Dextrose 10% or 50% in the treatment of hypoglycaemia out of hospital? A randomised controlled trial

C Moore, M Woollard

Methods

Participants

We included hypoglycaemic patients aged 18 years or over from south-east Wales (UK), whose level of consciousness and ability to cooperate did not allow administration of oral carbohydrates, whose blood sugar was <4 mmol/l, and in whom intravenous access had been gained in three or fewer attempts. We excluded conscious, cooperative patients, who were able to take oral carbohydrate or who were administered dextrose, glucagon, or Hypostop (Bio-diagnostics Ltd, Upton-on-Severn, Worcestershire, UK) before the arrival of the paramedics.

Interventions

To be consistent with the existing South-East Wales paramedic protocol for 50% dextrose, we randomised patients to receive either 10% or 50% dextrose in 5 g increments. This was considered appropriate as it allowed us to compare equivalent doses of the two solutions. To ensure that the dose of 10% dextrose was measured accurately, the paramedics used a syringe attached to a three-way tap to draw up 50 ml aliquots from a 500 ml infusion bag attached to a giving set. The 10 ml aliquots administered to the 50% dextrose group were measured using 5 ml calibration markings on the prefilled syringes. The paramedics were instructed to administer the 5 g bolus and wait for one minute before administering subsequent aliquots, until either the Glasgow Coma Scale (GCS) score had returned to 15 or the maximum cumulative dose of 25 g of dextrose had been administered. Time taken to regain GCS 15 was calculated from the time the first incremental dose was administered.

Results

To compare for each dextrose concentration the time to achieve a Glasgow Coma Scale (GCS) score of 15, and the dose required to obtain a blood glucose level of ≥4.5 mmol/l.

Conclusions:

Dextrose 10% delivered in 5 g (50 ml) aliquots is administered in smaller doses than dextrose 50% delivered in 5 g/10 ml aliquots, resulting in lower post-treatment blood glucose levels. We therefore recommend it as the intravenous treatment of choice for adult hypoglycaemia.
Outcomes

Our key outcome measure for this study was intergroup comparison of the time taken to regain a GCS score of 15 following the administration of two concentrations of dextrose. Secondary outcome measures included post-treatment blood glucose levels, the total dose of dextrose given, and the time required to achieve a capillary blood sugar level of >4.5 mmol/l, measured using Roche Accu-Check “Advantage” blood glucose meters and test strips (Roche Diagnostics Ltd, Bell Lane, Lewes, East Sussex, UK). The paramedics were asked to record incidences of extravasation and to score the convenience of administering each concentration of dextrose using a Likert scale. The researchers followed up all patients to determine whether there had been a recurrent episode of hypoglycaemia within 24 hours of treatment.

Consent

Due to the confused or unconscious state of hypoglycaemic patients it was not possible to obtain informed consent from the participants prior to recruitment into the trial. Instead, when they were recovered and oriented after treatment, the paramedics informed them that they had been recruited for a study that was comparing the efficacy of two different concentrations of dextrose. Each participant was given an information pack describing the trial with a form and preaddressed envelope so that participants could withdraw their data from the study at any time. Ethical approval was obtained from the Bro Taf Health Authority Local Research Ethics Committee.

Sample size

Following a pilot study, it was established that a total sample size of 50 was required (25 subjects per group) to detect a three minute difference between the groups in a return to full consciousness (GCS 15), with power of 0.85 and \( \alpha \) of 0.05.

Randomisation

A total of 240 study forms (120 per group) identifying the concentration of dextrose to be administered were pre-randomised for order using SPSS (version 10.0.5) and assigned a unique sequential number. Each form was put in an opaque envelope and packed in consecutively numbered groups of 10, which were then placed in participating ambulance service vehicles. Following confirmation that a subject met the inclusion criteria, paramedics responsible for their care opened the lowest numbered envelope remaining in the vehicle’s pack and administered the dextrose concentration detailed on the study form inside. The randomisation sequence was concealed and held by one of the chief investigators until recruitment was completed.

Blinding

Due to the differences in appearance of the two formulations of dextrose it was not possible to blind the paramedics to the concentration of dextrose given.

Figure 1  CONSORT flow chart illustrating the recruitment of patients for the present randomised controlled trial. hypo, hypoglycaemic episode in 24 hours.
Subjects with a further hypoglycaemic episode within 24 hours.

