

Prospective induction of peripheral neuropathy by the use of Tartarian Buckwheat



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ABSTRACT

Tartarian Buckwheat is an effective hypoglycemic medicinal herb. Its main active ingredients are flavonoids. We report here 5 cases of new onset polyneuropathy with dyskinesia prospectively induced by tartarian buckwheat products. Clinical and electrophysiological evidence along with laboratory tests were reviewed and analyzed. All patients were male, with an average age of 52.2 ± 10.9 years old (range: 40–66 years) and had a recent history of using tartarian buckwheat for diabetes therapy. The average time of use was 2.5 ± 1.0 months (range: 1.5–4 months). The average duration of the clinical course was 0.9 ± 0.2 months (range: 0.5–1 months). Symptoms included numbness and weakness of the limbs (5/5, 100%), hoarseness (4/5, 80%), dysphagia (1/5, 20%), bilateral facial paralysis (1/5, 20%), urinary disorders (3/5, 60%) and gonadal abnormality (4/4, 100%). Nerve conduction studies suggested more severe damages in motor nerves than sensory nerves. All the patients showed abnormality on Von Frey filaments determination. Hence, tartarian buckwheat products may cause toxic peripheral nerve lesion and the use of herbal medication needs to be better regulated and closely monitored.

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1. Introduction

Herbs have been used for disease treatment from the beginning of human society [1]. The arrival and rapid development of chemical synthetic drugs have made the use of herbs obsolete. However in recent years, people have paid more attention to organic food and natural herbal products. Herbal medicine has gained favor to be used as a complementary means for treatment of chronic diseases [2]. Currently, drugs used in 80% of the world's population are made from plants, directly or indirectly. Along with China, UK is one of the countries with the most abundant use of herbal products. According to the Global Industry Analyst, Inc. report the sales of herbal products worldwide are expected to reach about 107 billion dollars by the year 2017 [3], underlining the global impact of the herbal products market.

Buckwheat black tea composite tablets are made from tartarian buckwheat and used as a hypoglycemic health food. Tartary buckwheat is an archaic dicotyledon, which is also called *Fagopyrum tataricum* and

belongs to the Polygonaceae family [14]. The seeds of tartary buckwheat contain proteins with high quality and can provide essential amino acids for people [14]. The main active ingredients of buckwheat are flavonoids (2-phenyl-1,4-benzopyrone), also referred to as Vitamin P8 [14,15]. The flavonoids were considered to have hypoglycemic, lipid-lowering, anti-cancer, anti-mutagenic, immunity-enhancing, sterilizing, anti-atherosclerosis, anti-aging, and antioxidant effects [4,5]. Neurological damage caused by herbs could present in various forms. Its severity is often dose-related [6]. Poisoning of tartarian buckwheat products has been rarely reported. We report here five patients with peripheral neuropathy which was perhaps induced by tartarian buckwheat products.

2. Material and methods

2.1. Clinical characteristics

Five patients were admitted to the General Hospital of Chinese PLA between April and June 2013 and diagnosed with toxic peripheral neuropathy based on the recommended diagnostic criteria of toxic peripheral neuropathy [1], namely a dose–response relationship; consistent manifestations; temporal relationship for onset of symptoms and drug exposure; and improvement or at least non-progression after drug cessation. Patients showed presentation of toxic peripheral neuropathy after 10–14 day intake of buckwheat composite tablet, exclusive of peripheral lesion induced by other reasons. These patients were found during follow-up by the seller company and

Abbreviations: vFFs, Von Frey filaments; GC-MS, Gas chromatographic mass spectrometry; ICP-MS, Inductively coupled plasma mass spectrometry; NMR, Nuclear magnetic resonance spectroscopy; LC-MS, Liquid chromatography/mass spectrometer; GC, Gas chromatography; MCV, Motor conduction velocity; CMAP, Compound muscle action potentials; SCV, Sensory conduction velocity; SNAP, Sensory nerve action potential.

