

## **HYPERVITAMINOSIS B6 IN AUSTRALIA- FROM CLINICAL EXPERIENCE TO GOVERNMENT GUIDELINES:**

### **BARIATRIC CARE TEAM WERE A CRITICAL CATALYST FOR CHANGE**

#### **Background:**

Vitamin B6 (pyridoxine) is a water-soluble vitamin present in various food products as well as in dietary supplements<sup>i</sup>; with pyridoxal 5'-phosphate (PLP)<sup>ii</sup> being the biologically active form. Fasting plasma PLP concentrations most accurately reflect B6 body stores hence measured to determine systemic levels<sup>iii</sup>.

Daily B6 intake should not exceed 25 mg as an intake of 50 mg/day is associated with sensory<sup>iv v vi</sup> and in some instances mild motor neuropathy<sup>vii</sup>.

Other sources of high vitamin B6 include energy drinks,<sup>viii</sup> and type of bariatric operation which may alter the gut microbiota composition<sup>ix x xi</sup>.

#### **Introduction:**

The aim of this presentation is to encourage HCPs involved in the management of BMS patients to remain vigilant and employ adequate lifelong recall systems given that hypervitaminosis B6 toxicity can/does occur both in the early postop-period AND also years later, and has serious clinical implications.

Several, but not all, bariatric metabolic surgery [BMS] units in Australia routinely measure B6 levels in their patients at different time intervals pre- and post- surgery. The Bariatric physician [BP] at Site 1 observed the number of patients with raised B6 levels were increasing resulting in a self-directed audit.

Upon completion of the audit, the Site 1 BP shared the findings with the BP doctors network enquiring if other sites had similar experiences. This was the clinical impetus for this collaboration between sites, review of dietary intake including supplementation in BMS patients, review of the medical literature, investigation into B6 content in Australian supplements, submission to and subsequent changes in regulatory recommendations.

#### **Methods:**

Both Site 1 (AS) and Site 2 (DWLS) independently performed a retrospective audit of prospectively collected vitamin B6 blood test levels on all their BMS patients and agreed to collaborate. Their findings were shared with the Therapeutic Goods Administration (TGA) regulatory body of Australia.

Pubmed was utilized to review the literature for the years 2015–2023. The key terms used in the search were ‘vitamin B6 pharmacokinetics’, ‘vitamin B6 toxicity’ and ‘bariatric surgery’. The references of all retrieved articles were scanned to identify additional articles.

### **Results:**

High and excessively high vitamin B6 defined as >190nmol/L and >250nmol/L respectively

Site 1 (AS), N = 2953 blood test results between 2015-2019, 37% and 24% of total patients had high and excessively high B6 levels (B6 levels range: 20 – 7960 nmol/L).

Site 2 (DWLS), N= 612 blood test results between May 2021 – April 2022: 28% and 18% of total patients had high and excessively high B6 levels (B6 levels range: 34 – 5980 nmol/L).

Investigation into Australian supplement content and dosing identified that (i)Pyridoxine hydrochloride is the most used form used, which according to the literature is more likely to cause toxic effects than the active phosphate form (P5P) and (ii)some supplements had excessively high doses of B6.

In addition to this, up to 5 August 2022, the TGA had received 32 adverse event reports with sufficient information to establish a possible causal association between peripheral neuropathy and products containing vitamin B6<sup>ii</sup>. As a result, in October 2022, the TGA disseminated new guidelines on dosage, and labelling and encourages the ongoing reporting of all suspected adverse reactions to medicines, including over-the-counter supplements.

### **Conclusion:**

Neurological symptoms such as neuropathy might be associated with B6 toxicity in post-BMS patients and should prompt HCPs to carefully evaluate plasma B6 levels and dietary intake in these patients.

The general recommendations for vitamin B6 supplementation in all post-BMS patients should be revised towards individualized, tailored approaches according to actual plasma vitamin B6 levels in these patients. A regular follow-up of vitamin B6 plasma levels and critical evaluation of vitamin B6 supplementation, either as part of the multivitamin preparation or related to regular energy drink intake, is highly warranted and should be an integral part of the routine post-bariatric follow-up.

**Conflict of Interest** relevant to this presentation: nil

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<sup>ii</sup> Stover, P. J. & Field, M. S. Vitamin B-6. *Adv. Nutr.* 6, 132–133 (2015).

<sup>iii</sup> Stover, P. J. & Field, M. S. Vitamin B-6. *Adv. Nutr.* 6, 132–133 (2015).

<sup>iv</sup> Vrolijk, M. et al. The vitamin B6 paradox: Supplementation with high concentrations of pyridoxine leads to decreased vitamin B6 function. *Toxicol. In Vitro.* <https://doi.org/10.1016/j.tiv.2017.07.009> (2017).

<sup>v</sup> EFSA. (European Food Safety Authority, 2006).

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<sup>vi</sup> Schaumburg, H. et al. Sensory neuropathy from pyridoxine abuse: a new megavitamin syndrome. *N. Engl. J. Med.* 309, 445–448 (1983)

<sup>vii</sup> Morra, M. et al. Sensory and motor neuropathy caused by excessive ingestion of vitamin B6: A case report. *Funct. Neurol.* 8, 429–432 (1993).

<sup>viii</sup> Wolk, B. J., Ganetsky, M. & Babu, K. M. Toxicity of energy drinks. *Curr. Opin. Pediatr.* 24, 243–251. <https://doi.org/10.1097/MOP.0b013e3283506827> (2012).

<sup>ix</sup> Guo, Y. et al. Modulation of the gut microbiome: A systematic review of the effect of bariatric surgery. *Eur. J. Endocrinol.* 178, 43–56. <https://doi.org/10.1530/eje-17-0403> (2018).

<sup>x</sup> Paganelli, F. L. et al. Roux-Y Gastric bypass and sleeve gastrectomy directly change gut microbiota composition independent of surgery type. *Sci. Rep.* 9, 10979. <https://doi.org/10.1038/s41598-019-47332-z> (2019).

<sup>xi</sup> Aron-Wisnewsky, J. et al. Major microbiota dysbiosis in severe obesity: Fate after bariatric surgery. *Gut* 68, 70–82. <https://doi.org/10.1136/gutjnl-2018-316103> (2019).

<sup>xii</sup> <https://www.tga.gov.au/news/safety-updates/peripheral-neuropathy-supplementary-vitamin-b6-pyridoxine> (accessed January 2023)