

Prolonged ingestion of senna: weight loss, cyclic edema, dyspepsia and hepatoneuromyopathy

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Abstract

The authors present a case of a 31 year old female patient who, following prolonged ingestion of senna extract, developed severe weight loss, cyclic edema and dyspepsia, accompanied by an asymptomatic increase in markers of liver and muscle damage, dyslipidemia, electromyographic alterations and mitochondrial myopathy in the muscle biopsy, with some of these changes normalizing over several weeks after the suspension of senna

ingestion.

This clinical case is of particular significance, given that senna is widely used for its pharmacological properties, with failure to consider its potential toxic effects.

Keywords: senna, hepatopathy, neuropathy, myopathy, cyclic edema, weight loss, dyspepsia.

INTRODUCTION

From the primitive origins of mankind until the present day, Man has made use of natural resources with medicinal properties, particularly by-products of plants that are the cornerstone of natural medicine, and an important milestone in the development of many of the drugs used in conventional medicine.

Of the vast array of medicinal plants, the senna plant (*Cassia occidentalis*) is part of the *Cassia* genus which includes more than 600 species. It is a plant that is widely distributed in tropical and subtropical zones throughout the world, with the exception of the continent of Oceania. It grows preferably in fertile, cultivated soils, along river banks and in meadows and forests, from sea level up to altitudes of 900 metres. In cold, arid regions or seasons, its life cycle is 6-9 months, while in a warm, humid environment, the life cycle of the plant can extend up to four years (with the plant reaching up to 8 metres in height). It flowers and produces seeds throughout the year, or seasonally, depending on climatic conditions, giving flowers with yellow petals (about 2 cm long) and flat slightly curved brown pods, 5-12 cm long, with 40 or more brown-black ovoid seeds of about 4 mm

long, a high percentage of which germinate between 5 and 36 days after falling to the ground¹. The senna plant, along with dozens of others of the same genus, constitutes a rich source of phenolic, anthracene and anthraquinone derivatives (*Fig. 1*) to which the biological activity of the extract of various constituents of the plant (leaf, stems and pods/seeds) is attributed, in part, with numerous applications, some with questionable efficacy in both natural and conventional medicines². These include purgative, analgesic, antipyretic, antitumoral, expectorant, anti-inflammatory, diuretic, antifungal, bactericidal, antiparasitic, antiviral, antimalarial, antispasmodic, emetogenic and immunostimulant effects. The laxative effect is the most common indication of senna, as several of its constituents are converted by bacteria of the intestinal flora into irritant substances that act directly on the intestinal mucosa, increasing the motility of the colon and inhibiting the secretion of water and electrolytes, thereby exercising its effect, with an onset of action 6-12 hours after ingestion³. Examples of isolated bioactive isolated substances from the senna plant (*Fig. 1*) include 1,8-dihydroxy-anthraquinone (1), palmidin A, B, C and D, 1,8-dihydroxy-3-methyl anthraquinone, 1,8-dihydroxy-3-methoxy-6-methyl anthraquinone, torosaside A (2) and B (3), torosachryson-8-O-6"-malonyl-beta-gentiobioside (4) and torosachryson-8-O-gentiobioside (5)². These substances, among others yet to be discovered, are the basis of the medicinal effects described above, but are also related to its toxic effects when ingested in sufficient quantities and/or over a long period. There

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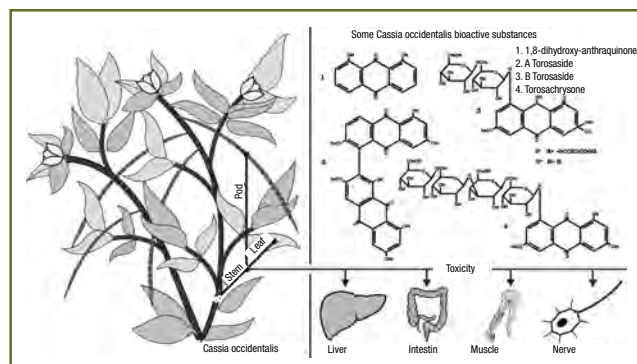


