Calcium homeostasis during i.v. infusion of 1.5% glycine in anaesthetized pigs

D. CHASSARD, K. BERRADA, J. P. TOURNADRE AND P. BOULÉTREAU

Summary

We have examined changes in plasma concentrations of calcium in seven anaesthetized pigs during i.v. infusion of irrigating fluid containing 1.5% glycine. Volumes infused were 875 ml at 20 min (22 ml kg⁻¹), 1475 ml at 40 min and 2075 ml at 60 min (75 ml kg⁻¹). Plasma concentrations of sodium decreased from 134.5 (SD 3.4) to 112.8 (6.7) mmol litre⁻¹ at 60 min and correlated with the volume of glycine infused ($r^2 = 0.73; P < 0.0001$). Changes in total calcium concentrations were not statistically significant. A decrease in ionized calcium concentration was observed at 40 min (1.12 (0.05) vs 1.24 (0.04) mmol litre⁻¹; $P < 0.05$) and reached 1.11 (0.05) mmol litre⁻¹ at 60 min ($P < 0.01$). However, when corrected for pH, this decrease was not statistically significant. These results suggest that changes in plasma concentrations of sodium rather than changes in calcium homeostasis are probably more important in the development of transurethral prostatic syndrome. (Br. J. Anaesth. 1996; 77: 271–273)

Key words

Resection of the prostate or endometrium by resectionoscope is a technique which requires the use of electrically inert near-isotonic solutions for irrigation. Resorption into the patient’s body of a large amount of glycine-containing irrigating fluid used for these procedures has been reported [1]. This complication includes biological disturbances such as dilutional hyponatraemia and hypo-osmolality [1]. Some clinical observations suggested that hypocalcaemia could be associated with these plasma disturbances [2]. However, there has been no controlled study evaluating calcium changes during i.v. infusion of irrigating fluid. In this study, we assessed the acute effects of i.v. infusion of glycine on calcium homeostasis in anaesthetized pigs.

Methods and results

After obtaining approval from our institution’s Animal Care Committee, we studied seven pigs (23–25 kg). Ketamine 8 mg kg⁻¹ i.v. was given i.m. after a 12-h fast. Anaesthesia was induced with propofol 5 mg kg⁻¹ i.v., sufentanil 3 µg kg⁻¹ i.v. and pancuronium 0.1 mg kg⁻¹ i.v., and was maintained with propofol 10 mg kg⁻¹ h⁻¹. Ventilation was adjusted to maintain an end-tidal carbon dioxide concentration of 4–5%.

A femoral vein and artery were cannulated to provide arterial pressure monitoring, arterial blood samples and a route for administration of glycine. Arterial blood samples were obtained for baseline measurements before a dose of 500 ml of 1.5% glycine (Glycocoll 1.5%, Baxter, Maurepas, France) was infused over 5 min, followed by a constant infusion of 1500 ml h⁻¹ over 55 min. This corresponds to an infusion rate of 34 ml kg⁻¹ during the first 20 min and 75 ml kg⁻¹ over the whole study. Repeated measurements were made 20, 40 and 60 min after the beginning of the infusion of glycine. Samples of blood for measurement of ionized calcium and pH-normalized ionized calcium concentrations were obtained anaerobically into pre-heparinized syringes and analysed immediately using the ICA II instrument (Copenhagen, Denmark). Plasma concentrations of sodium, potassium, magnesium, calcium, chloride, urea, protein, bicarbonate and blood glucose were analysed using the Astră 8 chemistry instrument (Beckman, Schiler Park, IL, USA). $P_{O_2}$, $P_{CO_2}$, and arterial pH were measured using a Radiometer ABL electrode system (Copenhagen, Denmark). The concentration of ammonia in blood was measured by the ACA III instrument (Du Pont, Wilmington, DE, USA). Osmolality was calculated using a standard formula: osmolality (mosmol litre⁻¹) = (sodium mmol litre⁻¹ $\times$ 2) + urea mmol litre⁻¹ + blood glucose mmol litre⁻¹.

Statistical significance was determined using analysis of variance (ANOVA) for repeated measures followed by Dunn’s test. $P < 0.05$ was considered statistically significant. Relationships between electrolyte concentrations and volume of glycine infused were assessed using Pearson’s product correlation coefficient ($r$) and coefficient of determination ($r^2$).

During the first 20 min of i.v. infusion (875 ml), there was a significant decrease in mean plasma concentrations of sodium from 134.5 (SD 3.4) to 121.2 (4.0) mmol litre⁻¹ ($P < 0.05$). At 40 min (1375 ml perfused), pigs demonstrated a more
Table 1. Changes in serum concentrations of protein, osmolality, calcium and other electrolytes during i.v. infusion of 1.5 % glycine (mean (SD) and median (range)). The volumes infused were 875 ml at 20 min, 1475 ml at 40 min and 2075 ml of 60 min. * \( P < 0.05 \), ** \( P < 0.01 \), *** \( P < 0.001 \) compared with baseline.

