SAFETY OF FOOD SUPPLEMENTS CONTAINING ALFA LIPOIC ACID: CLUES FROM THE ANALYSIS OF ADVERSE EVENTS SUBMITTED TO THE ITALIAN SURVEILLANCE SYSTEM

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Background. Alpha lipoic acid (ALA) plays a role in mitochondrial reactions, in particular as protector against reactive-oxygen species (ROS)-induced mitochondrial dysfunction (Packer et al., 1995). Dietary supplements containing ALA are currently in clinical use for the treatment of diabetic neuropathy, although their use is expanding in different diseases as supportive therapy (e.g., osteoporosis) (Koufaki et al., 2014). However, their safety profile is still incompletely characterized.

Aim. The aim of this study was to describe suspected adverse reactions (ARs) associated with food supplements containing ALA.

Methods. Spontaneous reports of suspected ARs to ALA were collected from the Italian Surveillance System of suspected ARs to Natural Health Products, from April 2002 to March 2017. The analysis and maintenance of this database is coordinated by the National Institute of Health, in collaboration with the Italian Medicines Agency and the Ministry of Health. Diagnosis are coded according to the Medical Dictionary for Regulatory Activities (MedDRA version 4). For serious cases, follow-up of patients is obtained from the hospital physician.

Results. Over the 15-year period, 85 reports concerning 160 suspected ARs to ALA food supplements were collected (5% out of 1589 total ARs entered in the database). The mean age was 60 years, and 69% of reports were related to females. ARs mainly consisted of symptoms related to allergy and/or hypersensitivity reactions (92 reactions, 58%), including various types of urticaria, rash and oedema. In the majority of cases a therapy was started, mainly corticosteroid and/or antihistamines. Hypoglycaemia occurred in 13 patients (8%); in eight of these cases presenting with hypoglycaemia, autoimmune insulin syndrome (also known as Hirata disease) was diagnosed. Thirty-three patients (39%) were hospitalised; in 41 (48%) concomitant drugs were present. Dechallenge was positive in 51 cases; rechallenge in 7 cases. The time-to-onset was 1 day in 35 cases, and within 1 week in 52 patients. Neuropathic pain, carpal tunnel syndrome and low back pain were the main reasons for use.

Discussion and conclusions. ALA food supplements were associated with a non-negligible proportion of ARs in Italy, represented by clinically-significant episodes of hypoglycaemia and Hirata syndrome (Gullo et al., 2014), as well as hypersensitivity reactions requiring hospitalization and/or drug interruption with medical management. In Italy, sales data of food supplements are not easily available for regulatory and research purposes, thus reporting rates cannot be calculated. The variegate uses, some of which without proven efficacy, require careful consideration by clinicians and pharmacists, who should remind consumers of potential risks, especially considering that ALA may be used as a self-medication. Continuous monitoring of food supplements safety is warranted.

Packer et al. (1995) Free Radic Biol Med. 19, 227-50

Koufaki et al. (2014) Expert Opin Ther Pat. 24, 993-1005

Gullo et al. (2014) Clin Endocrinol (Oxf). 81, 204-9