COLLECTION TUBES CONTAINING CITRATE STABILISER OVER-ESTIMATE PLASMA GLUCOSE

Rebekah Carey a, Helen Lunt b,c, Helen F. Heenan b, Christopher M A Frampton c, Christopher M Florkowski b,d.

a School of Medicine, University of Otago Christchurch, b Diabetes Centre, Christchurch Hospital, c Department of Medicine, University of Otago Christchurch, d Canterbury Health Laboratories, Canterbury District Health Board, Christchurch, New Zealand.

Aims and objectives: Blood collection tubes containing citrate lower pH, thereby inhibiting glycolysis. In Europe there is increased uptake of commercially available citrate tubes, aimed at minimising pre-analytical glucose loss associated with delayed processing (>30 minutes) of standard collection tubes. However, studies in healthy volunteers suggest that citrate introduces a positive bias in measured glucose. We measured this bias across a wider range of plasma glucose values. Samples collected into lithium-heparin tubes underwent immediate cooling and rapid plasma separation and were used as the primary comparator.

Methods: Participants with and without diabetes each donated nine tubes of blood, collected into lithium-heparin, or fluoride, or fluoride-citrate tubes. Plasma was separated immediately (‘time zero’) and at 2 and 24 hours. Preparation of the ‘time zero’ lithium-heparin and fluoride samples was optimised by processing these samples under cooled conditions. The remaining samples were prepared at room temperature. Plasma glucose was analysed in the routine clinical laboratory using the hexokinase method.

Results: Median plasma glucose for the 50 participants was 7.1 mmol/L (range 3.1-21.5). At ‘time zero’, fluoride-citrate glucose was 0.37 mmol/L (95% CI 0.26-0.48) higher than lithium-heparin glucose and 0.29 mmol/L (95% CI 0.21-0.36) higher than glucose from fluoride tubes. Following delayed plasma separation at 24 hours, glucose loss from the lithium heparin tubes averaged 0.2 mmol.L⁻¹.hr⁻¹. In contrast, the citrate tubes showed minimal glucose loss over 24 hours.

Conclusions: Citric acid stabilises glycolysis but causes a positive bias across a range of plasma glucose values, compared to blood collected into conventional tubes under cooled conditions. The magnitude of the positive bias seen with the fluoride-citrate tubes is unlikely to be due solely to the differential glucose stabilisation rates of acid, which is almost instantaneous, compared to cooling of blood, which takes several minutes.

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Our series of studies related to the 2015 NZSSD grant aimed to determine whether we should consider the introduction of citrate blood collection tubes into New Zealand. These collection tubes stabilise whole blood glucose prior to the laboratory measurement of plasma glucose. Local results mirror those of other recent publications, in that the citrate tubes tend to make glucose ‘read’ very slightly on the high side, when compared to conventional methods of sample collection. This is likely
to have the most impact in the diagnosis of GDM (gestational diabetes) using the oral glucose tolerance test and would cause an increase in the percentage of women being diagnosed with GDM.

At the moment there is also some uncertainty about the availability of the various different types of citrate collection tubes, both in New Zealand and also internationally. Whilst we would not currently recommend a change from fluoride to citrate tubes, our series of studies has highlighted the fact that if you want accurate plasma glucose values from standard fluoride tubes, then samples need to be analysed as quickly as possible after collection (IE short venesection-to-analyser times).

Helen Lunt, Christchurch Hospital, 14 October 2016