

Original Article

Whole blood viscosity determination in diabetes management: perspective in practice

Ezekiel Uba Nwose, Eugene Butkowski, Nathan Cann
Institute of Clinical Pathology and Medical Research, South West Pathology Service
Smollett Albury NSW, Australia.

Background: Antiplatelet and antioxidant nutritional therapies (ANT) are commonly used in diabetes management. Guidelines recommend identifying deficiencies of antioxidant vitamins and condition of no contraindication for nutritional and antiplatelet respectively. **Aim:** To determine whether the guidelines recommendations for diabetes patients to be assessed for (1) antioxidant vitamins' deficiencies and/or (2) whole blood viscosity (WBV) as indication of no antiplatelet contraindication. **Materials and Method:** Laboratory records were audited. 10,342 de-identified glycaemic index (HbA_{1c}) requests received in 2008 were sorted into three groups based on level of control. (1) Poor (n = 1962, HbA_{1c} ≥ 8.1); (2) Good (n = 5616, HbA_{1c} = 6.0 – 8.0) and (3) Excellent (n = 2764, HbA_{1c} ≤ 5.9). All 57 cases with haematocrit and total protein results in the poor (n=30) and excellent (n=27) groups were selected for calculation and comparison of WBV levels. **Results:** None of the two guidelines' recommendations are being followed as no case was requested for any antioxidant vitamin or WBV. Assessments of the latter show that WBV is statistically significantly lower (p < 0.05) in the group with excellent glycaemic control compared to the group with poor glycaemic control. **Conclusion:** Aspirin is one of the therapies in diabetes management. Its effect is modulated by WBV. ANT is alternative to aspirin and influences WBV. For patients that have full blood count and plasma protein results, WBV can be extrapolated at no extra cost to the health system. There is a need to raise awareness for the recommended guidelines for laboratory monitoring to be followed. (Nwose EU, Butkowski E, Cann N. *North Am J Med Sci* 2009; 1: 110-113).

Keywords: Antiplatelet therapy, antioxidant nutrition, diabetes mellitus, laboratory monitoring, whole blood viscosity.

Correspondence to: Dr. Ezekiel Uba Nwose, PhD, CSci, FIBMS, MAIMS. Institute of Clinical Pathology and Medical Research (ICPMR), South West Pathology Service, 590 Smollett Albury NSW 2640, Australia. Tel.: +61 260581651, Fax: +61 260581680. Email: ezekiel.nwose@gsahs.health.nsw.gov.au

Introduction

Observational studies have consistently supported the rationale for dietary therapy in diabetes mellitus [1]. This is shown in the evidence-based practice for Dietitians [2]. Antioxidants including glutathione (GSH), vitamin C and vitamin E amongst others have been identified as nutritional ingredients necessary for DM management [3]. The risk of harm from pro-oxidant radical forms of antioxidant vitamins is not in doubt. Hence, the Nutritionist's protocol includes assessment, intervention and follow-up for a person with diabetes [2].

The following points about micronutrients are also acknowledged on the guidelines viz:

- Diabetes is synonymous to a state of oxidative stress.
- Optimal amount of antioxidants from nutrition benefits some of diabetes sufferers.
- If deficiencies of antioxidant vitamins are identified, supplementation can be beneficial.
- There is potential toxicity associated with excessive amounts of antioxidant vitamin supplements and is not recommended for diabetes patients if there is no underlying deficiency.

- Routine supplementation of the diet with antioxidants is generally not recommended because of the prevailing controversies.

By inference, nutritional management of diabetes is hinged on oxidative stress and the guideline for discrete prescription of antioxidant supplement is recommended to be based on evidence of deficiencies. That is, the laboratory testing of antioxidant levels.

It is known that vitamin C in the blood is associated with lower endothelial dysfunction and inversely related to fibrinogen concentrations and blood viscosity [4]. This is due to the capacity of vitamin C in maintaining the levels of erythrocyte GSH and vitamin E; and in effect attenuates erythrocyte oxidative stress induced hyperviscosity. It is also known that hyperviscosity in diabetes is strongly influenced by the excellence of glycaemic control [5-7]. Therefore, it is possible that dietary management of diabetes in clinical practice would necessarily involve assessment of vitamins C and E levels as well as whole blood viscosity (WBV).

This article addresses a practical question on evidence-based nutrition practice and anti-platelet therapy guidelines for diabetes management viz: how are discrete choices and the

outcomes of antioxidant vitamins' nutrition and/or contraindication for anti-platelet therapy determined in clinical practice? Given the provisions in the guidelines and the available *in vitro* diagnostic tests for antioxidant vitamins C and E, as well as WBV in clinical practice, the objective of this work was to investigate how many diabetes patients have been tested and followed up for these antioxidants and WBV.

Materials and methods

Ethical considerations and samples: This evaluation of de-identified data was approved by the HREC of South West Pathology Albury. The Pathology Service Albury receives samples from the Albury Base Hospital and clinics from Albury-Wodonga communities. Samples were collected by either nursing staff or medical officers. In some occasions, out-patients come into the laboratory where dedicated phlebotomists collect the blood samples. Samples for vitamins C and E are referred to and tested at the Royal Prince Alfred laboratory Sydney, while WBV could be done on-sight.

It is assumed in this study that a number of patients would consult with dieticians, and that many would be medicating with aspirin. As participants in this study were de-identified and the outcome of this study provides for no direct or immediate personal clinical benefit to be offered, contact with patients was not made.

