

Abstract

Backgrounds: Sensory neuropathy from vitamin B6 toxicity was recognized since 1983. The lowest dose has been reported was 50 mg/day. High intakes of vitamin B6 from food and herb have not been reported to cause adverse effects. Turmeric is a herb that very rich source of pyridoxine. The data from United States Department of Agriculture National Nutrient data base indicates that turmeric 100 g contained pyridoxine 1.8 mg

Methods: This case report present A-76 year old woman present with progressive gait difficult for 3 years after turmeric consumption 1,000 mg/day for 5 years. Her physical examination showed sensory ataxia, impaired vibration and hyporeflexia both feet.

Results: Electrophysiological study showed evidence of distal sensory neuropathy on lower extremities. Laboratory investigation showed high level of vitamin B6 in serum. After cessation turmeric consumption 2 months but taking Gingko biloba leaves extract capsules and the “unknown vitamin” the sensory conduction study was mildly improved from previous study.

Conclusions: Long term use of Vitamin B6 from food source and unknown vitamin can cause sensory neuropathy.

Sensory neuropathy can cause by several etiologies, including vitamin B6 or pyridoxine that either a deficiency or an excess.

Pyridoxine must be obtained from the diet because humans cannot synthesize it. Vitamin B6 and its derivative pyridoxal 5'-phosphate (PLP) are essential to over 100 enzymes mostly involved in protein metabolism. In the nervous system, PLP catalyzes

Sensory Neuropathy Associated with Long Term Turmeric Consumption

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the synthesis of two major neurotransmitters: serotonin and dopamine. Other neurotransmitters, including glycine, glutamate, histamine, and γ -aminobutyric acid (GABA), are also synthesized in reactions catalyzed by PLP-dependent enzymes.¹

Pyridoxine toxicity is a recognized cause of sensory neuropathy. Schaumburg et al² described sensory neuropathy after pyridoxine misuse in 1983. Severe sensory peripheral neuropathy in individuals following ingestion of large doses of vitamin B6. Symptoms of toxicity include hyperaesthesia, paraesthesia, muscle weakness, numbness and loss of proprioception and vibration sense. Electrophysiological measurements and examination of nervous tissue by biopsy in some individuals have

demonstrated nerve damage. The lowest dose reported to have been followed by symptoms consistent with sensory nerve damage is 50 mg per day. The data from EUROPEAN COMMISSION HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Vitamin B6 (expressed on 19 October 2000) indicate that severe toxicity can be produced at doses of 500 mg/day or more, and that minor neurological symptoms may be apparent at doses of 100 mg/day or more if consumed for long periods.³ The US National Institute of Health has established Upper Intake Levels for vitamin B6 that apply to both food and supplement intakes⁴

Upper Intake Levels for vitamin B6 that apply to both food and supplement intakes

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months	Not possible to establish*	Not possible to establish*		
7–12 months	Not possible to establish*	Not possible to establish*		
1–3 years		30 mg		30 mg
4–8 years		40 mg		40 mg
9–13 years		60 mg		60 mg
14–18 years		80 mg	80 mg	80 mg
19+ years		100 mg	100 mg	100 mg

*Breast milk, formula, and food should be the only sources of vitamin B6 for infants.

High intakes of vitamin B6 from food sources have not been reported to cause adverse effects.⁵

Turmeric (*Curcuma longa*) is grown throughout India, other parts of Asia, and Central America. Historically, turmeric has been used in Ayurvedic medicine.

Today, turmeric is used as a dietary supplement for inflammation, arthritis, stomach, skin, liver, and gallbladder problems, cancer and

other conditions.⁶ Turmeric is very rich source of many vitamins including pyridoxine. The data from USDA National Nutrient data base indicates that turmeric 100 g contained pyridoxine 1.8 mg⁷ which may too excess from Recommended Dietary Allowances.

This case report presents sensory neuropathy with vitamin B6 toxicity that may be associated with long term turmeric consumption.

Recommended Dietary Allowances. B6 table

Age	Male	Female	Pregnancy	Lactation
Birth to 6 months	0.1 mg*	0.1 mg*		
7–12 months	0.3 mg*	0.3 mg*		
1–3 years	0.5 mg	0.5 mg		
4–8 years	0.6 mg	0.6 mg		
9–13 years	1.0 mg	1.0 mg		
14–18 years	1.3 mg	1.2 mg	1.9 mg	2.0 mg
19–50 years	1.3 mg	1.3 mg	1.9 mg	2.0 mg
51+ years	1.7 mg	1.5 mg		

* Adequate Intake (AI)

Case Presentation

A-76 years old woman visited out patient department with the progressive difficult gait problem for 3 years. She was sent to the neurology clinic. She had progressive unsteady when walking for 3 years ago. One year ago, she cannot walk without her tripods cane. She didn't have any weakness, numbness or tingling. She didn't have dizziness, nausea or vomiting. She didn't have hearing problem.

