Blood glucose concentration profile after 10 mg dexamethasone in non-diabetic and type 2 diabetic patients undergoing abdominal surgery

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Background. Dexamethasone prevents postoperative nausea and vomiting but may increase blood glucose. We compared blood glucose concentrations after dexamethasone in non-diabetic and type 2 diabetic patients undergoing surgery and looked for any association with preoperative glycosylated haemoglobin [HbA (1c)] and BMI.

Methods. Sixty three patients were enrolled: 32 were non-diabetic (Group ND) and 31 type 2 diabetic (Group D) without insulin treatment. Anaesthesia was induced using i.v. anaesthetic agents and maintained with sevoflurane. All patients received 10 mg dexamethasone at induction. Blood glucose concentrations were measured at induction and then every 60 min for 240 min. Data were analysed using ANOVA. Effects of HbA (1c) and BMI were investigated using linear correlation and logistic regression.

Results. Blood glucose concentrations increased significantly over time and peaked at 120 min after 10 mg dexamethasone in both groups. The magnitude of increase was comparable between the groups [mean (SD) 29 (19) and 35 (19)% of baseline in Group D and Group ND, respectively]. Maximum concentrations were higher in Group D [8.97 (1.51) mmol litre\(^{-1}\), range 6.67–12.94 mmol litre\(^{-1}\)] than in Group ND [7.86 (1.00) mmol litre\(^{-1}\), range 5.78–10.00 mmol litre\(^{-1}\)]. There was a significant correlation between the maximum concentrations and BMI (R\(^2\)=0.21) or HbA (1c) (R\(^2\)=0.26). Logistic regression analysis revealed that the higher the BMI, the lower the HbA (1c) threshold associated with an increased probability (>0.5) of observing blood glucose levels higher than 8.33 mmol litre\(^{-1}\) during 240 min after dexamethasone administration. Similarly, the higher the HbA (1c), the lower the BMI threshold associated with the same probability.

Conclusions. After 10 mg dexamethasone, blood glucose levels increase in non-diabetic and type 2 diabetic patients undergoing abdominal surgery. Poorly controlled diabetes and severe obesity can influence the development of hyperglycaemia.

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Dexamethasone administered alone or in combination with other antiemetic drugs has proven efficacious in preventing nausea and vomiting after different types of surgery\(^1\) and when morphine is used for patient-controlled analgesia.\(^2\) In addition, it is used in an attempt to decrease brain oedema, alleviate nerve damage and inhibit the inflammatory response.\(^3,4\) It also reduces pain induced by administering i.v. propofol.\(^5\) However, dexamethasone, even after single-dose administration, has been shown to increase blood glucose during surgery.\(^6\) This effect may be related to an increase in neoglucogenesis and the development of insulin resistance, which have been demonstrated in both animals and humans.\(^7,8\) Hyperglycaemia is known to be a significant risk factor of adverse outcome in patients at risk of ischaemia.\(^9,10\) Hence, it may be of interest to determine factors that may influence blood glucose concentrations during the perioperative period.
Finally, dexamethasone has been reported to increase blood glucose concentrations in non-diabetic patients but has not been investigated in diabetics. The aims of this study were to compare blood glucose concentrations after a bolus of 10 mg of dexamethasone in non-diabetic and type 2 diabetic patients undergoing routine surgery, and to look for any association between increased glycosylated haemoglobin [HbA (1c)] or BMI and increased blood glucose concentrations in the perioperative period.

