

Supplemental to the Vitamin B6 Citizen Petition dated September 17, 2021

Abstract

Vitamin B6, also known as pyridoxine, is a water-soluble vitamin, extensively promoted as food supplement for health maintenance and wellness.¹ Due to the COVID-19 pandemic, Americans are turning to vitamins and supplements to boost immune function. The percentage of supplement users in the United States has increased from 47% to 76%.^{5,6} Prior to the pandemic, 28-36% percent of the US population reported use of supplements that contained vitamin B6.^{1,2} More than half of Americans believe that Vitamins and Supplements available over-the-counter (OTC) have been evaluated by the FDA. Nearly one-third believe that if a supplement has a potential for toxicity, it would not be sold in the US.⁶

It is well established that when taken in excess, Vitamin B6 can cause symptoms of peripheral neuropathy and neurotoxicity.^{1,2} Doses ranging from 50-500 mg are widely available over the counter (OTC) at pharmacies, resulting in numerous cases of Vitamin B6 toxicity in patients. Submittal of this citizen petition resulted in patients contacting Emery Pharma to discuss their experience with Vitamin B6 toxicity. This case report summarizes major findings from patients experiencing Vitamin B6 toxicity.

Introduction

During the COVID-19 pandemic, there have been numerous reports of Vitamin B6 reducing COVID-19 severity, without proper clinical data to substantiate these claims.³ In our society, there has been an increase in the use of social media by patients across the healthcare spectrum. Platforms such as Facebook, have enabled patients to create support groups and communities. Patients use these platforms to discuss new treatments, compare notes, and overall, find support from those facing the same medical conditions.⁴ Many Facebook groups exist, such as "Exploring B6 Toxicity" which has approximately 3,000 members, "B6T Smart is Understanding B6 toxicity using Western Research", which consists of 3,400 members. Surveys were obtained from anonymous patient volunteers suffering from B6 Toxicity, and the results are outlined in Table 1. All patients participating in this survey have given consent to be contacted by the FDA if needed.

Table 1: Summary of Patient-Reported Adverse Effects

Patient	Date of Birth	Vitamin B6 Daily Dose and Manufacturer	Blood Test: B6 Level Reported (nmol/L)** Normal range: 20-125 nmol/L	Duration of Therapy	Symptoms Reported
1	10/6/1986	250 mg	254 nmol/L	6 months 15 days	peripheral neuropathy, numbness, twitching, joint pain/cracking, rashes, temperature intolerance, tinnitus, paresthesia, heart palpitations, dead limbs in the morning, facial pain, temporomandibular joint dysfunction (TMJ), sore throat, burning and numbness, hip pain/burning
2	7/25/1958	50 mg	360 nmol/L	1 year 7 days	peripheral neuropathy, numbness, twitching, joint pain/cracking, temperature intolerance
3	3/25/1983	N/A	1292 nmol/L	10 years 7 months 3 days	peripheral neuropathy, joint pain/cracking, rashes, temperature intolerance, erythromelalgia
4	3/12/1985	Varied between a prenatal, energy drinks, to a different MVI with 10 mg pyro HCl, and liquid IV.	123.9 nmol/L	6 years 6 months	peripheral neuropathy, numbness, twitching, joint pain/cracking, rashes, temperature intolerance, tinnitus, paresthesia, dexterity issues in my hand, postural orthostatic tachycardia syndrome, anxiety
6	7/6/1973	Emergen-C 30 mg	147.5 nmol/L	11 months 18 days	peripheral neuropathy, numbness, joint pain/cracking, dizziness, nausea, muscle weakness, anxiety, shortness of breath
7	1959	7 mg	611.8 nmol/L	20 years	peripheral neuropathy, numbness, twitching, joint pain/cracking, tinnitus, paresthesia, lightheaded, burning feet
8	1/18/1964	Country Life 24 mg	131.7 nmol/L	25 years 10 months 28 days	peripheral neuropathy, numbness, temperature intolerance

