



Perspective

Prescribing vitamin B complex: Need for reassessment

Vitamins are the largest selling segment of global dietary supplement market registering a revenue of USD 37.64 billion in 2018¹. North America and Europe together account for 55.74 per cent of the global vitamin and mineral market share followed by the Asia-pacific region. According to estimates over 33 per cent of population in the United States of America and in many European countries like United Kingdom, Denmark, and Sweden regularly use multi vitamin mineral (MVM) preparations as dietary supplements². Studies assessing the prescribing behaviour of doctors in various parts of India reveal that vitamins constitute about 24-25 per cent of all prescribed drugs, however, the rationale behind this practice is not clear³. MVM preparations are also readily available over the counter and are often consumed by patients and general public as health tonics¹. The reason for their sales possibly includes a belief that these are required for the well-being of an individual.

B-vitamins are a class of water-soluble vitamins that are commonly used as a dietary supplement. These are a diverse group of chemical substances comprising of thiamine (B1); riboflavin (B2); niacin (B3); pantothenic acid (B5); pyridoxine (B6); biotin (B7); folic acid (B9) and cyanocobalamin (B12) which are collectively referred to as 'vitamin B complex'. These are essential for meeting the metabolic demands of the body as most of them serve as co-enzymes involved in various metabolic pathways (Table I⁴). Many of these are also available as fixed dose combinations (FDCs) with other vitamins and minerals (MVM).

B-vitamins are used for the treatment of specific vitamin deficiency disorders such as beriberi (thiamine); pellagra (niacin) or certain non-nutritional disorders like Wernicke-Korsakoff syndrome (thiamine) and hyperlipidaemia (niacin)⁵. B-vitamins are also given prophylactically to prevent adverse effects of drug therapy, for example, those receiving isoniazid (300 mg or more)

are given vitamin B6 (pyridoxine) in a dose of 10 mg daily to prevent peripheral neuropathy while those receiving cycloserine would require pyridoxine in a dose of 100-150 mg/day to reduce the incidence of its neurological adverse effects⁶. However, there is so far no clear evidence that vitamin B complex is beneficial in the treatment of peripheral neuropathy from other causes such as diabetes mellitus and alcoholism. The routine use of B-vitamins may be indicated in some population groups. For example, folic acid is recommended for women of childbearing age and vitamin B-12 for adults of age above 50 yr. There is a strong evidence that a daily intake of at least 450 µg dietary folate equivalents in non-pregnant non-lactating women decreases the incidence of neural tube defects (NTDs) in newborns⁷.

B-vitamins are often used in conditions not characterized with a vitamin B deficiency for which evidence for efficacy is lacking (Table II⁸⁻¹⁷). Clinical studies and guidelines have consistently reported no clear benefits or possible harm of using B-vitamins or MVM supplements for decreasing morbidity and mortality due to major chronic diseases¹⁸. For example, the use of B-vitamins like folic acid has been found harmful in those with high baseline homocysteine levels¹⁹. Similarly, the use of MVM supplements containing beta carotene increases the risk for lung cancer and those with high-dose vitamin E increases overall mortality among users²⁰.

There is ample evidence to discourage the use of B-vitamins or MVM supplements in well-nourished adults¹⁸. However, notwithstanding the above clinical situations, B-vitamins are often prescribed or self-administered by people regularly as nutrition supplements. It is even more perplexing how vitamin B complex, a FDC of B vitamins for which there is no evidence of efficacy at all is prescribed or used.

There are many FDCs of vitamin B complex available in the market. These contain different B