She had many underlying diseases; hypertension, coronary artery disease with bypass graft and hyperlipidemia. Her current medication are aspirin, atorvastatin, carvedilol and omeprazole.

Physical examination showed that she could walk slowly without cane. Her gait was slightly wide. Her motor tone was normal and her motor power was full all extremities. Romberg test was positive. Cerebellar signs were normal. Her deep tendon reflexes reduced both knees and absent both ankles. Babinski signs were plantar flexion. Pain and temperature sensation were normal, but impaired vibration both feet.

Nerve conduction study include motor nerve conduction (right median nerve, right ulnar nerve, both peroneal nerves and both tibial nerves), sensory nerve conduction (right median nerve, right ulnar nerve and both sural nerves) and F-wave

study (right tibial nerve) were done. The electrophysiologic study showed normal motor conduction in all tested nerves and normal F-wave study at right tibial nerve. The sensory nerve action potentials (SNAP) were abnormal in all tested nerves; mildly increased peak latency and reduced peak amplitude in right median nerve, mildly increased peak latency in right ulnar nerve and absent response in both sural nerves.

Laboratory work up included: vitamin B1, B6, B12 level, copper level, serum immunoelectrophoresis were done. All result was normal except vitamin B6 level, It was higher than normal (41.02 microgram/L; normal range 8.70-27.20)

We evaluated her medication use include herbal and food supplement use. She had the "turmeric power" 2 capsules (each capsule contains turmeric powder 500 mg) every day for 5 years and didn't have any other pyridoxine supplement before. She told that she bought the turmeric powder from the Thai traditional herbs shop for "improve bone condition".

We advised the patient to stop using the turmeric powder and follow-up 2 months later. She still complaint "not improved" her difficult gait so we re-evaluated the sensory conduction test (right median nerve, right ulnar nerve and both sural nerves). The results were the sensory conduction of right ulnar nerve was normal, but other nerves still same as compared to previous study. We also follow-up vitamin B6 level, it showed higher level compared to previous study (50.08 microgram/L (compared to previous 41.02); normal range 8.70-27.20 microgram/L). She confirmed stopping "turmeric powder capsule" but later she confessed that had taking Gingko biloba leaves extract capsules (2 capsules per day for 2 months) and the "unknown vitamin" to relive her symptoms from the

pharmacy shop. The Ginkgo biloba contained “Gingkotoxin” the neurotoxin which structured related to vitamin B6 and can interfered serum vitamin B6 level. The “Unknown vitamin” that can buy over the counter in Thailand included vitamin B1, B6, B12, Vitamin B complex and Vitamin C. The patient already took the all “unknown vitamin”

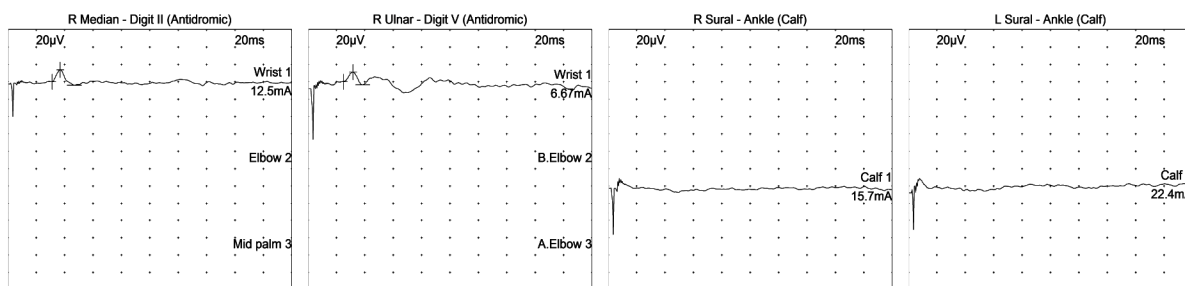
and thrown away all its packages. We strongly advised her to stop using all herbals and vitamin supplements and follow-up next 2 months.

Her serum vitamin B6 level at the next 2 months showed lower level compared to previous study (30.24 microgram/L (compared to previous 50.08); normal range 8.70-27.20 microgram/L).