Glasgow Coma Scale (GCS), or the proportion of participants experiencing a maximum consciousness (GCS of 15), median post-treatment recovery of normal consciousness. There were no significant differences between the groups in age or sex characteristics or the number of patients with insulin dependent diabetes. Pretreatment GCS and blood sugar levels were also similar in both groups (table 1).

We analysed the data on an intention to treat basis to determine the maximum permitted dose of dextrose administered, time to recovery, time on scene, and ease of administration. StatsDirect (version 2.2.78, CamCode, Ashwell, UK) was used to calculate p values and 95% confidence intervals for intergroup differences in proportions with regard to sex, insulin dependent diabetes, and post-treatment recurrent hypoglycaemia.

We used SPSS to conduct the Mann–Whitney U test for intergroup comparisons of age, pretreatment and post-treatment GCS and blood sugar, total dose of dextrose administered, time to recovery, time on scene, and ease of administration.

**Table 1** Comparison of the demographic data of the two study groups. Values are median (range, interquartile range)

<table>
<thead>
<tr>
<th></th>
<th>10% Group (n = 25)</th>
<th>50% Group (n = 26)</th>
<th>Difference, p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>56 (22 to 93, 38 to 74)</td>
<td>54 (22 to 81, 43 to 66)</td>
<td>-2, p = 0.692</td>
</tr>
<tr>
<td>Pretreatment GCS</td>
<td>4 (3 to 14, 3 to 8)</td>
<td>6 (3 to 14, 3 to 12)</td>
<td>+2, p = 0.400</td>
</tr>
<tr>
<td>Pretreatment blood glucose (mmol/l)</td>
<td>1.50 (0.00 to 3.80, 1.20 to 1.80)</td>
<td>1.40 (0.00 to 3.70, 0.78 to 1.83)</td>
<td>-0.1, p = 0.317</td>
</tr>
<tr>
<td>Proportion (%)</td>
<td>Proportion (%)</td>
<td>Difference (95% CI, p)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>15/25 (60)</td>
<td>16/26 (62)</td>
<td>+2% (-28 to +25%, p = 1)</td>
</tr>
<tr>
<td>Insulin dependent diabetes</td>
<td>21/25 (84)</td>
<td>22/26 (85)</td>
<td>+1% (-22 to +21%, p = 1)</td>
</tr>
</tbody>
</table>

GCS, Glasgow Coma Scale

**Table 2** Differences in outcome measures between the two study groups. Values are median (range, interquartile range)

<table>
<thead>
<tr>
<th></th>
<th>10% Group (n = 25)</th>
<th>50% Group (n = 26)</th>
<th>Difference, p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total dose of dextrose (g)</td>
<td>10 (5 to 30, 10 to 15)</td>
<td>25 (10 to 25, 15 to 25)</td>
<td>+15, p = 0.001</td>
</tr>
<tr>
<td>Post-treatment blood glucose (mmol/l)</td>
<td>6.20 (4 to 17, 5.15 to 9.10)</td>
<td>9.40 (4.30 to 18.50, 8.28 to 11.60)</td>
<td>+3.2, p = 0.003</td>
</tr>
<tr>
<td>Post-treatment GCS</td>
<td>15 (6 to 15, 15 to 15)</td>
<td>15 (3 to 15, 15 to 15)</td>
<td>0, p = 0.400</td>
</tr>
<tr>
<td>Time to GCS 15 (min)</td>
<td>8 (1 to 30, 5 to 15)</td>
<td>8 (2 to 19, 4 to 11)</td>
<td>0, p = 0.733</td>
</tr>
<tr>
<td>Time on scene (min)</td>
<td>40 (13 to 75, 30 to 51)</td>
<td>35 (15 to 61, 23 to 45)</td>
<td>-5, p = 0.162</td>
</tr>
<tr>
<td>Ease of administration score</td>
<td>2 (1 to 4, 1 to 3)</td>
<td>1 (1 to 5, 1 to 2)</td>
<td>-1, p = 0.142</td>
</tr>
</tbody>
</table>

GCS, Glasgow Coma Scale

Time on scene was moderately higher for the 10% dextrose group, and paramedics rated administration of 10% dextrose as being slightly less easy than for the 50% solution. However, neither finding reached statistical significance. There were no reported incidences of extravasation in either group.