Data was acquired by downloading 2008 archived results, from the Auslab Laboratory Information System (LIS). All results of blood samples that were tested for glycaemic index (HbA1c) for the period of 1st January to 31st December 2008 were included. 10,342 results were pooled and sorted into three glycaemic control categories on the basis of decisive interpretation. (1) Poor (n = 1962, HbA1c \geq 8.1); (2) Good (n = 5616, HbA1c = 6.0 – 8.0) and (3) Excellent (n = 2764, HbA1c \leq 5.9).

In this study, HbA1c was discretionally used as selection criteria to identify the otherwise de-identified diabetes subjects who are undergoing management and monitoring. Blood glucose level was part of information used in decisive interpretation of the result based on which sorting into groups has been done.

Laboratory records for each case were audited to identify any test for vitamins C, vitamin E and/or WBV. The tabulated results from this patient audit when possible included additional tests results for haematocrit and serum proteins, which were used to determine level of WBV according to the method of Tamariz and his group [8]. A total of 102 cases have results for haematocrit and plasma proteins, of which 57 cases comprising excellent group (n = 30) and poor group (n = 27) were selected for comparison of WBV levels. Statistical analysis was performed using 'Student's *t*-test assuming equal variances'. The hypothesis in the comparison was that hyperviscosity as a physiological

manifestation of diabetes-induced oxidative damage would be less in the excellent group than in the poor group.

Results

None of the cases tested for glycaemic controls in 2008 were tested for any antioxidant vitamin deficiency or WBV. This is evidence of non-observance of the recommended guidelines.

Calculated whole blood viscosity seems close or similar in the two groups. However, analysis of the inter-quartile range shows it is statistically significantly lower ($p < 0.05$) in the group with excellent glycaemic control compared to the group with poor glycaemic control (Table 1).

Table 1 Relative values in the two glycaemic control groups

	Poor	Excellent
N	30	27
Mean	11.93	11.50
Median	11.95	11.43
Standard deviation	1.37	1.30

Discussion

There is evidence that antioxidant vitamins are not being assessed in clinical practice as part of diabetes management. Two probable reasons may be responsible for this observation. Based on a clause in the guidelines that identification is difficult to ascertain [2], it is likely that practitioners are unaware that the laboratory tests are available in clinical practice. This calls for awareness to be raised.

The impression (that identification of deficiencies of antioxidant vitamin level is difficult to ascertain) needs to be corrected, because validated methods for *in vitro* diagnostic use exist for vitamins C and E. In Australia, the tests can be bulk billed by public laboratories, which means the government has provided for it as service to citizens.

The second possible reason for non-observance of the guidelines' recommendations may be the controversy surrounding antioxidant efficacy. However, this reason in the face of increasing awareness for antioxidant nutrition and over-the-counter antioxidant supplements is unhelpful to the patients. This is especially given the acknowledged fact of antioxidant toxicities.

The same concern follows antiplatelet therapies such as aspirin. It was also observed that none of the participants were requested for WBV tests. A major reason may be the fact that the results from scientific research are quickly and erroneously categorized as relevant or irrelevant. Regrettably,

reports on WBV fall into the latter category and attempts to discuss WBV most often turns out a waste of time [9].

WBV was assessed in this study, in patients for whom the haematocrit and plasma proteins were performed for different reason. The result shows that people with poorly controlled glycaemic index have statistically significantly ($p < 0.05$) higher level of viscosity compared to those that are excellently controlled (Table 1). This is expected as those with poor control would be experiencing more hyperglycaemia-induced oxidative stress with consequential reduced erythrocyte deformability and increased WBV [5-7].

This report provides further evidence that WBV is worse in poorly controlled diabetes. It further demonstrates that extrapolation of WBV level from haematocrit and plasma protein values is a valuable alternative method. A major insight to perspective in practice is that WBV can be determined for patients that have full blood count and plasma protein results, but at no extra cost to the health system.

It is known that WBV attenuates the efficacy of antiplatelet agents [10]. The significance is that individuals with low WBV would not benefit from antiplatelet agents. Therefore, until blood rheology problems are duly recognised and monitored in clinical practice, those who suffer from diabetes, but have low WBV will continue to be disadvantaged with antiplatelet therapy. Given that guidelines recommend identifying deficiencies of antioxidant vitamins and condition of no contraindication for nutritional and antiplatelet respectively; and given the result presented in this report; the question is: what is there to lose in laboratory monitoring of WBV in clinical practice? This audit did not seek to establish the reference value of WBV in the diabetes and healthy population. Beside the method adopted in this study, different methods exist for the determination of WBV and associated with this is different normal values. Perhaps, what needs to be established is what should be regarded as a reference values. This is especially important given the closeness in central values for the poorly and excellently controlled groups.

Conclusions

Clinical algorithms have been suggested to guide the use of dietary therapy using laboratory measures [3, 11]. However, the suggestions neither include the identifiable antioxidants, nor the index of effective pathophysiological haemorheology. Thus, the crucial factor of oxidative stress being managed by antioxidant nutrition is being overlooked. Furthermore, it is known that anticoagulants are not safe because of associated bleeding complications and treatment with antiplatelet as a substitute does not offer better safety. Aspirin is still one of the main therapies in diabetes management and its effect is modulated by WBV, which in turn is influenced by antioxidant nutritional therapy. Utilizing the available laboratory tests for antioxidant vitamins status in patients during dietician's assessment would be keeping with

guidelines. Determining WBV levels would be invaluable to optimize antioxidant nutrition outcomes, in addition to keeping with the guidelines for antiplatelet therapy.

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