



# Healthy adults with severe stress and hypomagnesaemia benefit from a combination of magnesium and vitamin B6

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This randomised, single-blind, clinical study investigated the effects of magnesium supplementation compared with combined administration of magnesium and vitamin B6. Whilst there were no significant differences between the study arms in the case of moderate stress, patients with hypomagnesaemia and severe or very severe stress benefitted from a combination of magnesium and vitamin B6.

For the first time, a randomised study has compared the effects of supplementation with magnesium alone with those of a combined administration of magnesium and vitamin B6 [1]. Whilst there were no significant differences between the two arms of the study in the case of moderate stress, patients with hypomagnesaemia exposed to severe or very severe stress benefitted from a combination of magnesium and vitamin B6.

Everyday stress is part of modern life and can have a major influence on mood, well-being, behaviour and health. Daily stress factors increase the probability that physical and mental health problems will occur. The present study investigated the effects of a combined magnesium-vitamin B6 supplement compared with those of magnesium alone on stressed adults with low magnesium levels.

After potassium, magnesium is the second most common intracellular cation. Hormones released during stress bring about a movement of magnesium from the intracellular to the extracellular space leading to increased excretion of magnesium in the urine and a subsequent fall in serum magnesium concentrations. Low levels of serum magnesium in turn cause an increase in the release of stress-associated hormones such as catecholamines, adrenocorticotrophic hormones and cortisol as a response to stress and impair their access to the brain. The result is a vicious circle of reduced resistance to stress and a further loss of magnesium.

Vitamin B6 exerts modulatory effects on neurotransmitters that affect depression and anxiety; it may reduce blood pressure and act peripherally to reduce the physiological

effects of corticosteroid release. One possible reason is that vitamin B6 facilitates the cellular uptake of magnesium, which both limits its excretion and increases its effectiveness.

Animal studies have shown that a specific combination of magnesium and vitamin B6 in a ratio of 10:1 relieves the symptoms of magnesium deficiency more rapidly than magnesium alone [2]. The present study examined the question of whether healthy stressed adults react in a comparable way. Stress levels were evaluated using the stress subscale of the validated Depression Anxiety Stress Scales (DASS-42) self-assessment tool [3]. The DASS are suitable for recording psychological forms of stress with or without somatic symptoms. The long version (DASS-42) contains 14 items for each of the three subscales (depression, anxiety and stress) that are rated on a four-point scale from “0: Did not apply to me at all” to “3: Applied to me very much, or most of the time”.

Healthy adults with a stress subscale score of > 18 corresponding to at least moderate stress and serum magnesium concentrations of 0.45 to 0.85 mmol/l were investigated in this Phase IV study. 264 patients were randomly assigned to one of the two study arms and received either a magnesium-vitamin B6 combination (daily dose 300 mg magnesium and 30 mg pyridoxine) or magnesium alone (daily dose 300 mg magnesium). Participants received six coated tablets per day, two to be taken at the time of each of the three main meals.

The distribution of subjects across the DASS-42 stress subscale levels in each treatment arm was similar, with approx. 60%

in each group classified as having severe or extremely severe stress. 130 patients in each study arm completed the study and were included in the evaluation. The study endpoints were the change in DASS-42 stress subscale scores from the start of treatment to week 4 and then up to the primary endpoint in week 8 and the incidence of adverse drug reactions (ADRs).

In the modified intention-to-treat analysis (N = 264 subjects) both treatment arms showed a considerable reduction in the DASS-42 stress subscale score from the start of treatment to week 8 (Mg-vitamin B6 combination 44.9% versus Mg 42.4%). The difference between the two arms was not statistically significant ( $p > 0.05$ ). However, when the subgroup of 162 adults with severe to extremely severe stress (DASS-42 stress subscale score  $> 25$ ) was analysed, then a 24% larger and hence significant improvement in the magnesium-vitamin B6 study arm compared with magnesium alone was observed in week 8 ( $p = 0.0203$ ).

With regard to ADRs, 12.1% of the subjects treated with a magnesium-vitamin B6 combination and 17.4% of those treated with magnesium alone reported side effects possibly related to the treatment. The most frequent was diarrhoea, which was reported by 4.5% of subjects in the magnesium-vitamin B6 combination arm and 7.6% in the magnesium-only arm. One subject in the magnesium-only arm had gastroenteritis. All subjects recovered from the side effects.

## Summary

These results suggest that oral magnesium supplementation relieves stress in healthy adults with hypomagnesaemia. At normal levels of stress, the addition of vitamin B6 to magnesium was not superior to supplementation with

magnesium alone. In the case of patients with severe to extremely severe stress, this study demonstrated a clinical benefit for the combination of magnesium and vitamin B6. The benefits of the observed reduction in stress might – if they were maintained over a long period, have considerable positive effects on the physical and mental health of those affected.

## Literature

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