Both the median total dose of dextrose administered and post-treatment blood sugar level were significantly higher in the 50% group, and these subjects were more likely to have received the maximum permitted dose of 25 g (table 2).

An exploratory analysis of patients without a maximum GCS score of 15 following treatment is shown in table 3. Although all three patients had euglycaemic post-treatment blood sugar levels, all required hospital admission. One of these patients was suspected of being under the influence of illegal drugs, one was a known alcoholic, and one had a serious intercurrent urinary tract infection.

**Table 3** Analysis of patients not achieving a Glasgow Coma Scale (GCS) score of 15

<table>
<thead>
<tr>
<th>Unique identifier</th>
<th>Group</th>
<th>Blood sugar</th>
<th>GCS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre, pretreatment</td>
<td>Post, post-treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>82</td>
<td>10%</td>
<td>1.3</td>
<td>11.4</td>
</tr>
<tr>
<td>212</td>
<td>10%</td>
<td>3.8</td>
<td>9.7</td>
</tr>
<tr>
<td>23</td>
<td>50%</td>
<td>1.1</td>
<td>8.7</td>
</tr>
</tbody>
</table>

**DISCUSSION**

We did not find any difference in the efficacy of treatment between the two groups in the present study. However, despite both cohorts having similar GCS and blood sugar levels before treatment, subjects in the 50% group received a median of 15 g more glucose than those in the 10% group, and subsequently had post-treatment blood glucose levels that were a median of 3.2 mmol/l higher. Patients
administered 50% dextrose were more likely to have received the maximum dose of 25 g than those given the 10% concentration. The reasons for this are unclear, but may be related to the presentation of the 50% solution or to usual practice before the trial. It is also possible that the pharmacokinetics of the two solutions are different, and that 50% dextrose delivered in 5 g (10 ml) boluses has a slower onset of action, encouraging the administration of additional increments before initial aliquots have taken effect.

Two of the subjects contacted by the researchers after treatment reported that before the study they had often had difficulty bringing their blood glucose back to their expected usual level after being treated by paramedics using 50% dextrose. This might imply that the lower cumulative doses administered with the 5 g (50 ml) aliquots of 10% dextrose could assist patients in controlling their post-treatment blood sugar levels. Evidence suggests that administration of dextrose can have a detrimental effect on patients at risk of cerebral ischaemia, such as victims of stroke, cardiac arrest, or head trauma. Avoidance of hyperglycaemia has a neuroprotective effect and reduces mortality and morbidity in the critically ill. The relatively lower post-treatment blood sugar levels associated with the use of 10% dextrose administered in 5 g (50 ml) aliquots may, therefore, offer a safer option for the treatment of hypoglycaemia in these categories of patient.

Limitations of the study
Follow up data were not available for three patients in the 10% group and four in the 50% group, but these missing data would not have significantly changed this study’s primary finding. The total number of patients who presented with hypoglycaemia in the study area during the trial period was also not available. Although this did not influence the randomisation process, it is possible that the outcome of those patients not recruited for the trial could have altered its results had they been included.

CONCLUSIONS
Dextrose 10% administered in 5 g (50 ml) aliquots was found to be as effective and safe as 50% dextrose delivered in 5 g (10 ml) aliquots. Patients in the 10% dextrose group received a median of 15 g less glucose than those in the 50% group, were less likely to receive the maximum permitted dose, and consequently had post-treatment blood glucose levels that were 3.2 mmol/l lower on average. We therefore recommend 10% dextrose administered in 5 g (50 ml) aliquots as the first choice intravenous therapy for the treatment of hypoglycaemia in adults.

ACKNOWLEDGEMENTS
The authors would like to thank all the paramedics who participated in this study, in particular, K Dwyer who asked the question “If we can use 10% dextrose for pregnant females, why can’t we use it for all adults?” A Smith, K Roberts, and K Pitt helped identify relevant papers. R Whitfield provided expert advice about the randomisation strategy and E Green, P Burrows, and P Wilkins helped with preparation of the data collection forms.

AUTHORS’ CONTRIBUTIONS
C Moore had the idea for the study and collected the data. M Woollard and C Moore designed the study, analysed the data, and wrote and edited this paper.

REFERENCES
Dextrose 10% or 50% in the treatment of hypoglycaemia out of hospital? A randomised controlled trial
C Moore and M Woollard

doi: 10.1136/emj.2004.020693