Table I. Vitamins of B complex⁴

Vitamins	RDA [#]	Deficiency cause	Deficiency syndrome and symptoms	Dose
Thiamine (B1)	1.2-1.7 mg/day	Dietary deficiency	Beri Beri, Wernicke's encephalopathy-Korsakoff psychosis	P: 2-10 mg/day T: 100 mg/day IV
Riboflavin (B2)	1.4-2.1 mg/day	Dietary deficiency	Ariboflavinosis	T: 2-20 mg/day
Niacin (B3)	16-21 mg/day	Dietary deficiency (maize, jowar and bajra eaters)	Pellagra	P: 20-50 mg/day T: 200-500 mg/day
Pantothenic acid (B5)	No recommendation	Dietary deficiency	Rare, fatigue, paresthesia, numbness, muscle cramp	T: 10-50 mg/day
Pyridoxine (B6)	2 mg/day	Dietary deficiency; drugs (isoniazid)	Peripheral neuropathy, glossitis, anorexia	P: 2-5 mg/day T: 50-200 mg/day
Biotin (B7)	No recommendation	Consuming raw egg whites	Rare, rashes, brittle hair, anemia, lethargy, anorexia, myalgia	No defined dose
Folic acid (B9)	200 µg/day	Dietary deficiency	Megaloblastic anemia	P: 0.5 mg/day T: 1.5-5 mg/day
Cyanocobalamin (B12)	1 µg/day	Dietary deficiency (vegetarian diet) Malabsorption (pernicious anemia)	Megaloblastic anemia Peripheral neuropathy	P: 3-10 µg/day T: 100-1000 µg/week IV

[#]RDA refers to the amount of dietary nutrient required by a reference adult male (body weight 60 kg) to meet their physiological needs as per the dietary standards for the Indian population. P, prophylactic dose; T, therapeutic dose; RDA, recommended dietary allowance

vitamins, sometimes other vitamins and minerals in variable quantities. The quantity of individual vitamin many a time does not coincide with their therapeutic or prophylactic doses. This aspect is not considered many times while prescribing. The analysis of the five most popular oral preparations of vitamin B complex available in the Indian market showed that half of the B-vitamins are present in their therapeutic doses while some are in their prophylactic dose along with other vitamins which do not have any recommended intake (Table III)²¹. It is unlikely that the users of these multivitamins know these differences and their clinical implications. For example prescribing an MVM preparation containing folic acid, as shotgun therapy for treating vitamin B12 deficiency can not only obscure the possible diagnosis of pernicious anaemia but can also pose a risk of developing serious neurological complications²⁰. The prophylactic dose of folic acid during pregnancy is 0.5 mg/day while its dose for the treatment of established anaemia is 5 mg/day but MVM preparations in the market have a variable composition of folic acid ranging from 0.5 to 5 mg⁴. A hypochromic anaemia which is not responsive to iron therapy may be benefited with pyridoxine (pyridoxine responsive hypochromic anaemia)²². Pyridoxine is also a cofactor for enzyme dopa

decarboxylase and its use in a Parkinson's patient taking l-dopa may result in therapeutic failure¹⁴.

The Government of India through a gazette notification banned an FDC of vitamin B complex containing vitamin B1, B6, and B12 from January 1, 2001. A core group of experts appointed by the Supreme Court of India concluded that there was no rationality of this combination and it should be phased out from the market to prevent improper use. However, the pharmaceutical companies added other B-vitamins (vitamin B2; B3 and B5) to this combination, and this new recipe when marketed reported sales of over ₹161 crores in 2017²³. It is considered to be among the top-selling FDC of vitamin B complex in the country. Introspection is needed as to how adding more drugs to a banned FDC will make it rational. Another dangerous trend that has emerged is combining drugs acting on different organ systems with vitamins. Few of such FDC's (atorvastatin + vitamin B6/B9/B12 + vitamin D; ammonium citrate + vitamin B9/B12) also featured in the list of 344 FDC's which were banned by the Government of India citing no therapeutic justification and potential risk to people²⁴.

The economic consequences of irrational use of MVM as nutritional supplements can be realized

Table II. Current available evidence on using vitamin B for prophylaxis or management of diseases