FIG. 1

are numerous reports that confirm a detrimental effect of senna in animals^{4,5} and humans^{6,7} following accidental ingestion of high quantities, or ingestion of smaller quantities for prolonged periods, and the spectrum of toxic manifestations includes liver damage, neuropathy, myopathy, nephropathy, weight loss and death. The toxicity, of unclear etiopathogenesis, is attributed to the anthraquinone glycosides, and the various available histopathological studies carried out on animals and some humans indicate, in a fully consistent manner, a decrease in histochemical activity of cytochrome oxidase and other mitochondrial enzymes⁴, notably in the anatomopathological study of the muscle biopsy of sacrificed animals, and in the diagnostic study of humans. Adverse effects associated with ingestion of senna include: a slight increase in transaminases (usually asymptomatic), liver failure, muscle damage (with atrophy), weight loss, diarrhea, cutaneous rash, colorectal necrosis (possible increased risk of colorectal cancer), changes in urine colour (red/pink to black/brown), dyspepsia, fatigue, melanosis coli (pigmentation of the colonic mucosa), hydroelectrolytic changes (metabolic acidosis, metabolic alkalosis, hypokalemia, hypocalcemia, edema) and abdominal pain^{3,8}.

CASE REPORT

Female patient, 31 years of age, Caucasian, unemployed (degree in management), single, born and resident in Cova da Beira, came to the Internal Medicine Service on the indication of the gastroenterologist in charge of her case, with the following case history: the occurrence, about two years ago, of an episode of gastrointestinal disturbance, beginning about an hour after dinner, which was manifested as watery diarrhea,

anorexia, food vomiting, and heartburn, with no fever or abdominal pain. The symptoms continued throughout the night, with persistent nausea and anorexia the following morning, and with complete resolution by lunch time of the same day. This episode was preceded by other gastroenteritis that members of the family entourage. Two to three weeks later, for the first time, she reported the appearance of severe but painless bilateral and symmetrical edema in both legs, affecting the portions below the knees, occurring in the evenings, which disappeared spontaneously after 2-3 days without any therapeutic intervention. Since then, the edema, with the same characteristics as in the first episode, has occurred cyclically at intervals of two to three weeks. Patient reports taking an infusion of senna extract for a period of about ten years, to relieve constipation (1 teaspoon of extract of senna leaves in a litre of water, drinking 1 litre each day and then taking approximately half of this amount after the episode of diarrhea). The patient also reports dyspepsia with heartburn and postprandial fullness, having lost about 7 kg since the aforementioned episode of gastroenteritis, presenting a body weight of 33 kg on the first day of hospitalization. Finally, the patient's medical history revealed an eating disorder accompanied by some clinical characteristics of anorexia nervosa (extreme thin appearance, amenorrhea, feeling of fullness and abdominal distension, lanugo, hypothermia, bradypnea, bradycardia, hypotension, peripheral edema and hypertrophy of the parotids), but with the preservation of a correct self-perception of her body (awareness of accentuated thin appearance), stabilization of body weight for ten years (with no tendency to further weight loss), a strict diet both in quality and quantity for several years, with adequate nutritional value for her biophysiological needs (as assessed by the hospital nutritionist) and absence of analytical indicators of malnutrition (normal hemoglobin, albumin, urea and creatinine).

The physical examination revealed her biotype to be asthenic, conscious, oriented in space and time, cooperating, with dysthymic mood and some emotional lability, severe emaciation (body weight: 33 kg, height: 1.61 m, body mass index: 12.7 kg/m², 15 kg below the normal weight), with the skin and mucous membranes well colored and hydrated, uniform hypertrophy of the axial and appendicular muscle mass, few skin folds, hypertrophy of the parotid glands, and a generalized hyporeflexia in