9	3/24/1983	Neurobion 200 mg	N/A	1 months 5 days	peripheral neuropathy, numbness, tinnitus, paresthesia, Lhermitte's sign, anxiety and depression, loss of appetite, muscle weakness, heart palpitations, chest pain, insomnia, eustachian tube dysfunction.
10	5/13/1958	Rainbow Lite Multivitamin 25 mg	666.7 nmol/L	1 year 4 months 2 days	peripheral neuropathy, numbness, temperature intolerance, tinnitus, paresthesia, anxiety
11	1/5/1993	Bragg Nutritional Yeast 7.2 mg	294.9 nmol/L	3 years	peripheral neuropathy, numbness, twitching, temperature intolerance, tinnitus, paresthesia, depression
12	9/12/1977	100 mg per day, then a three- month break, resumed 75 mg per week until June	320 nmol/L	5 months 19 days	peripheral neuropathy, numbness, twitching, joint pain/cracking, rashes, tinnitus, paresthesia, pudendal neuralgia, premature menopause
13	3/26/1979	Greenbrier International Inc. 40 mg	297.9 nmol/L	3 months 19 days	peripheral neuropathy, twitching, tinnitus, anxiety, fatigue
14	8/4/1958	Spring Valley 100 mg	N/A	17 years 6 months 26 days	peripheral neuropathy, tinnitus, paresthesia, flushing, blurry vision
15	5/24/1952	Life Extension two a day multi vitamin 75 mg	450 nmol/L	5 months 21 days	peripheral neuropathy, numbness, twitching, joint pain/cracking, temperature intolerance, tinnitus, paresthesia, visual impairment, anxiety, orthostatic hypotension, dizziness, involuntary muscle movements, irritable bowel syndrome, muscle pain and spasm
16	Information not provided	75 mg	609.7 nmol/L	1 month 1 day	peripheral neuropathy, twitching, rashes, tinnitus, anxiety, trigeminal neuralgia, mouth burning, tremors, hair loss. muscle wasting and weight loss, visual changes

17	3/17/1973	Livol Multi, Apovit B- Komplex, Sanofi Magne B6 30 mg	N/A	3 years	peripheral neuropathy, numbness, twitching, seizures
18	10/23/1982	FaBB tablets 25 mg	297.7 nmol/L	12 years	peripheral neuropathy, numbness, rashes, temperature intolerance, short term memory loss, dry eyes, pruritus, insomnia
19	8/1/1955	B complex and multivitamin 100mg	142.2 ng/mL	19 years 10 months	peripheral neuropathy, numbness, joint pain/cracking, tinnitus, abdominal pain
20	1/24/1976	Bioceuticals Nature's Energy, Centrum 50-300 mg	535 nmol/L	7 years 2 months 18 days	peripheral neuropathy, numbness, twitching, joint pain/cracking, tinnitus, paresthesia, weakness, fatigue, postural orthostatic tachycardia syndrome, blurry vision, foot and hand atrophy
21	6/12/1952	Alive women's 55+ 40 mg	719.8 nmol/L	6 years 6 days	peripheral neuropathy, joint pain/cracking
22	8/2/1971	NOW and Nature Made (Nature Made Super B Complex + various name brand multi vitamins) 100 mg	351 nmol/L	16 years 8 months 9 days	peripheral neuropathy, numbness, twitching, joint pain/cracking, rashes, paresthesia, fatigue, dizziness, headaches, heartburn, dry eyes, constipation, sexual dysfunction
23	7/1/1956	Generic multivitamin for "women over 50" 6 mg	1,059 nmol/L	2 months 24 days	peripheral neuropathy, numbness, temperature intolerance, paresthesia
24	10/12/1996	Subneuro B6 20mg pyridoxine 20 mg	N/A	1 month 14 days	peripheral neuropathy, numbness, joint pain/cracking, rashes, temperature intolerance, tinnitus, paresthesia, hypothermia, sinus problems, histamine issue, fatigue, weakness, back pain, body pain, headache, stomach pain, muscle pains, anxiety, depression, decline in mental health, postural orthostatic tachycardia syndrome,

