LETTER TO THE EDITOR

THIAMINE ADMINISTRATION IN ALCOHOL-DEPENDENT PATIENTS

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Thiamine (vitamin B1) is a water-soluble vitamin that is involved in the metabolism of glucose and lipids as well as in the production of glucose-derived neurotransmitters (see Cook et al., 1998). Its deficiency leads to a variety of neurological and cardiovascular symptoms and signs. Early symptoms may include fatigue, weakness and emotional disturbance, whereas prolonged gradual deficiency may lead to a form of polyneuritis (known as dry beriberi), cardiac failure or peripheral oedema (wet beriberi) (Thomson, 2000).

Severe thiamine deficiency (TD) may result in the development of Wernicke’s encephalopathy (WE). The classical signs of WE are ocular motility disorders (nystagmus, ophthalmoplegia), ataxia and mental changes (confusion, drowsiness, obtundation, clouding of consciousness, pre-coma and coma), although minor episodes of ‘subclinical’ encephalopathies are frequent (Reuler et al., 1985). An appropriate treatment may correct most of these abnormalities; in contrast, the lack of a diagnosis of WE may result in serious consequences (Reuler et al., 1985). When patients with WE were inappropriately treated with low doses of thiamine, mortality rates averaged ~20% and Korsakoff’s psychosis (KP) developed in ~85% of survivors (Thomson et al., 2002).

KP is characterized by anterograde and retrograde amnesia, disorientation, poor recall and impairment of recent memory coupled with confabulation: approximately 25% of patients who are affected by KP require long-term institutionalization (Reuler et al., 1985). Because of the close relationship between WE and KP, these two disorders are usually termed as the Wernicke–Korsakoff syndrome (WKS) and considered as a single disease (Thomson, 2000).

Alcoholism is the most frequent cause of TD in Western countries and the prevalence of WKS is 8–10 times higher in alcoholics than in the general population (12.5 and 0.8%, respectively) (Reuler et al., 1985). WKS is a clinical emergency that requires the rapid administration of high doses of thiamine; however, clear guidelines have not been provided in terms of the required dosage and the duration of treatment in alcoholic patients (Day et al., 2004). The present letter is intended to provide some element of discussion on thiamine dosage, route of administration and duration of treatment in alcoholics.

The daily requirement of thiamine is ~1.5 mg; on deprivation, TD occurs within 2–3 weeks (Thomson, 2000). In normal subjects, the absorption of thiamine does not exceed 4.5 mg even when large doses of thiamine are administered orally (Thomson, 2000). In alcoholics, the oral absorption of thiamine is extremely variable, with some patients showing little or even no absorption (Thomson, 2000). About 80% of alcoholics develop TD as the likely consequence of inadequate nutritional intake, reduced absorption and impaired utilization of thiamine (Singleton and Martin, 2001). In malnourished alcoholics, maximal absorption of thiamine after a single oral dose is only 0.8 mg or less when alcohol has been consumed shortly beforehand (Cook et al., 1998).

Parenteral administration of thiamine is unanimously considered the route of choice to replenish thiamine stores as rapidly as possible (Reuler et al., 1985). However, physicians apparently seldom prescribe parenteral administration of thiamine. As an example, a recent retrospective study found that only one-fifth of patients, who were hospitalized for head injury and at risk for TD, received thiamine (Ferguson et al., 2000). Among the latter, 75% were given thiamine orally for a short period and at low doses. Physicians tend to be concerned about possible adverse reactions such as anaphylaxis, dyspnoea/bronchospasm and rash/flushing (Cook et al., 1998) following parenteral administration. Nevertheless, it should be noted that these reactions have been found to be 10–100 times less frequent than those secondary to penicillin administration (Cook et al., 1998). Moreover, a slow infusion of thiamine (i.e. over a 30-min period) appears to reduce the possible occurrence of adverse reactions (Thomson et al., 2002).

Some recent papers by Cook, Thomson and colleagues (Cook and Thomson, 1997, Thomson and Cook, 1997, Cook et al., 1998, Hope et al., 1999, Cook, 2000, Thomson, 2000, Thomson et al., 2002) describe in detail both the prophylaxis and the treatment regimen of WKS in terms of thiamine dosage and duration of treatment. Specifically, the prophylactic treatment for at-risk patients consists of an intramuscular administration of 250 mg thiamine (plus other B vitamins and ascorbic acid), once daily for 3–5 consecutive days. Cases of established WE should be treated empirically with a minimum of 500 mg thiamine (plus other B vitamins and ascorbic acid), i.v. or i.m., three times daily, for at least 2 days. In patients with ataxia, polyneuritis, confusion or memory disturbance, the treatment should be continued until clinical improvement is registered.

Adherence to the above suggestions requires appropriate pharmaceutical preparations. In Italy, thiamine content in
parenteral preparations that are available presently varies from 2 to 100 mg per ampoule. According to the above-mentioned indications for WKS treatment, an Italian patient should receive, as a minimum, the improbable number of 15 ampoules per day.

It is highly predictable that the lack of an adequate preparation, along with the lack of clear guidelines on dosage and duration of treatment, will continue to result in the prescription of a quantity of thiamine that does not concur with those deemed to be effective.

REFERENCES


