LETTERS TO THE EDITOR

BNF Recommendations for the Treatment of Wernicke’s Encephalopathy: Lost in Translation?

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We have written extensively about the diagnosis and treatment of Wernicke’s encephalopathy (Thomson et al., 2008, 2009) highlighting the need for prompt treatment with intravenous thiamine. We are concerned that recent British National Formulary (BNF) recommendations are not clearly written and risk causing confusion and delay in the treatment of patients with this disorder, which is potentially reversible if treated appropriately.

Recent NICE clinical guidelines on alcohol-use disorders (CG 100 and 115, NICE 2010, 2011) set out clear recommendations regarding the use of thiamine in the urgent treatment of suspected Wernicke’s encephalopathy.

Clinical Guideline 100 recommended that thiamine be given in doses ‘toward the upper end of the BNF range’ and that it should be given ‘parenterally’. This NICE guideline was published in June 2010, so it is likely that it was referring to what was written in BNF 58 (September 2009). BNF 58 did not specifically outline the treatment of suspected Wernicke’s encephalopathy. It recommended that Pabrinex intravenous high potency injection, 2–3 pairs every 8 h, be used in the following situation:

Coma or delirium from alcohol, from opioids, or from barbiturates, collapse following narcosis.

No indication was given in BNF 58 as to the duration of treatment, although NICE Clinical Guideline 100 specified a minimum of 5 days (CG 100, 1.2.1.4).

BNF 58 also contained important information in a box, highlighted in blue, on p548 referring to MHRA/CHM Advice (September 2007), concerning potentially serious allergic reactions that rarely occur during or shortly after parenteral administration of thiamine, specifically that this ‘should not preclude the use of parenteral thiamine in patients where this route of administration is required, particularly in patients at risk of Wernicke–Korsakoff syndrome where treatment with thiamine is essential’.

Since September 2011 the BNF guidance (BNF 62 and 63) for the treatment of Wernicke’s encephalopathy with thiamine is more specific and is as follows:

by intravenous infusion of I/V High Potency or by deep intramuscular injection into the gluteal muscle of I/M High Potency, 2 pairs 3 times daily for 2 days; if no response discontinue; if symptoms resolve after 2 days give 1 pair daily for 5 days or for as long as improvement continues.

The evidence would indicate that intramuscular thiamine treatment may not, in all patients, provide an adequate circulating level of thiamine to traverse the blood brain barrier and correct the dangerously low availability of thiamine in the brain cells of alcohol-dependent patients (Thomson, 2000; Thomson and Marshall, 2006). In our view the treatment of suspected Wernicke’s encephalopathy should be as set out below in Table 1.

Even if the intramuscular route could guarantee adequate replenishment of thiamine, such high volume and painful injections into gluteal muscles of malnourished alcohol-dependent patients are neither possible nor practical.

The safety profile of parenteral B vitamin preparations compares favourably with commonly used drugs such as Penicillin (Wrenn and Slovis, 1992; Cook et al., 1998).

The dose required to treat Wernicke’s encephalopathy is not based on randomized clinical trials because these are not ethically possible (Cook et al., 1998; Royal College of Physicians, 2001; Lingford-Hughes et al., 2004, 2012; Sechi and Serra, 2007; Thomson et al., 2008, 2012; BNF, 2009; Day et al., 2009). The NICE Clinical Guideline 100 ‘adopted a consensus-based approach to the review of the literature, synthesizing previously published narrative reviews to assist in development of the recommendations for this guideline’ (NICE, CG 100, 2010).

We are concerned that the BNF changed its recommendations for the treatment of Wernicke’s encephalopathy after the publication of the NICE Clinical Guidelines to include I/M High Potency thiamine. This recommendation is not based on scientific evidence. Clinicians suspecting Wernicke’s encephalopathy in a patient should treat it as an emergency and provide optimum intravenous treatment in order to avoid permanent brain damage (Kopelman et al., 2009; Thomson et al., 2012).