					exercise intolerance, loss of appetite, blood pressure instability
25	7/31/1951	Celebrex Bariatric Multi and Nature Made B6 100 mg	800 nmol/L	4 months 15 days	paresthesia, anxiety
26	9/11/1985	Rainbow Light Multivitamin 20 mg	459 nmol/L	11 months 15 days	peripheral neuropathy, joint pain/cracking, temperature intolerance
27	4/26/2000	AOV 20 mg	396 nmol/L	8 days	peripheral neuropathy, numbness, twitching, rashes, temperature intolerance, nausea, muscle pain, constipation, photosensitivity, hyperesthesia
29	4/4/1991	4 mg	N/A	3 years 10 months 2 days	peripheral neuropathy, numbness, twitching, joint pain/cracking, rashes, temperature intolerance, tinnitus, paresthesia, depression, anxiety
30	3/29/1967	Centrum silver Multivitamin 6 mg	247.8 nmol/L	1 year 4 months 15 days	peripheral neuropathy, numbness, temperature intolerance, tinnitus, paresthesia, vertigo, insomnia, depression
31	10/16/1973	Nature Bounty Hair, Nail, and Skin 5 mg	1,225 nmol/L	10 years (dates not specified)	peripheral neuropathy, twitching, tinnitus, paresthesia
32	4/5/1986	Melatonin 10 mg	159.3 nmol/L	2 years 11 months	peripheral neuropathy, numbness, twitching, rashes, tinnitus, paresthesia, muscles weakness hemiparesis, blurred vision, headaches, chest pain
33	11/18/1953	FutureBiotics, Emergen-C 10 mg	771.7 nmol/L	10 years 4 months 14 days	peripheral neuropathy, numbness, twitching, joint pain/cracking, tinnitus, paresthesia, pain and discomfort in feet, hands, and calves

34	2/25/1963	Now Foods B100 100 mg	181 nmol/L	15 years 7 months 29 days	temperature intolerance, tinnitus, insomnia, post exertional malaise, eye pain, blurry vision
36	9/22/1982	Swiss multivitamin 40 mg	1000 nmol/L	1 month 6 days	peripheral neuropathy, twitching, temperature intolerance, low blood pressure, postural orthostatic tachycardia syndrome, chronic fatigue syndrome
37	9/4/1961	Centrum Silver 2 mg	284.2 nmol/L	16 years 9 months 30 days	numbness
38	8/18/1977	Walgreen's generic 100 mg	612 nmol/L	1 weeks 2 days	peripheral neuropathy, tinnitus, paresthesia, tremor, alopecia, gastrointestinal issues
39	7/6/1977	GNC Women's Ultra Mega Woman Energy & Metabolism Vitamin 50mg	610 nmol/L	5 years 8 months 4 days	peripheral neuropathy, numbness, joint pain/cracking, tinnitus, paresthesia, neck and shoulder pain
40	3/29/1967	Centrum Silver 6 mg	247.8 nmol/L	1 years 6 months 15 days	peripheral neuropathy, numbness, temperature intolerance, tinnitus, paresthesia, insomnia, vertigo.
41	9/21/1975	Children's vitamin with 35% of RDA	847 nmol/L	8 months 14 days	peripheral neuropathy, numbness, paresthesia, cramping, pain, neuroma
42	6/10/1975	Cenovis MegaB 50 mg	1420 nmol/L	2 months 22 days	peripheral neuropathy, numbness, twitching, joint pain/cracking, tinnitus, paresthesia, burning cold sensations, increased eye floaters
43	8/17/1980	2 mg	950.6 nmol/L	7 years	peripheral neuropathy, numbness, twitching, joint pain/cracking, tinnitus, paresthesia, photosensitivity
44	5/5/1985	Pyroll protect 150 mg	200 nmol/L	3 days	peripheral neuropathy, numbness, twitching, joint pain/cracking, tinnitus, dizziness, muscle twitches, vertigo
45	3/2/1986	Natrol Melatonin ER Tablets 10 mg	448 nmol/L	4 years 2 months 4 days	peripheral neuropathy, numbness, twitching, paresthesia

