TOXICOLOGY INVESTIGATION

A Trial Investigating the Symptoms Related to Pine Nut Syndrome

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Abstract During the last few years, thousands of cases of pine nut-related dysgeusia have been reported. The symptoms involved are predominantly related to taste disturbances such as a constant bitter or metallic taste. The taste disturbance has been reported to occur 1-2 days after ingestion of pine nuts from the species of *Pinus armandii*. This paper describes a small trial where six volunteers consumed six to eight pine nuts suspected to cause dysgeusia. Incubation periods, symptoms and their duration were recorded. The trial showed that all subjects had developed symptoms of pine nut-related dysgeusia. Four out of six subjects experienced the classical bitter and metallic taste 1-2 days after ingestion. Two subjects experienced minor symptoms such as dryness and a sensation of enlarged tonsils. After the disappearance of symptoms, laboratory tests determined the pine nuts to originate from the species of P. armandii. A follow-up conversation with the subjects after 1 year showed no recurrent symptoms.

Keywords Dysgeusia · Pine mouth syndrome · Pine nut syndrome · Pine nuts · *Pinus armandii*

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Introduction

From 2009 through 2011, thousands of people in Europe and the USA have experienced and reported symptoms of pine nut-related dysgeusia [1, 2]. Pine nut-related dysgeusia is, in the public, referred to as pine mouth syndrome, or pine nut syndrome (PNS). The symptoms involved in PNS are predominantly related to taste disturbances such as a constant bitter or metallic taste. In additional to these classical symptoms, nausea, headache, diarrhoea and vomiting have been reported [1]. The taste disturbance has been reported to occur 1–3 days after ingestion of pine nuts from the species of *Pinus* armandii. PNS was first described in 2001 [3]. In 2010, reports showed up in the literature again, and a recent paper documents more than 3,100 cases of pine nut-related dysgeusia in France, with a peak in occurrences in 2009 [1]. PNS is, however, still relatively unknown, as most cases have been described within the past 3 years. Despite the recent scientific focus, the causative agent responsible for PNS is not known, but the dysgeusia have so far been related to pine nuts from the species of P. armandii [2, 4]. A few PNS cases have been reported [3, 5], but to our knowledge, no controlled trials have yet been published. The aim of this small trial is to document the incubation periods, symptoms and their duration. In addition, a follow-up conversation with the volunteers was performed after 1 year to investigate possible recurrent symptoms or other side effects.

Material and Method

Pine Nuts

The Danish Veterinary and Food Administration collected the pine nuts from an importer after several consumers had complained about a specific lot from China. All complaints were about pine nut-related dysgeusia. After the trial, the pine nuts were subjected to species determination through comparison of individual fatty acids [7]. The fatty acid analysis was performed by an accredited gas chromatographic method [6].

Trial

Complaints to the Danish Veterinary and Food Administration about a pine nut-related dysgeusia encouraged us to investigate the phenomenon further. A convenience sample of six adults (numbered 1 to 6) agreed to participate in the trial after they were informed about the possible side effects in a form of bitter and metallic taste. A control group was not established. The volunteers had no prior knowledge of PNS except for subject 5. No subjects had experienced PNS earlier in life. The volunteers consisted of four women and two men who were all healthy and did not receive any regular medication. Subjects 6 and 4 were smokers. The subjects 1 and 5 consumed pine nuts on a regular basis several times a month prior to the trial. Subjects 2, 3, 4 and 6 did not consume pine nuts on a regular basis prior to the trial but were familiar with pine nuts and their taste.

On November 3, 2010 (day 1), the subjects were given a portion of six to eight pine nuts and asked to chew and swallow the nuts as they would normally do with consumption of nuts. The portion size is considered a typical intake regardless of how the nuts are presented, i.e., as a snack, added to a salad or as a pesto. Symptoms were individually recorded on a daily basis. No physical examination was performed. Incubation periods and symptoms are presented in Table 1. After 1 year, a follow-up conversation was performed.

Results and Discussion

The presented results will be strictly descriptive with no statistical analysis of intensity and duration of symptoms or incubation periods. The symptoms and incubation periods reported in the present trial are in close agreement with real case stories [1, 5]. However, none of the volunteers experienced nausea, headache, diarrhoea or vomiting, nor did they experience symptoms lasting more than a week, as reported elsewhere [1, 5]. These differences in symptoms and their duration might be related to the amount of intake or difference in susceptibility. A difference in susceptibility is shown in this trial as the volunteers reacted very differently from the same pine nut intake. Subjects 1, 2, 3 and 4 experienced the classical pine mouth symptoms of intense bitter and metallic taste. These symptoms lasted from 2 to

the species of Pinus armandii from nuts experienced symptoms after ingestion of pine and the volunteers on Data

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Subject (age)				Symptoms				
	Day 1 (10:30 a.m.)	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8
1 (33) female	Ingestion of 6–8 pine nuts	No symptoms	Intense bitterness, a strange feeling in the mouth, a dryness in the back part of the mouth	Intense bitterness	Disappearing	None		
2 (43) female	Ingestion of 6–8 pine nuts	Strange taste	Intense bitterness especially in relation to food and drink intake	Intense bitterness	Continues	Itching in the throat	None	
3 (44) female	Ingestion of 6–8 pine nuts	No symptoms	A taste of iron or metal in the back of the mouth	Sudden disappearance	None			
4 (44) female	Ingestion of 6–8 pine nuts	No symptoms	Intense bitterness especially in relation to food and drink intake; had to avoid coffee and red wine	Continues	Disappearing	Disappearing	Disappearing	None
5 (38) male	Ingestion of 6–8 pine nuts	No symptoms	Dryness and a feeling of enlarged tonsils	Continues	Disappearing	Disappearing	None	
6 (53) male	Ingestion of 6–8 pine nuts	No symptoms	Dryness	None				

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5 days. The remaining subjects 5 and 6 were both men and only slightly affected for a maximum of 4 days. The fact that the two least affected volunteers were men is in agreement with another report that shows females to be more frequently affected than men [1].

The accredited gas chromatographic analysis of the individual fatty acids present in the pine nuts was compared with literature data [7]. The results showed a perfect match with *P. armandii*. So far, *P. armandii* is the only pine nut species associated with PNS [2, 4].

A follow-up conversation was performed in November 2011, 1 year after the trial. During that year, none of the subjects had experienced recurrent symptoms or other side effects they could relate to the trial. However, other long term effects cannot be ruled out as the causative agent, and its mode of action is unknown. Further evaluation into potential molecular causes for the symptoms should be explored. Subjects 1 and 5, without considering the identity of the species, have eaten pine nuts several times every month after the trial without experiencing PNS. Subjects 2, 3, 4 and 6 have not eaten pine nuts since the trial. This and other studies might increase the awareness of the symptoms involved in PNS, and especially, physicians could benefit from this knowledge in their diagnostic work.

Conflicts of Interest None.

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