Nutrivigilance

Seizures associated with consumption of a food supplement containing melatonin designed to promote sleep

ANSES received a report of life-threatening seizures following consumption of the food supplement Novanuit® Triple Action by a man with no history of epilepsy. Causality of the product was deemed to be very likely in this case. Given the severity of the adverse effect described, ANSES is bringing this case to the attention of the general public and healthcare professionals. It recommends paying close attention to the adverse effects that could occur following consumption of any product containing melatonin, and calls for such effects to be reported to the national nutrivigilance scheme.

As part of the nutrivigilance scheme that it has been running since 2009, ANSES received a report of seizures potentially associated with consumption of the food supplement Novanuit® Triple Action marketed by Sanofi. This product, designed to promote sleep, contains melatonin, California poppy (Eschscholzia californica), lemon balm (Melissa officinalis), passion flower (Passiflora incarnata) and vitamin B6.

The alert

The report concerned a 47-year-old man with no history of epilepsy. He was not taking any long-term medication, and only drank alcohol at weekends. In 2020, while suffering from sleep disorders, he began to take the food supplement Novanuit® Triple Action. After nine days of use, he experienced involuntary contractions of the muscles around the eye, along with dizziness, which soon disappeared without treatment. On the tenth day of taking the product, he had a seizure that caused him to fall. The medical examination, which included a brain scan, Holter heart rhythm monitor, electroencephalogram (EEG), electrocardiogram (ECG), cardiac ultrasound and computed tomography angiogram, found nothing unusual and ruled out a recent ischemic or haemorrhagic stroke. The biological test results did not reveal any abnormalities. The patient returned home and continued taking the food supplement until the sixteenth day, when a new seizure occurred. In the hospital emergency room, the patient’s brain imaging results (MRI) were unremarkable, the clinical and biological examinations showed no particular anomaly, the blood alcohol level was zero and the ECG was normal.

He stopped taking Novanuit® Triple Action and began an anti-epileptic treatment after consultation with a neurologist. The neurologist prescribed neurological monitoring and the continuation of the anti-epileptic treatment. The subsequent outcome was favourable and the patient did not experience any further seizures under treatment.

Link with use of the food supplement

The causality of the food supplement in the occurrence of the seizures was assessed using the method developed for the nutrivigilance scheme [1]. Causality takes four components into account: the onset time, the outcome after discontinuing the product, whether or not the effect reappears upon reintroduction, and the absence of any other possible explanation for the observed adverse effect. For the food supplement Novanuit® Triple Action, the time to onset of the effect was considered “compatible”. The outcome was described as “suggestive”, although specific treatment was initiated because this adverse effect was life threatening to the patient.

2. The Holter device records heart rate and rhythm over an extended period of time.
3. Clogged vessel.
4. Ruptured vessel.
Reintroduction would have been considered "positive" if the effect had reappeared after each intake and "negative" if it had not. As the seizures did not occur systematically each time the product was taken, it was not possible to reach a conclusion on the reintroduction component; it was therefore classified as "inconclusive". The aetiological investigation ruled out the most common causes of seizures through tests of neurological, cardiac, hepatic and renal function and biological analyses. The Novanuit® Triple Action product was therefore deemed very likely responsible for the occurrence of the seizures, i.e. I4 on a scale ranging from I0 (excluded) to I4 (very likely).

Have similar cases been described in the scientific literature?

The literature search focused on possible human cases of seizures and epilepsy associated with the active ingredients of the food supplement Novanuit® Triple Action, namely California poppy (*Eschscholzia californica*), lemon balm (*Melissa officinalis*), passion flower (*Passiflora incarnata*), vitamin B6 and melatonin.

The available studies on melatonin's influence on the onset of epileptic seizures are contradictory, with some reporting an anticonvulsant action while others showed a proconvulsant effect. In addition, they were conducted with doses ranging from 1.5 mg/d to 10 mg/d. Novanuit® Triple Action contains 1 mg of melatonin per tablet.

The literature search did not identify any studies or clinical cases reporting seizures related to the other active ingredients in the food supplement Novanuit® Triple Action.

Have similar cases been reported to the nutrivigilance scheme?

To date, no other similar cases concerning the food supplement Novanuit® Triple Action have been reported to the nutrivigilance scheme.

Conclusions and recommendations

The causality of the food supplement Novanuit® Triple Action in the occurrence of seizures in a patient with no history of epilepsy was deemed highly likely. One of its ingredients, melatonin, has already been the subject of an opinion by ANSES [2]. This opinion advised against the consumption of food supplements containing melatonin by people suffering from epilepsy without seeking the advice of their doctor.

In general, ANSES recommends that consumers of food supplements:

- notify a healthcare professional of any adverse effect occurring after consumption;
- comply with the conditions of use specified by the manufacturer;
- avoid taking food supplements on a multiple, prolonged or repeated basis throughout the year without having sought the advice of a healthcare professional (doctor, dietician, etc.);
- exercise great vigilance with regard to improper claims;
- exercise great vigilance regarding the purchase of products sold through alternative channels (internet, gyms, etc.) and without personalised advice from a healthcare professional.

ANSES also reminds healthcare professionals that they must report to its nutrivigilance scheme any cases of adverse effects they suspect are associated with the consumption of food supplements.

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References:

[1]. ANSES. 2019. "Revised ANSES opinion of 10 July 2019 on updating the method for determining causality in reports of adverse effects in nutrivigilance".