Interference of creatinine measurement in CAPD fluid is dependent on glucose and creatinine concentrations

T. W. L. Mak¹, C. K. Cheung¹, C. M. F. Cheung¹, C. B. Leung², C. W. K. Lam¹ and K. N. Lai²

Departments of ¹Chemical Pathology and ²Medicine, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong

Abstract

Background. High glucose concentration in CAPD fluid is known to interfere with creatinine measurement, which is required for assessment of peritoneal membrane permeability and adequacy of dialysis. Correction formulae have been proposed but they may be method/analyser-dependent. We studied such interference in detail.

Methods. CAPD fluid was diluted to prepare six specimens with glucose concentrations ranging from 9.1 to 154.4 mmol/l. To each specimen, creatinine standard was added to give five different concentrations from 50 to 800 μmol/l. The 30 specimens were assayed for creatinine with six routine clinical chemistry analysers (Hitachi 911 and 747, Technicon RAXT and SMAC3, Beckman CX7, and Kodak Ektachem 700). Creatinine interference was calculated by subtracting the apparent creatinine concentration with corresponding baseline creatinine concentration (measured at glucose = 9.1 mmol/l) in the same series.

Results. At constant creatinine concentration, interference increased with increasing glucose concentration to varying extents (up to 200%) amongst the six analysers. At constant glucose concentration, interference decreased with increasing creatinine concentration in analysers using the alkaline picrate reaction but increased in the Kodak analyser using enzymatic assay.

Conclusion. Interference of creatinine measurement in CAPD fluid is dependent on glucose and creatinine concentrations, and each centre should derive specific correction formulae for its analytical system.

Key words: CAPD fluid; creatinine measurement; glucose interference

Materials and methods

Creatinine standard was purchased from BDH Chemicals Ltd, Poole, UK. CAPD fluid containing 4.25% (w/v) dextrose was obtained from Baxter Healthcare Corporation, Deerfield, IL, USA.

CAPD fluid was diluted with distilled water to prepare specimens with six different glucose concentrations of 9.1, 18.3, 35.5, 67.6, 105.6 and 154.4 mmol/l. For each series of glucose concentration, creatinine standard was added to form a range of five different creatinine concentrations of 50, 100,

© 1997 European Renal Association–European Dialysis and Transplant Association
Interference of creatinine measurement in CAPD fluid by glucose

200, 400, and 800 mmol/l. Thirty specimens with different combinations of glucose and creatinine concentrations were thus prepared.

The specimens were assayed in duplicate for creatinine with six commonly used routine clinical chemistry analysers: Hitachi 911 and 747 (Boehringer Mannheim, Mannheim, Germany), Technicon RAXT and SMAC3 (Technicon, Tarrytown, NY, USA), Beckman CX7 (Beckman Instrument Corp. Brea, CA, USA), and a Kodak Ektachem-700 (Eastman Kodak Co. Rochester, NY, USA) The first five systems employed the alkaline-picrate reaction. The Kodak analyser used creatinine specific enzymes creatinine aminohydrolase and creatine aminohydrolase. Interassay coefficients of variation (CV) of these methods were <5% at creatinine concentrations ranging from 100 to 153 mmol/l.

For each series of specimens with the same creatinine but different glucose concentrations, the creatinine concentration measured in the sample containing 9.1 mmol/l of glucose was taken as the baseline creatinine concentration. Glucose at this concentration or below did not cause significant interference in all the analytical systems being studied. The creatinine interference was calculated by subtracting the apparent creatinine concentration from the corresponding baseline creatinine concentration in the same series.

Glucose was measured with a hexokinase method on a Hitachi 911 analyser using commercial reagents (Boehringer Mannheim, Mannheim, Germany). Interassay CV were 2.1 and 2.9% at glucose concentrations of 2.1 and 10.1 mmol/l, respectively.

Results

Interference of creatinine measurement varied with both glucose and creatinine concentrations to different extents in the different analytical systems. These variations are shown in Figure 1a–f.

It was observed that creatinine interference increased with increasing glucose concentration in all six analytical systems. For a given creatinine concentration, the relationship between creatinine interference and glucose concentration was approximately linear at glucose concentrations above 18.1 mmol/l.