Methods

After approval from the regional hospital Ethics Committee and informed consent, 63 consecutive patients undergoing early morning elective abdominal surgery were enrolled over a period of 3 months in this prospective open non-randomized study. They neither received dexamethasone nor insulin before surgery. Thirty-two of them were non-diabetic (Group ND). The other 31 patients suffered from type 2 diabetes mellitus (Group D) which was treated exclusively by oral anti-diabetic drugs. These drugs were all previously not known to be a diabetic, presented with a HbA (1c) threshold above which this probability was higher than 0.5, and the same BMI thresholds for a given HbA (1c) value. The equation of the model served to draw a surface-response curve illustrating the relationship (Matlab software, version 7.0.1., Mathworks Inc., Natick, USA). The obtained model allowed calculating, for a given BMI value, HbA (1c) threshold above which this probability was higher than 0.5, and the same BMI thresholds for a given HbA (1c) value. The equation of the model served to draw a surface-response curve illustrating the relationship (Matlab software, version 7.0.1., Mathworks Inc., Natick, USA). The potential effect of surgical stress was investigated by comparing CRP values measured the day after surgery between groups of patients, using two-tailed unpaired t tests. The same test was used to compare maximum observed blood glucose levels. Patient characteristic data were compared using χ² or two-tailed unpaired t tests. In all cases, P-values of less than 0.05 were considered statistically significant. Power calculations were performed using the G-POWER® software.16

Results

Patient characteristics, HbA (1c), BMI and CRP mean values, and length and type of surgery are presented in Table 1. All recruited patients were ASA II. One of the patients, previously not known to be a diabetic, presented with a HbA (1c) concentration of 6%. The diabetes of this patient was diagnosed during hospitalization. However, in order to be consistent with selection criteria of patients, he was considered as belonging to Group ND for the purpose of statistical analysis.

More than 50% of the patients underwent bariatric surgery, which can explain high BMI values in both groups. Bariatric surgeries and non-bariatric laparotomies were significantly more frequent in Group D than in Group ND. Patients in Group D were significantly older than those in Group ND. Unsurprisingly, they also had significantly higher HbA (1c) [6.0 (0.4) vs 5.4 (0.4) %, respectively] and BMI values [40.4 (6.7) vs 34.6 (6.8), respectively], consistent with their metabolic disorder.

The time course of blood glucose concentrations in the two groups is shown in Figure 1. At induction of anaesthesia, blood glucose concentration was 7.05...
Blood glucose was significantly higher in diabetic than in non-diabetic patients and peaked at T2, amounting to 8.69 (1.48) mmol litre$^{-1}$ and 7.51 (0.90) mmol litre$^{-1}$ in Group D and Group ND, respectively. Maximum blood glucose concentration measured during the study period was significantly higher in Group D [9.0 (1.5) mmol litre$^{-1}$, range 6.7–12.9 mmol litre$^{-1}$] than in Group ND [7.9 (1.0) mmol litre$^{-1}$, range 5.8–10.0 mmol litre$^{-1}$] (Table 1).

When considering the whole sample of patients, the maximum blood glucose concentration observed for each patient was significantly and linearly correlated to BMI ($R^2=0.21$, $P<0.01$) (Fig. 3A), and HbA (1c) ($R^2=0.26$, $P<0.01$) (Fig. 3B). According to binary logistic regression (Fig. 4), patients whose BMI was, for example, 20 kg m$^{-2}$ had an increased risk (>0.5) of presenting blood glucose levels higher than 8.33 mmol litre$^{-1}$ (150 mg dl$^{-1}$) during the 240 min after dexamethasone if their HbA (1c) was higher than 8.33%. The same threshold was considerably lower (5.40%) for a BMI of 40 kg m$^{-2}$. Similarly, patients whose HbA (1c) was 5.5% had the same increased risk if their BMI was higher than 40 kg m$^{-2}$. The same BMI threshold was 33 kg m$^{-2}$ for a HbA (1c) of 6.5%.

There was no significant difference in mean CRP at day 1 between Group D and Group ND (Table 1). The power of detecting a significant difference in mean CRP at day 1 between the groups was 0.97 when considering a $\alpha$ threshold of 0.05, a clinically relevant difference in mean CRP of 2, a variance of 2 and a total number of patients of 63.