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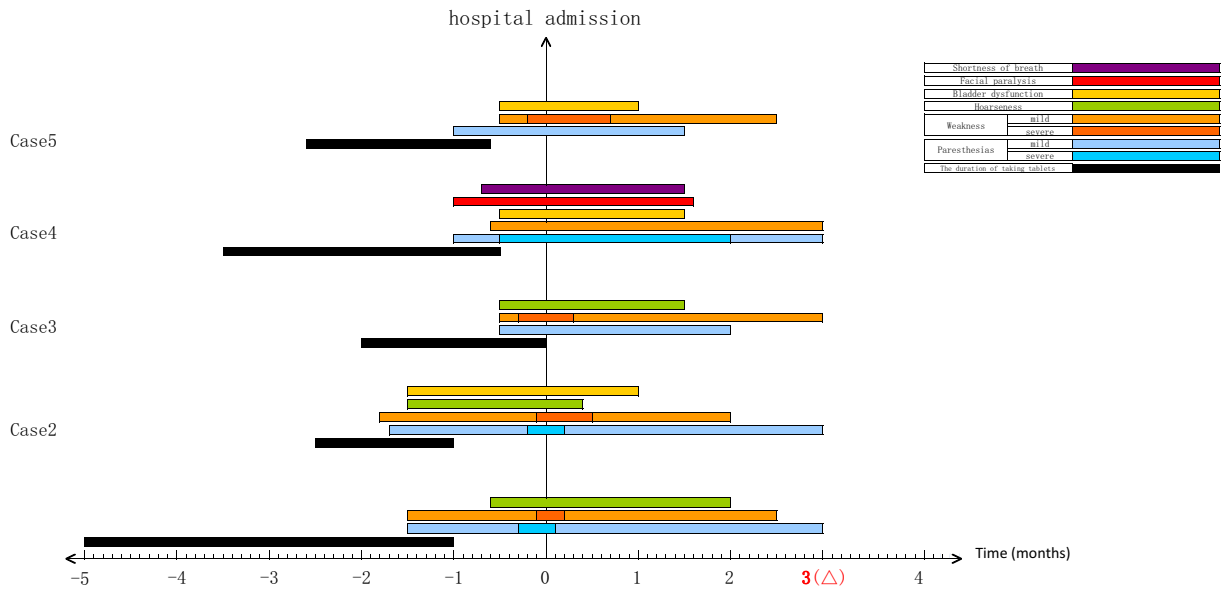


Fig. 1. The symptoms and signs of 5 patients after taking Tartarian Buck wheat composite tablets.

then sent to our hospital. The patients were not related and came respectively from different areas of Yunnan, Hunan, and Guizhou province. However, the medical history revealed that all the buckwheat products were from the same batch making one possibility that contamination or poisoning happened in this batch. All of them had no symptoms of peripheral neuropathy until they took this drug. In addition, these symptoms developed quickly after taking this drug and stopped after withdrawing from it. Routine blood test, assays on blood chemistry, tumor markers, rheumatism and immunization markers, neurological electrophysiology, and Von Frey filaments (vFFs) were performed. Four of them underwent function test on thyroid gland and gonads. Three of them underwent routine chemical assay of neurolymph as well as a 24 hour-video electrocardiogram examination. Three of them underwent visual evoke examination. These 5 patients had no symptom and sign showing lesions in CNS. Brain MRI scanning was performed on 3 patients, which showed normal findings. All patients were enrolled in the current study after obtaining signed informed consent.

2.2. Von Frey filaments examination

Determination of Von Frey filaments was performed using the Tactile allodynia method. Patients were supine in a quiet environment for 30 min at room temperature. vFFs of different pressures were used to touch and press skin from distal to proximal limbs. A bent of 90° with no feeling was regarded as non-response. vFFs were replaced by pressure from lighter to heavier.

Table 1 Clinical examinations of the five patients.

Items	N (%)	Value	Reference value
Creatine kinase	3 (60)	274.5 (217.3–317.3)U/L	(2–200) U/L
Isoenzyme creatine kinase	1 (20)	27.2 U/L	(0–24) U/L
Serum ferritin	3 (60)	751.6(412–1145) ng/ml	(30–400) ng/ml
Albumen cerebrospinal fluid	2 (0.40)	597 mg/L	150–400 mg/L
Cerebrospinal fluid IgA	1 (0.20)	0.677 mg/dl	0–0.5 mg/L
Cerebrospinal fluid IgG	2 (0.40)	4.79 mg/dl	0–3.4 mg/dl

2.3. Toxicology testing

Blood and urine samples of the patients and the sample of buckwheat black tea composite tablet were qualitatively or quantitatively analyzed by toxicology testing, including rapid emergency drug profiling system (REMEDi HS), gas chromatographic mass spectrometry (GC-MS), inductively coupled plasma mass spectrometry (ICP-MS), nuclear magnetic resonance spectroscopy (NMR), liquid chromatography, liquid chromatography/mass spectrometer (LC-MS), gas chromatography (GC), and chemical method.

2.4. Statistical analysis

Numeration data was expressed as frequency and percentage and measurement data was expressed as mean ± standard deviation. Differences on numeration data and measurement data were analyzed by Person chi-square analysis and *t* test, respectively. A *p* value ≤0.5 was considered significant and *p* ≤0.01 as considered highly significant. Student *t* test was used if homogeneity of the overall variance was shown (*p* > 0.05). Dunnett *t* test was used if heterogeneity of the overall variance was shown (*p* ≤ 0.05).

3. Results

3.1. General characteristics

All the patients were male, aged between 40 and 66 years (52.2 ± 10.9 years), with the course of disease of 0.5–1 (0.9 ± 0.2) months. All

Table 2 The incidence of acute neurotoxic symptoms secondary to receiving drug.

Symptoms	No (%)
Paresthesias	5 (100)
Weakness	5 (100)
Shortness of breath	1 (20)
Hoarseness	4 (80)
Dysphagia	1 (20)
Facial paralysis	1 (20)
Bladder dysfunction	3 (60)

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