First electrodiagnostic study

SNC

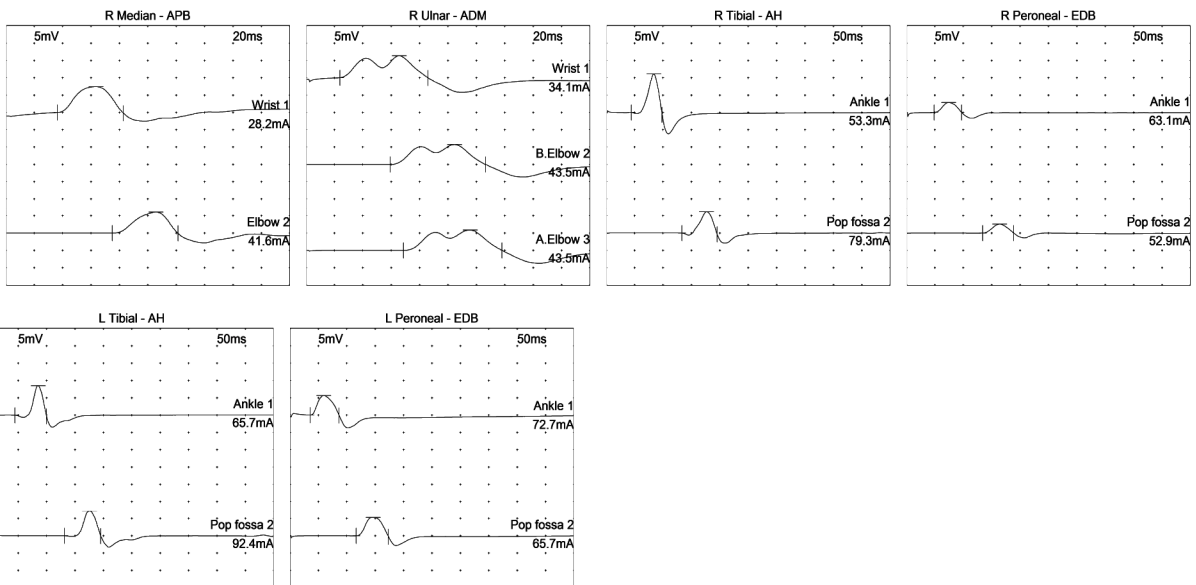
Nerve / Sites	Rec. Site	Onset Lat ms	Peak Lat ms	NP Amp µV	PP Amp µV	Segments	Distance mm	Velocity m/s	Intensity
R Median - Digit II (Antidromic)									
Wrist	Dig II	3.13	3.70	13.9	18.0	Wrist - Dig II	136	44	12.5mA
Ref.			≤3.40	≥15.0	≥20.0	Ref.			
R Ulnar - Digit V (Antidromic)									
Wrist	Dig V	2.50	3.18	11.2	14.8	Wrist - Dig V	113	45	6.67mA
Ref.			≤3.10	≥10.0	≥15.0	Ref.			
R Sural - Ankle (Calf)									
Calf	Ankle	NR	NR	NR	NR	Calf - Ankle	140	NR	15.7mA
Ref.			≤4.20	≥5.0	≥5.0	Ref.			
L Sural - Ankle (Calf)									
Calf	Ankle	NR	NR	NR	NR	Calf - Ankle	140	NR	22.4mA
Ref.			≤4.20	≥5.0	≥5.0	Ref.			



MNC

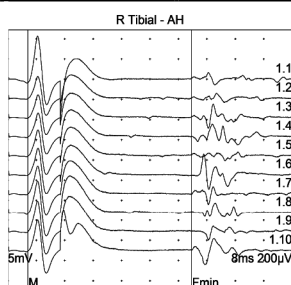
Nerve / Sites	Muscle	Latency ms	Amplitude mV	Rel Amp %	Duration ms	Segments	Distance mm	Lat Diff ms	Velocity m/s	Area mVms	Stim.
R Median - APB											
Wrist	APB	3.65	7.46	100	4.64	Wrist - APB	59			20.89	28.2mA
Ref.		≤4.40	≥4.00			Ref.					
Elbow	APB	7.50	6.07	81.4	4.64	Elbow - Wrist	211	3.85	54.75	15.34	41.6mA
Ref.						Ref.			≥49.00		
R Ulnar - ADM											
Wrist	ADM	2.40	6.37	100	6.20	Wrist - ADM	49			22.40	34.1mA
Ref.		≤3.60	≥5.00			Ref.					
B.Elbow	ADM	5.94	5.73	90	6.72	B.Elbow - Wrist	191	3.54	53.93	22.00	43.5mA
Ref.						Ref.			≥49.00		
A.Elbow	ADM	6.88	5.85	102	6.93	A.Elbow - B.Elbow	60	0.94	64.00	23.39	43.5mA
Ref.						Ref.			≥49.00		