### Discussion

The main finding of this study is that over a 240 min period after a bolus of 10 mg dexamethasone given at induction of

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**Table 1** Patient characteristics, HbA (1c), BMI, CRP at day 1, maximum blood glucose (MBG) observed (absolute and % of baseline), length of surgery and type of surgery in Group ND and Group D. Results of statistical analysis are also displayed (in that last column, the numbers between parentheses are the degrees of freedom). *$P<0.05$ compared with ND group. Data are given as mean (SD) or absolute numbers.

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>ND</th>
<th>D</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>32</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>35.9 (22–67)</td>
<td>41.5 (28–59)*</td>
<td>$t_{61}=2.25$</td>
</tr>
<tr>
<td>Male/female (n)</td>
<td>12/20</td>
<td>12/19</td>
<td>$\chi^2_{(1)}=0.01$</td>
</tr>
<tr>
<td>HbA (1c) (%)</td>
<td>5.4 (0.4)</td>
<td>6.0 (0.4)*</td>
<td>$t_{61}&gt;100$</td>
</tr>
<tr>
<td>BMI (kg m$^{-2}$)</td>
<td>34.6 (6.8)</td>
<td>40.4 (6.7)*</td>
<td>$t_{61}&gt;3.4$</td>
</tr>
<tr>
<td>CRP at day 1 (mg dl$^{-1}$)</td>
<td>5.1 (3.1)</td>
<td>4.5 (2.1)</td>
<td>$t_{61}=0.78$</td>
</tr>
<tr>
<td>MBG (mmol litre$^{-1}$)</td>
<td>7.9 (1.0)</td>
<td>9.0 (1.5)*</td>
<td>$t_{61}=3.5$</td>
</tr>
<tr>
<td>MBG (% of baseline)</td>
<td>35 (19)</td>
<td>29 (19)</td>
<td>$t_{61}=1.47$</td>
</tr>
<tr>
<td>Length of surgery (min)</td>
<td>114.3 (42.0)</td>
<td>131.7 (41.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Surgery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bariatric surgery (n)</td>
<td>16</td>
<td>22*</td>
<td></td>
</tr>
<tr>
<td>Non-bariatric laparoscopy (n)</td>
<td>15</td>
<td>5*</td>
<td>$\chi^2_{6.7}=7.7$ $P&lt;0.05$</td>
</tr>
<tr>
<td>Non-bariatric laparotomy (n)</td>
<td>1</td>
<td>4*</td>
<td></td>
</tr>
</tbody>
</table>
anaesthesia, blood glucose concentrations remain significantly higher in type 2 diabetic than in non-diabetic patients undergoing routine abdominal surgery. Blood glucose concentrations peaked 120 min after dexamethasone in both groups. The magnitude of increase (as % increase from the baseline) was not different between the diabetic and the non-diabetic patients.

Dexamethasone has already been reported to produce significantly larger increases in blood glucose concentrations in non-diabetic patients undergoing elective craniotomy. Patients not taking dexamethasone before surgery but receiving it during and after operation have been reported to have a greater increase in blood glucose concentrations from preinduction values than patients who did not receive dexamethasone or those normally on dexamethasone and who also received it during operation. However, this is the first study to demonstrate that the profile of blood glucose levels, although parallel, is significantly higher in diabetic than in non-diabetic patients after 10 mg of dexamethasone given as single dose. This dose may seem to be high in the context of routine abdominoal surgery and prevention of postoperative nausea and vomiting, as opposed to doses used for prevention and treatment of brain oedema. However, several studies investigating the antiemetic effect of dexamethasone used at least 8 mg, and Lee and colleagues have reported higher satisfaction rates in patients receiving between 8 and 12 mg. This is the reason why we chose 10 mg dose in this study.

