PE1408/S

Scottish Parliament - Petition: PE 1408

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The Pernicious Anaemia Society

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We thank you for advising us of the resumption of our petition, following the issue last month of the awaited updated guidelines on the Diagnosis & Treatment of Cobalamin and Folate Disorders, as prepared by the British Committee for Standards in Haematology (BCSH). We have had an opportunity to plough through the wealth of information the document contains and the BCSH are to be commended for the degree of attention given to these disorders and, in particular, pernicious anaemia (PA).

We are pleased to say that we feel real progress has been made, and specifically that definite problems have finally been admitted by the BCSH in the way this condition has been diagnosed and treated to date. We are also encouraged by some of the recommendations made and are now focussed on ensuring they are implemented in such a way as to provide patients with the confidence of knowing they can challenge their treatment when it fails to correspond to these recommendations.

At the moment, diagnosis and treatment of PA is extremely haphazard with every variation being seen in the way many of our members are being treated. This leads to confusion, disappointment and real despair when patients report such variance between GP surgeries.

We detail below the specific points made in the new guidelines which we feel are of most relevance:

1. *"The clinical picture is the most important factor in assessing the significance of test results assessing cobalamin status since there is no 'gold standard' test to define deficiency . . . In the presence of discordance between the test result and strong clinical features of deficiency, treatment should not be delayed to avoid neurological impairment."*

This is one of the most crucial aspects of treatment. Symptoms must no longer continue to be overlooked in favour of laboratory results. We have recently had several members report that their injections had been stopped solely based on their serum levels, and their symptoms completely disregarded. This is despite the existing guidance, which has also been reiterated in the updated guidelines, specifically saying:

> *"No further testing for cobalamin levels is required."*

2. *"Neurological presentation . . . may occur in the absence of haematological changes, and early treatment is essential to avoid permanent neurological disability . . . Furthermore, patients with strong clinical features of cobalamin deficiency may have serum cobalamin levels which lie within the reference range . . . The absence of a raised MCV cannot be used to exclude the need for cobalamin testing since neurological impairment occurs with a normal MCV in 25% of cases."*

These are common problem areas for our members. It is often reported that treatment has been refused because *"there is no macrocytic anaemia"* or the patient's serum B12 level is *"normal."* Injections may also be withdrawn once a patient's B12 returns to as little as low normal.

3. Re the serum cobalamin test: *"it lacks the specificity and sensitivity required of a robust diagnostic test . . . Some assays may give false normal results in sera with high titre anti-intrinsic factor antibodies."*

Re Holotranscobalamin (HoloTC) test: *“an immunoassay for this fraction is now available . . .*

Recommendation: “*Holotranscobalamin is suggested as a suitable assay for assessment of cobalamin status in a routine diagnostic laboratory in the future”*

It is a relief that the failings of the serum B12 test has now been recognized and a possible replacement test suggested.

4. *“ . . . the finding of a negative intrinsic factor antibody assay does not therefore rule out pernicious anaemia . . . Patients negative for intrinsic factor antibody, with no other causes of deficiency, may still have pernicious anaemia and should be treated as anti-intrinsic factor antibody negative pernicious anaemia. Lifelong therapy should be continued in the presence of an objective clinical response . . . All patients with anaemia, neuropathy or glossitis, and suspected of having pernicious anaemia, should be tested for anti-intrinsic factor antibody regardless of cobalamin levels.”*

Maybe we can now be hopeful that patients will not have their symptoms and low cobalamin level trivialized by the lack of IF antibodies, and have treatment refused on the strength of it. Equally, this test should still be done solely based on symptoms, rather than cobalamin level. Again, it is wonderful to see confirmation that therapy be *‘lifelong’* once an objective response is evident, since we encounter patients whose therapy is stopped for no valid reason, such as their serum level is now normal.

Perhaps we could also add that it can, on occasions, take considerably longer than a fortnight for someone to respond to initial loading injections and it may therefore be inappropriate to assume they are not going to respond. Realistically, the only way to manage this is to consider allowing any patient in this situation an extended course of loading injections if they have failed to notice any obvious improvement at the end of the recommended six injections within a two-week period.

5. *“ . . . a group of disorders characterised by gastric hypochlorhydria due to age-related gastric atrophy or secondary to drugs such as the proton pump inhibitors.”*

This is a widespread problem, with a high percentage of members being prescribed acid-suppressant medicine for indigestion without proper investigation to first determine their gastric acid level. In the presence of undiagnosed hypochlorhydria, it is obviously the worst medicine they could then be given. It is not unusual for these members to obtain significantly more digestive relief by making their own decision to stop the acid-suppressant and instead adding in a substitute for hydrochloric acid, in the form of Betaine HCL, or even simply drinking fresh lemon juice in hot water. Betaine HCL is not available on the NHS and it is alarming that patients are being driven out of desperation to experiment with a potentially harmful substance just to gain relief from the misery of constant indigestion.

Finally, I’m sure you would be surprised if we did not have some negative comments and, fortunately, these are very few. One statement in particular though cannot be left unchallenged.

“A Cochrane review on the use of oral cobalamin suggests it is as effective as intramuscular B12, with benefit of fewer visits to health centres and reduced discomfort of injections . . . High dose oral cobalamin would be a reasonable alternative as maintenance in patients unable to tolerate IM injections provided there is good compliance with treatment. On the other hand, some patients may prefer IM injection therapy in order to assure effective treatment.”

Please be assured that no patient prefers injections! We would all be on high-strength B12 tablets if we found they provided effective control of our PA. Many of our members have tried them, or supplement in addition to their injections, but we cannot recall anyone tell us they could manage

on tablets (or the other supplemental forms) alone, and for many others they have no obvious effect, other than to elevate their serum level, which increases the chance that their doctor will stop the injections too!

We also see no mention made of the many patients who cannot manage on even 2-monthly injections, and these form the vast majority of our members. As one myself who needs three injections a week on a permanent basis, this matter is of great concern to me and is the main focus of this petition. What recommendation is being made for this large group of patients? We realise it is impractical to expect both the GP surgery and the patient to have such frequent injections administered by the practice nurse, but here is where another major change can be considered. At present, B12 injections are given intramuscularly but quite a few members who have had to self-inject without tuition lack the confidence to inject into muscle and have chosen the subcutaneous (SC) route instead (the same method as diabetics use). Most of them find SC injections equally effective and it may be time to approach the manufacturers of injectable cobalamin to investigate having the preparation licensed for SC use too. This would then make it easier, safer and much more cost-effective to teach patients who need very frequent injections to manage them themselves, as I have done for the last five years.

We hope the above comments will be taken into consideration and, in summary, would be very interested to learn what now happens to these BSCH guidelines and recommendations. Are they to be submitted to the department which oversees the British National Formulary (BNF) and, if so, are they under any obligation to accept them and incorporate them into the BNF in due course?

Thank you once again for all the care taken to produce such an in-depth and promising document,

Yours faithfully,

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