Nerve / Sites	Muscle	Latency ms	Amplitude mV	Rel Amp %	Duration ms	Segments	Distance mm	Lat Diff ms	Velocity m/s	Area mVms	Stim.
R Peroneal - EDB											
Ankle	EDB	4.90	2.84	100	4.84	Ankle - EDB	80			7.73	63.1mA
Ref.		≤6.20	≥2.00			Ref.					
Pop fossa	EDB	13.44	2.61	91.8	5.47	Pop fossa - Ankle	350	8.54	40.98	7.71	52.9mA
L Peroneal - EDB											
Ankle	EDB	3.59	5.64	100	5.05	Ankle - EDB	56			16.83	72.7mA
Ref.		≤6.20	≥2.00			Ref.					
Pop fossa	EDB	11.67	5.32	94.4	5.68	Pop fossa - Ankle	360	8.07	44.59	18.15	65.7mA
R Tibial - AH											
Ankle	AH	4.43	11.09	100	5.42	Ankle - AH	69			23.69	53.3mA
Ref.		≤6.00	≥3.00			Ref.					
Pop fossa	AH	13.33	6.16	55.5	6.20	Pop fossa - Ankle	370	8.91	41.54	16.51	79.3mA
Ref.						Ref.			≥39.00		
L Tibial - AH											
Ankle	AH	4.43	8.57	100	5.57	Ankle - AH	77			16.53	65.7mA
Ref.		≤6.00	≥3.00			Ref.					
Pop fossa	AH	13.13	7.23	84.4	6.41	Pop fossa - Ankle	352	8.70	40.47	17.48	92.4mA
Ref.						Ref.			≥39.00		



F Wave

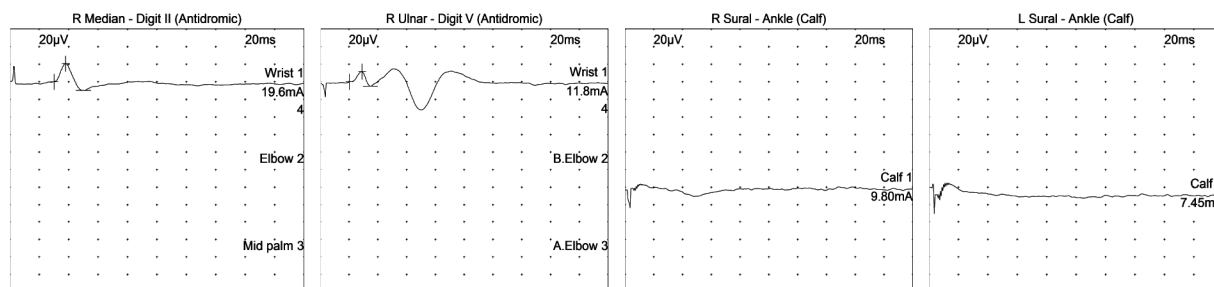
Nerve	F Lat ms	Ref. ms	M Lat ms	Ref. ms	F-M Lat ms
R Tibial - AH	51.7	≤58.0	5.6	≤32.0	46.0



Follow up study

SNC

Nerve / Sites	Rec. Site	Onset Lat ms	Peak Lat ms	NP Amp μ V	PP Amp μ V	Segments	Distance mm	Velocity m/s	Temp. $^{\circ}$ C	Intensity
R Median - Digit II (Antidromic)										
Wrist	Dig II	3.02	3.80	20.7	31.0	Wrist - Dig II	149	49	31.2	19.6mA
Ref.			\leq 3.40	\geq 15.0	\geq 20.0	Ref.				
R Ulnar - Digit V (Antidromic)										
Wrist	Dig V	2.03	2.92	11.6	16.8	Wrist - Dig V	111	55	31.3	11.8mA
Ref.			\leq 3.10	\geq 10.0	\geq 15.0	Ref.				
R Sural - Ankle (Calf)										
Calf	Ankle	NR	NR	NR	NR	Calf - Ankle	140	NR	30.8	9.80mA
Ref.			\leq 4.20	\geq 5.0	\geq 5.0	Ref.				
L Sural - Ankle (Calf)										
Calf	Ankle	NR	NR	NR	NR	Calf - Ankle	140	NR	31.9	7.45mA
Ref.			\leq 4.20	\geq 5.0	\geq 5.0	Ref.				



Discussion

From this case, the sensory conduction was slightly better after stop using the turmeric powder that we suspected the source of pyridoxine supplement but the serum vitamin B6 level still high maybe interfered from Ginkgotoxin from Ginkgo biloba extract⁸. We suspected that the long term use of turmeric were the cause of vitamin B6 toxicity induced sensory neuropathy.

Vitamin B6 toxicity from food sources have not been widely report. The dosage of vitamin B6 that this patient received per day was lower that any report (She had turmeric powder 1,000 mg/day (0.018 mg of pyridoxine) for 5 years. So we suspected that

- Vitamin B6 from food source can cause neurotoxicity

- Long term use, small dose of vitamin B6 can cause sensory neuropathy

The result from previous study shown that the effect of vitamin B6 toxicity persist for up to 6 months for recovery.

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