiazepines as anticonvulsant.

4. Conclusion

Without questioning the efficacy of medicinal plants, there is a false perception of safety and the absence of side effects in their use. Currently, herbaceous poisonings can be considered a public health problem, because they are a frequent cause of morbidity and mortality, and because they are preventable and controllable conditions, if the corresponding prevention and control methods are applied. Additionally, the doctor's knowledge of herbal medicine is deficient and

the patient's relatives do not provide information on the administration of these products. Although star anise is used in a traditional way, its commercialization must be regulated by health authorities, due to its high risk of neurotoxicity and hepatotoxicity; especially in young children. In addition, the pediatrician and the general or family doctor should educate the general population about the possible adverse effects and consequences of the use of star anise, but preferably it is recommended not to use in infants.

Compliance with ethical standards

Disclosure of conflict of interest

All authors declare that they have no conflict of interest.

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