INTRODUCTION

The calculation of serum osmolality from measured analytes, when used in conjunction with the measured osmolality, is a useful tool in determining the likelihood of ingestion of low molecular weight substances. The difference between the calculation (in mmol/L) and the measurement (in mOsm/kg) of osmolality is the Osmolar Gap. With allowance for the uncertainty of measurement it represents the contribution of analytes not measured which may include poisons such as methanol or ethylene glycol.

When it comes to which algorithm to use for the osmolality calculation there is little consensus. A review by Fazekas et al. described 36 variations of varying complexity. The three most commonly used calculations in the clinical chemistry laboratory are those of:

- **Bhagat et al.**: 1.89xNa + 1.03xUrea + 1.08xGlucose + 7.45
- **Weisberg**: 1.87xNa + urea + glucose + 8.55
- **the simple calculation**: 2xNa + urea + glucose.

In this study we determined reference intervals for these three calculations using data from the Aussie Normals study. This was a large scale “a priori” study of almost 1800 healthy individuals (ages 20 to 87 years) from the Canberra region with the intention of developing reference intervals with over 80 analytes measured. Patients were excluded based on known disease states (e.g. renal or cardiovascular disease) and some medications. The sodium, potassium, urea and glucose concentrations were measured using the Abbott Architect ci8200.

We also performed a small comparison between the calculated osmolality and the measured osmolality (by freezing point depression) using 15 patient samples. Samples for this study were selected based on their varying sodium, glucose and urea concentrations.

METHODS

From the complete Aussie Normals cohort we excluded those samples where the glucose concentration had not been measured - which resulted in 796 samples (417 F and 379 M). From these we calculated osmolality using the three common formulas.

Reference intervals were calculated using Shapiro-Wik. Six low osmolality results were excluded using a 3.5 SD exclusion rule.

To compare the calculated osmolality with the measured osmolality (Advanced Instruments Osmometer) we selected 15 patients with varying sodium (mmol/L), urea (mmol/L) and glucose (mmol/L) concentrations.

RESULT

Using the Shapiro-Wilk test to determine the reference interval for the simple calculation yielded an interval of 281 to 299 mmol/L, the Weisberg (1975) calculation 272 to 288 mmol/L and the Bhagat et al (1984) calculation a RI of 280 to 297 mmol/L.

Compared to the measured osmolality the Deming regression fit for the simple calculation was 0.92x + 18.3, for the Weisberg Calculation it was 0.87x + 24.4 and for the Bhagat et al calculation it was 0.88x + 22.2.

CONCLUSION

The Bhagat et al (280 to 297 mmol/L) and the simple calculation (281 to 299 mmol/L) had similar reference intervals whilst that of the Weisberg calculation was considerably lower (272 to 289 mmol/L). The study compared well with our current reference range (using the Bhagat et al calculation) of 280 to 300 mmol/L. It is important to note there is a considerable uncertainty of measurement of approximately ± 5 mmol/L. All three calculation formulas underestimated the actual osmolality.

In our limited comparison of the three calculations, with the measured osmolality the simple calculation was the closest. At the recent AACB/RCPA Harmonisation Meeting (2015) a consensus was reached to use the simple calculation and this study has demonstrated that there would be little effect from such a change.