46	1/27/1960	Centrum multivitamin 5 mg	495 nmol/L	20 years 6 months 26 days	peripheral neuropathy, numbness, twitching
47	5/16/1959	Solaray 100 mg	456 nmol/L	3 years 9 months	peripheral neuropathy, numbness, twitching, joint pain/cracking, rashes, temperature intolerance, tinnitus, paresthesia, insomnia
48	1/22/1989	100 mg for 2 months, then 10 mg for 2 months	537 nmol/L	4 months	numbness, twitching, temperature intolerance, involuntary muscle movements.
49	11/29/1976	50-100 mg	196.7 nmol/L	3 months	peripheral neuropathy, numbness, twitching, joint pain/cracking, paresthesia, pruritus

*Patient data has been anonymized and is available upon request to the Food and Drug Administration (FDA) under confidentiality

** The assumption was made that patients were taking Pyridoxal-5-phosphate. All units were converted to nmol/L.

Conclusion

Based on the self-reported data collected through this survey, most patients are experiencing or have experienced peripheral neuropathy as a result of high-dose Vitamin B6 consumption. Through the data collected from these surveys, as well as case studies available in the literature, it can be concluded that when taken in excess, Vitamin B6 poses a risk of peripheral neuropathy and neurotoxicity.

Emery Pharma is petitioning the agency that once all evidence is considered and thoroughly reviewed, they will find Vitamin B6 is misbranded. Emery Pharma urges the Food and Drug Administration to implement safe guidelines for the use of this widely abused vitamin. Manufacturers of Vitamin B6 or B-Complexes should include labeling regarding the potential toxicity of Vitamin B6. Labeling should include a warning to consumers to discontinue B6 supplementation if they experience signs or symptoms of toxicity. Additionally, doses greater than 10 mg should be sold “behind the counter”, with a prescription and under the supervision of a physician. When considering the consequences of inaction and the health of the public, we hope that the FDA will follow these recommendations.

References

1. Office of Dietary Supplements - Vitamin b6." NIH Office of Dietary Supplements, U.S. Department of Health and Human Services, ods.od.nih.gov/factsheets/VitaminB6-HealthProfessional/.
2. Morris MS, Picciano MF, Jacques PF, Selhub J. Plasma pyridoxal 5'-phosphate in the US population: the National Health and Nutrition Examination Survey, 2003-2004. *Am J Clin Nutr* 2008;87:1446-54.
3. Kumrungsee T, Zhang P, Chartkul M, Yanaka N and Kato N (2020) Potential Role of Vitamin B6 in Ameliorating the Severity of COVID-19 and Its Complications. *Front. Nutr.* 7:562051. doi: 10.3389/fnut.2020.562051
4. Eckler, Petya and Worsowicz, Gregory and Rayburn, J. Wesley (2010) Social media and healthcare : an overview. *PM&R*, 2 (11). pp. 1046-1050.
5. Kumrungsee T, Zhang P, Chartkul M, Yanaka N and Kato N (2020) Potential Role of Vitamin B6 in Ameliorating the Severity of COVID-19 and Its Complications. *Front. Nutr.* 7:562051. doi: 10.3389/fnut.2020.562051
6. "Murphy, Jill. "Survey Finds 3 in 10 Americans INCREASED Supplement Use Since Covid-19 Pandemic." *Pharmacy Times*, *Pharmacy Times*, 23 July 2021, www.pharmacytimes.com/view/survey-finds-3-in-10-americans-increased-supplement-use-sincecovid-19-pandemic.