<table>
<thead>
<tr>
<th>Ionized calcium (mmol litre(^{-1}))</th>
<th>pH-normalized ionized calcium (mmol litre(^{-1}))</th>
<th>Cobalt (g litre(^{-1}))</th>
<th>Ammonia (mmol litre(^{-1}))</th>
<th>Potassium (mmol litre(^{-1}))</th>
<th>Magnesium (mmol litre(^{-1}))</th>
<th>Sodium (mmol litre(^{-1}))</th>
<th>Calcium (mmol litre(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial</td>
<td>Baseline</td>
<td>122–124 (6.1–7.7)</td>
<td>54.2 (4.9–63.4)</td>
<td>45.1 (41.5–52.5)</td>
<td>44.4 (4.9)</td>
<td>134 (130–140)</td>
<td>250 (240–350)</td>
</tr>
<tr>
<td>20 min</td>
<td>121.7 (6.6)</td>
<td>45.1 (41.5–52.5)</td>
<td>44.4 (4.9)</td>
<td>45.1 (41.5–52.5)</td>
<td>44.4 (4.9)</td>
<td>135.6 (133–140)</td>
<td>250 (240–350)</td>
</tr>
<tr>
<td>60 min</td>
<td>122 (130–140)</td>
<td>45.1 (41.5–52.5)</td>
<td>44.4 (4.9)</td>
<td>45.1 (41.5–52.5)</td>
<td>44.4 (4.9)</td>
<td>135 (130–140)</td>
<td>250 (240–350)</td>
</tr>
</tbody>
</table>

marked decrease in plasma concentrations of sodium of 17 mmol \( (P < 0.05) \). At 60 min (1875 ml perfused), this decrease was 22 mmol (mean plasma sodium concentration 112.8 (6.7) mmol litre\(^{-1}\)) \( (P < 0.001) \). This decrease was correlated significantly with the volume of glycine infused \( (r = 0.85, r^2 = 0.73, P < 0.0001) \). A statistically significant decrease in calculated osmolality was seen at 40 min \( (P < 0.05) \) and 60 min \( (P < 0.001) \). Protein, urea, ammonia and other electrolyte concentrations, including potassium, magnesium and phosphate, did not change significantly from baseline during the study (table 1).

A 12 % decrease in plasma concentrations of calcium occurred after infusion of glycine but this decrease was not significant (table 1). In contrast, ionized calcium decreased significantly at 40 min but remained greater than 1.10 mmol litre\(^{-1}\). When ionized calcium was correlated for arterial pH, there was no significant change.

There were no statistically significant correlations between calcium, ionized calcium or pH-corrected ionized calcium, and volume of glycine infused \( (r = -0.46, -0.68, -0.54 \) and \( r^2 = 0.21, 0.46, 0.29 \), respectively) and no relationship between ionized calcium and changes in serum protein concentration.

Comment

It is generally believed that transurethral resection of the prostate syndrome (TURPS) is the results of dilutional hyponatraemia caused by the direct toxicity of glycine and by hyperammonia [1]. Recently, hypocalcaemia has been proposed in the physiopathology of TURPS [2].

Hypocalcaemia denotes low concentrations of biologically active calcium in blood. In fact, symptoms caused by altered concentrations of calcium reflect changes in the serum concentration of ionized calcium [3]. Only one case report expressed interest in the ionized calcium concentration rather than the total calcium concentration during TURPS [2].

In this study, we evaluated changes in plasma calcium concentrations during i.v. infusion of 1.5 % glycine. We found no statistically significant changes in serum calcium concentrations throughout the study. However, a significant decrease in ionized calcium was noted after infusion of glycine 1475 ml over 40 min. Nevertheless, concentrations of ionized calcium were in the normal range for our laboratory and pH-normalized ionized calcium was not decreased significantly by infusion of glycine. Thus, within the limitations of our study, we found that infusion of glycine was not associated with significant disturbances in serum calcium.

Few studies have examined calcium homeostasis during absorption of irrigating solutions such as glycine, despite the crucial role of calcium in neurological and cardiovascular function. Malone and colleagues reported a perioperative decrease in plasma calcium; further changes were not observed in the postoperative period [4]. In seven healthy volunteers, glycine 1 litre i.v. over 20 min (20 ml kg\(^{-1}\)) significantly decreased plasma concen-
trations of calcium [5]. A decrease in plasma calcium concentration (2.04 vs 2.16 mmol litre$^{-1}$) was also seen after 1.57 litre (22 ml kg$^{-1}$) of fluid absorption [6]. The clinical significance of these studies is limited as none measured pH-normalized ionized calcium.

Several events may induce acute hypocalcaemia during anaesthesia: transient hypomagnesaemia, an increase in plasma albumin concentration, administration of citrate and hyperphosphatemia are more common causes [3]. It must be remembered that the concentration of ionized calcium is dependent on arterial pH: acidosis increases and alkalosis decreases the concentration. In our study, none of these factors was present: phosphorus concentration was decreased and the decrease in plasma magnesium concentration was not statistically significant.

Volumes of glycine absorbed during TURPS are generally 500–4000 ml [1, 6]. The volumes administered in our animal study were 875 ml at 20 min and 1875 ml at 60 min (34 and 75 ml kg$^{-1}$). For humans weighing 60–70 kg, this corresponds to values of 2000–5000 ml. Moreover, serum concentrations of sodium were less than 120 mmol litre$^{-1}$, a value known to be the threshold for the development of TURPS [1]. Despite this, calcium homeostasis was not altered.

Acknowledgements

We thank Mrs Finzi for technical assistance, Mrs Didierjean for help in the preparation of the manuscript and Dr Peix for help in animal preparation.

References