TABLE I

Endpoints	Days of blood sample collection							Normal
	1 st day	3 rd day	9 th day	16 th day	23 th day	30 th day	40 th day	
LDK	1131,5	1008	915,9	656,8	600,1	531,3	318,2	240-480 U/L
CK	775,1	565	468,8	398,1	206,9	172,4	71	26-192 U/L
CKMB	59,8	—	22,4	—	21,6	18,9	4,2	0,6-6,3 ng/mL
Myoglobin	178,2	—	75,4	—	68,1	50,1	23,6	14,3-65,8 ng/mL
GOT	62,9	50	43,2	50,5	37,4	39,8	17,7	0,0-32 U/L
GPT	93,8	77	69,7	67,4	51,7	50,5	21,6	0,0-31 U/L
GGT	124,9	76	106,7	75,7	59,1	49,3	22,5	7,0-39,0 U/L
C-TOTALI	230,2	—	—	—	172,2	165,5	—	100-200 mg/dL
— Senna Intake →		Definite withdrawal of senna intake						

the absence of sensitive or motor focal neurologic signs. The additional analytical study on admittance (day 1) showed a significant increase in liver injury (AST, ALT and GGT) and muscle markers (CK, CKMB and myoglobin), an increase in LDH (lactate dehydrogenase) and a hypercholesterolemia (Table I), without any other changes in the other analytical parameters assessed (thyroid function, pituitary and gonadal function, electrophoretic proteinogram, autoimmunity, iron, vitamin B12 and folic acid). Upper digestive endoscopy and colonoscopy revealed no pathological changes. Electromyography revealed an axonal neuropathy with a reduction in the amplitude of action potentials of the motor and sensory nerves, and needle EMG showed findings of non-specific myopathy. Anatomopathological study of muscle biopsy showed diffuse atrophy of the muscle fibers, an accumulation of lipids in the majority of the fibres observed, and a moderate amount of fibres with decreased histochemical activity of the cytochrome oxidase enzyme (histopathological characteristics suggestive of a mitochondrial myopathy). Nerve biopsy was not performed. Based on the above data, a conservative clinical approach was instituted, with total and immediate suspension of ingestion of senna (with close surveillance of the intestinal tract, due to the risk of intestinal constipation/obstruction due to a possible withdrawal effect after prolonged ingestion of senna), vitamin B complex supplementation, metoclopramide to relieve the functional dyspepsia, and attempt to implement an appropriate diet, which the

patient refused, continuing to eat exactly the same foods that she had already eaten for ten years. With these measures, and the periodic evaluation of the analytical parameters, a consistent and progressive decrease was documented in the initially high enzyme levels (LDH, CK, CK-MB, Myoglobin, SGOT, SGPT, GGT) and cholesterolemia (total-C), shown in Table I, with the disappearance of cyclic edema and dyspepsia and slight weight gain (+ 2.5 kg at the end of hospitalization, on the 40th day). The EMG and muscle biopsy were not repeated after the suspension of senna ingestion.

DISCUSSION

Nowadays, ingestion of senna extract to treat constipation and other indicated uses of the natural medicine has become very common in the scope of medical prescription (Pursennide®, Bekunis®, Mucinum®), self-medication, and the recommendation of herbalists, leading to an increased number of cases of acute and chronic intoxication, especially in patients with chronic and continuous ingestion of the extract, and those who use infusions of the senna plant instead of dosage tablets. Current knowledge that reconciles the finding of toxicity in animals (accidental cases and laboratory experiments) and humans, laboratory, anatomopathological and pharmacological demonstration of the biological effects of some chemical components of the senna plant, and the present clinical case, reveal toxic effects with preferential effect on the neurological, muscle and

liver tissues, resulting in an asymptomatic increase of liver enzymes, mitochondrial myopathy with muscle atrophy, weight loss, and electromyographic changes in axonal lesions, among other clinical manifestations of unclear etiopathogenesis that form part of the range of adverse effects reported for the senna plant. Based on the facts presented here, it is feasible to include the ingestion of senna in the vast range of differential diagnoses of asymptomatic increase in liver and/or muscle enzymes, forming the basis of healthcare that focuses on close observation of patients medicated with senna (warning of the dangers of prolonged ingestion and recommending only sporadic and non-continuous use, particularly in individuals with eating disorders who continually use diuretic teas to voluntarily reduce body weight) and the preferential use of dosed medication over infusions. ■

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