Review	Condition	Conclusion
Ang <i>et al</i> ⁷ , 2008	Peripheral neuropathy	Evidence is insufficient to determine whether vitamin B is beneficial or harmful for treating peripheral neuropathy
Raval <i>et al</i> ⁹ , 2015	Diabetic Kidney Disease (DKD)	No evidence to recommend the use of vitamin B therapy alone or in combination for delaying progression of DKD
Day ¹⁰ , 2013	Wernicke-korsakoff syndrome (WKS)	Evidence is insufficient to determine the dose, frequency, route or duration of thiamine treatment for prophylaxis against WKS or its treatment due to alcohol abuse
Rodríguez ¹¹ , 2001	Alzheimer's disease	Sample size in studies was <50 and the reported results were inadequate to suggest regarding the efficacy of thiamine in Alzheimer's diseases.
Schandelmaier ¹² , 2017	Cardiovascular disease (CVD)	Evidence suggests that niacin does not reduce cardiovascular mortality from myocardial infarction or stroke but is associated with side effects
Malouf ¹³ , 2003	Cognitive impairment	No evidence for short-term benefit from vitamin B6 supplementation in mood or cognitive functions could be found especially among elderly and people with dementia
Salam ¹⁴ , 2015	Pregnancy and/or labour	Evidence is insufficient to determine the clinical benefits of vitamin B6 supplementation in pregnancy and/or labour. One clinical trial suggests protection against dental decay
De-Regil <i>et al</i> ⁸ , 2015	Neural tube defects (NTDs) and other congenital anomalies (including cleft palate)	Folic acid, prevents NTDs, but does not have a clear effect on other birth defects
Lassi <i>et al</i> ¹⁵ , 2013	Pregnancy outcomes (haematological and biochemical parameters during pregnancy)	No conclusive evidence to suggest that folic acid supplementation during pregnancy improves pregnancy outcomes like preterm birth and still birth/ neonatal deaths
Shea <i>et al</i> ¹⁶ , 2013	Rheumatoid arthritis and its treatment side effects	Supplementation with folic or folinic acid has a protective effect on patients with rheumatoid arthritis during treatment with methotrexate (MTX)
Malouf and Areosa Sastre ¹⁷ , 2003	Cognitive impairment in demented and healthy elderly people	Insufficient evidence to determine the efficacy of vitamin B12 in improving the cognitive function among people with dementia and low serum B12 levels

Table III. Popular fixed dose combinations (FDCs) of vitamin B complex in Indian market²¹

Vitamins	Brand-A	Brand-B	Brand-C	Brand-D	Brand-E	Remarks
Thiamine (B1)	10 mg	10 mg	10 mg	10 mg	10 mg	Prophylactic dose
Riboflavin (B2)	10 mg	10 mg	10 mg	10 mg	10 mg	Therapeutic dose
Niacin (B3)	100 mg	100 mg	100 mg	45 mg	45 mg	Prophylactic dose
Pantothenic acid (B5)	50 mg	50 mg	50 mg	50 mg	50 mg	Therapeutic dose
Pyridoxine (B6)	3 mg	3 mg	3 mg	3 mg	3 mg	Prophylactic dose
Biotin (B7)	100 µg	100 µg	100 µg	-	-	No recommendation
Folic acid (B9)	1500 µg	1500 µg	1500 µg	-	-	Therapeutic dose (low)
Cyanocobalamin (B12)	15 µg	15 µg	15 µg	15 µg	15 µg	Prophylactic dose
Other vitamins/minerals	vitamin-C	-	vitamin-C; zinc	-	-	

from the fact that the global vitamin supplements market is expected to reach over USD 81 billion by the year 2025 with a significant rise in the vitamin-B product segment, soaring at a growth rate of 6.6 per

cent during 2019-2025²⁵. The Asia Pacific region, due to rapid urbanization and increased inclination towards preventive healthcare is expected to be the fastest emerging market for vitamin supplements.

Both China and India are projected to witness a growth rate of over 7.92 per cent in vitamin and mineral supplement market²⁵. In countries like India where 70 per cent of healthcare expenses are met by out-of-pocket expenditure by patient and medicines account for over half of this expenditure, it is important to reduce indiscriminate use of multivitamin preparations, and the savings could be better spent elsewhere.

India is facing over-nutrition and obesity as serious emerging public health problems over an existing burden of under-nutrition. Like other medicines, vitamins must be prescribed for specific indications as per the scientific evidence and their indiscriminate use for health promotion or prevention of chronic diseases should be stopped. Evidence-based guidelines for the use of vitamin/mineral supplements must be developed by building consensus among experts from the fields of nutrition, pharmacology and clinicians across various specialties. These guidelines should be formulated considering the dietary needs of Indian population and must also clarify the role of nutritional supplements in individuals otherwise taking a regular diet. The formulation of such guidelines can not only check the indiscriminate use of MVM preparations but can also serve as a benchmark to ban irrational or harmful FDCs. There needs to be a stringent regulatory system in place to prevent marketing of FDCs which do not have a concrete scientific basis. The consumers and prescribers must also be educated as regards to the importance of balanced diet *vis-a-vis* nutritional supplements, which are often not needed for maintaining health but can cause harm and a wastage of economic resources. This holds true even more so for B-vitamins, a much-misused vitamin complex.

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