INTRODUCTION OF MARKERS TO INDICATE AND DISTINGUISH DEATH DUE TO ALCOHOLIC KETOACIDOSIS, DIABETIC KETOACIDOSIS AND HYPEROSMOLAR HYPERGLYCEMIC STATE

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INTRODUCTION

Recent information from the International Diabetes Federation (IDF) states that the number of people diagnosed with and dying from diabetes continues “on a relentlessly upward trajectory” with no signs of abating. Worldwide one person dies every 7 seconds from diabetes and by 2030 one adult in ten will be diabetic. (1)

Diabetes is the fifth most common cause of death globally and is one of the most challenging problems faced by the NHS accounting for approximately 10% of their entire budget. (2)

One third to one half of diabetics are undiagnosed at any given time and, therefore, many deaths due to diabetes may go unrecognised. (2)

The two main conditions causing death directly as a result of diabetes are Diabetic Ketoacidosis (DKA) and Hyperosmolar Hyperglycemic Hyperosmolar State (HSS). Mortality rates are 2–5% for DKA and 15% for HHS. (4)

Aims

A study was undertaken to investigate the markers to identity and distinguish between HHS, DKA and ketoacidosis from other causes e.g. Alcoholic Ketoacidosis (AKA). (5)

Blood beta-hydroxybutyrate (βHB) and vitreous humor glucose (where available) concentrations were measured in 191 post-mortem cases. Blood acetone was also detected in these cases during routine screening for ethanol using headspace-gas chromatography (HS-GC).

RELATIONSHIP BETWEEN βHB AND ACETONE

Unlike βHB, acetone does not dissociate to hydrogen ions and therefore is not a contributory factor to acidosis. In addition, endogenous acetone accounts for only 2% of all ketone bodies and the source of acetone detected could be extrinsic e.g. intoxication with acetone based solvent. (6)

Therefore, whilst acetone is relatively quick and easy to detect it should not be used in isolation to diagnose ketoacidosis.

βHB accounts for 78% of the total ketone body concentration and is the main compound responsible for the elevated anion gap seen in ketotic patients and so is a better marker of ketoacidosis. (6)

TABLE 1: Cases with blood acetone at 2 mg/dL

<table>
<thead>
<tr>
<th>Case</th>
<th>Blood acetone (mg/dL)</th>
<th>Blood βHB (µg/mL)</th>
<th>VH Glucose (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>&gt;50</td>
<td>&gt;1.4</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>90</td>
<td>N/A</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>242</td>
<td>&gt;0.3</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>330</td>
<td>N/A</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>879</td>
<td>18.4</td>
</tr>
</tbody>
</table>

Whilst there is good correlation between βHB and acetone concentration there is also variation. Cases analysed subsequent to the study demonstrate the variation in βHB results at the limit of detection (2 mg/dL).

A limit of detection of 2 mg/dL is essential to ensure all cases of ketoacidosis are recognised.

CONCLUSION

• βHB is the preferred marker of ketoacidosis.
• Acetone can be used as an indicator and all cases involving ketoacidosis will be identified providing analysis for ethanol using HS-GC is carried out.
• βHB only needs to be measured if acetone is detected >2 mg/dL.
• Vitreous humor glucose should be routinely measured to distinguish DKA from ketoacidosis of other causes and to identify HHS.

REFERENCES

(2) http://www.diabetes.co.uk/nhs
(6) Ph.D. Salvador, F. Sera, Technically Speaking. The Department of Laboratory Medicine and Pathology Newsletter, vol. 4, no. 8, 7-7-2010.