In order to optimize guidelines for the treatment of acute Wernicke’s encephalopathy, there needs to be an informed debate on a number of issues, including the use of I/M and I/V thiamine, formulations that include other vitamins and mineral products, and who should have the responsibility for prescribing and administering these products. Once general guidelines have been agreed there needs to be a consensus on how these should be written so that they can be readily implemented without confusion by the average doctor/clinician. The

<table>
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<tr>
<th>Table 1. The immediate treatment of Wernicke’s encephalopathy</th>
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<tr>
<td>• Thiamine 500 mg IV t.i.d. for 2–3 days and 250 mg daily for the</td>
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<td>next 3–5 days given over 30 min diluted in 50–100 ml of normal saline</td>
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<tr>
<td>• Thiamine 100 mg p.o. t.i.d. for the rest of the hospital stay and during outpatient treatment. Absorption will be &lt;4.5 mg daily (10)</td>
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<tr>
<td>• Multivitamins IV</td>
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<td>• Replace magnesium: average deficit 2 mEq/Kg</td>
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<td>- Replace as outlined by Flink (1969) (33): check renal impairment</td>
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<tr>
<td>• Replace fluid and electrolyte losses: monitor electrolytes, blood pressure and renal function</td>
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Reproduced with permission from Thomson et al. (2009).
prescribing of thiamine/Pabrinex for acute Wernicke’s encephalopathy is currently ambiguous and constantly changing, sometimes leading to unfortunate consequences for patients. We would recommend that prescribing changes should be avoided unless prompted by new scientific evidence.

We appreciate the comments of two anonymous referees and would welcome further debate in these columns.

REFERENCES


BNF Response to ‘BNF Recommendations for the Treatment of Wernicke’s Encephalopathy: Lost in Translation?’

BNF Editorial Team

The doses of thiamine in the BNF were reviewed following the publication of the NICE guidelines (CG 100) on Alcohol-use Disorders (June 2010); the Pabrinex® Summaries of Product Characteristics (SPCs), The Maudsley Prescribing Guidelines in Psychiatry 10th edition (2009) and other sources were taken into account. The following change in dose (under Pabrinex®, made for BNF 61 (March 2011), was approved by our clinical expert advisers and agreed by the BNF’s Joint Formulary Committee:

‘Treatment of Wernicke’s encephalopathy, by intravenous infusion of I/V High Potency or by deep intramuscular injection into the gluteal muscle of IM High Potency, 2 pairs 3 times daily for 2 days; if no response, discontinue; if symptoms resolve after 2 days, give 1 pair once daily for 5 days or for as long as improvement continues.’

For BNF 64 (September 2012), in response to comments from the manufacturer of Pabrinex®, and in line with the latest Maudsley guidelines (11th edition (2012)), the dose was amended to remove mention of the use of intramuscular Pabrinex® at the outset of treatment:

‘Treatment of Wernicke’s encephalopathy, by intravenous infusion of I/V High Potency, 2–3 pairs 3 times daily for 2 days; if no response, discontinue; if symptoms respond after 2 days, give by intravenous infusion of I/V High Potency or by deep intramuscular injection into the gluteal muscle of IM High Potency, 1 pair once daily for 5 days or for as long as improvement continues’.

We are aware of that there is a lack of randomized controlled trials to guide recommendations. The BNF sometimes deviates from doses in the product literature in order to give doses that reflect clinical practice.

Patients at high risk of developing Wernicke’s encephalopathy are discussed in BNF section 4.10.1 (along with other aspects of treating alcohol dependence). The need to follow parenteral thiamine treatment with oral thiamine is mentioned in BNF section 4.10.1 and in section 9.6.2.

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Baclofen and Risperidone Association Increases Dramatically Triglycerides Level

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Baclofen, a centrally acting muscle relaxant Gaba-B agonist drug, is used for many years in the treatment of spasticity.