It was also observed that the slopes of the regression lines were affected by the concentration of creatinine present in the specimens. In systems using the alkaline-picrate reaction, interferences by the same concentration of glucose were smaller for specimens with higher creatinine concentrations. This phenomenon was most apparent in the Hitachi 747 analyser. The effect in the Kodak Ektachem analyser was in the opposite direction such that interference increased with increasing creatinine concentration. For illustrative purpose, the multiple correction formulae for glucose interference at different creatinine concentrations in the Kodak Ektachem are tabulated in Table 1.

Discussion

The alkaline-picrate reaction for creatinine assay is one of the oldest analytical method still in common use nowadays. It is inexpensive and reliable in most clinical situations. The principle involves the formation of a chromogen by creatinine with picrate in an alkaline medium, and the end-product is measured spectrophotometrically. When adapting this reaction to routine analytical systems, many minor variations in reaction condition have been made. These include the buffer pH, concentration of picrate, time of measurement, end-point or kinetic mode, and time of reaction. These variations do not give rise to significant differences in creatinine measurement in most clinical specimens.

Table 1. Formulae for correcting creatinine interference by glucose on the Kodak Ektachem-700 analyser

<table>
<thead>
<tr>
<th>Measured creatinine (mmol/l)</th>
<th>&lt;100</th>
<th>100–200</th>
<th>200–400</th>
<th>400–800</th>
<th>800–1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>1.9</td>
<td>1.1</td>
<td>2.2</td>
<td>4.7</td>
<td>6.9</td>
</tr>
<tr>
<td>Slope</td>
<td>0.048</td>
<td>0.098</td>
<td>0.26</td>
<td>0.58</td>
<td>0.72</td>
</tr>
</tbody>
</table>

Creatinine interference = [Glucose concentration] × Slope + Intercept.
Corrected creatinine concentration = [Measured creatinine concentration] – [Creatinine interference].
Although creatinine measurement has been known to be affected by high glucose concentration for a long time [2], this is not usually problematical except with severe diabetic complications. However, when measuring creatinine in CAPD fluid, most if not all analytical systems have been incapable of producing accurate results without correction. If the interference was dependent on glucose concentration alone, like Farrell and Bailey [1] had suggested, a single correction formula could be used. In this study we demonstrated that interference is dependent both on glucose and creatinine concentrations. Hence, multiple correction formulae, each applicable for a range of creatinine concentrations, are required to make appropriate adjustments.

We believe that the glucose interference is due to the formation of an interfering chromogen by glucose with picrate. This chromogen might have a much smaller absorption in the measuring wavelength. At physiological concentrations of glucose, this effect is insignificant. In specimens with very high glucose concentration, like the CAPD fluid, this effect becomes important. As reaction conditions differ among different analytical systems, the magnitude of this interference varies.

Our observation of the creatinine dependent phenomenon is more difficult to explain. We postulate that this might be due to the competition of creatinine and glucose for the limited amount of picrate. For any given concentrations of glucose and picrate, the higher the creatinine concentration, the more target chromogen will be formed. This would reduce the formation of glucose-picrate interfering chromogen.

Positive interference by glucose was also observed with the enzymatic creatinine method on the Kodak Ektachem analyser. The pattern of interference was, however, quite different from the alkaline-picrate method. The magnitude of interference was actually higher at higher creatinine concentrations. This is in contrast to what was observed in the picrate method, but is in agreement with the positive interference reported for a similar enzymatic method [2]. The cause of this interference is uncertain but it may be related to the detection system and/or the enzyme [4]. It is important to adjust for the glucose interference of creatinine measurement in CAPD fluid. Without such correction, other derived indices would also be inaccurate and misleading.

As the pattern of interference varies with the method and also the instruments used, a common correction formula for all the systems evaluated cannot be drawn. It is thus recommended that each centre performing creatinine assay should conduct our simple experiment to derive specific correction formulae for the interference.

Acknowledgements. We thank Dr Anthony Shek and Miss Judy Lai for their assistance in measuring some of the specimens with their analysers.

References

Received for publication: 29.4.96
Accepted in revised form: 10.9.96