In our study, we also investigated the effect of HbA (1c) and BMI on blood glucose concentrations. In any individual, HbA (1c) is known to reflect blood glucose values over the two previous months. Hence, it reflects the efficacy of treatment in diabetic patients. A significant linear correlation was observed between HbA (1c) and maximum blood glucose concentrations: the higher the HbA (1c), the higher the blood glucose concentration. Maximum glucose concentration was also linearly correlated with BMI. Therefore, obesity and poor control of diabetes appear to be determinant factors of hyperglycaemic response to surgery after dexamethasone administration.

The maximum blood glucose concentrations measured in this study were not excessively high (highest value: 12.9 mmol litre$^{-1}$ or 232.2 mg dl$^{-1}$) and were of debatable clinical significance. However, it is worth noting that poor control of intraoperative blood glucose concentration with values higher than 7.78 mmol litre$^{-1}$ (140 mg dl$^{-1}$) may be associated with a worsened outcome in cardiac surgery patients. In stroke patients, a level of 10 mmol litre$^{-1}$ has been reported as the threshold for definitive intervention to prevent secondary brain damage. Hence, checking for normality of glycaemia during surgery and knowing about factors that can affect blood glucose profile may be important, at least in the patients described above. A blood glucose concentration slightly higher than normal should have no consequence in the majority of surgical patients, but even moderate hyperglycaemia may have disastrous consequences when associated with ischaemia. The logistic regression model described here allows determining the risk of a given patient for attaining such blood glucose levels, as a function of his/her BMI and HbA (1c) values. For example, a type 2 diabetic patient with a low BMI of 20 kg m$^{-2}$ will be at an increased risk if his/her HbA (1c) is 8.33% or higher, indicating a poorly controlled diabetes. Similarly, a non-diabetic patient will be at increased risk if his/her BMI is very high (i.e. in the range of 40 kg m$^{-2}$). However, it must be kept in mind that this may only have

![Blood glucose concentration expressed as % of baseline (mean (SD)) in non-diabetic (ND, open squares) and type 2 diabetic (D, closed squares) patients from T1 to T4. The way of calculating % of baseline can be found in the text. *Blood glucose concentration in % of baseline significantly higher at T2 than at T1, T3 and T4 in both groups. +Blood glucose concentration significantly higher at T3 than at T4 in both groups.](image-url)
clinical consequences in patients submitted to major surgery and that blood glucose levels can be corrected during the course of surgery.

The lack of randomization in this study deserves comments. The main purpose of our study was to compare blood glucose profiles in diabetic and non-diabetic patients having received dexamethasone. This was done in a prospective non-randomized manner. Although length of surgery and protocol of anaesthesia were similar in both groups, post-hoc selection of patients based on their diabetic status has artificially biased repartition of types of surgeries. Blood glucose concentration has previously been shown to increase significantly over the course of surgery in patients who do not receive dexamethasone. Such an increase could be attributed to the stress response characterized by changes in serum norepinephrine, epinephrine and cortisol levels. It is therefore possible that the degree of surgical stimulus could have biased the results of this study. However, CRP is considered a reliable index to quantify the magnitude of surgical trauma and patient’s inflammatory response to surgery. In our study, there were no differences between groups in CRP measured at day 1 and the power of detecting a clinically relevant difference was high. We can therefore assert with reasonable confidence that the degree of surgical stimulus was comparable between our two groups of patients.

Another potential confounding factor is the use of clonidine. Our patients all received a fixed amount of 300 μg. As clonidine is known to affect glycaemic response to surgery and as BMI was significantly higher in Group D than in

Fig 3 Least square linear regression between maximum blood glucose concentration observed during the study period and BMI (A) or HbA (1c) (B). The equation of the regression line is given, and the squared correlation coefficient.

$y = 0.087x + 5.1525$

$R^2 = 0.2093$

$y = 1.3731x + 0.6294$

$R^2 = 0.2355$
Group ND, one could wonder to what extent clonidine differently affected blood glucose in the two groups of patients. Indeed, clonidine attenuates stress-induced blood glucose elevations through its blocking effects on the adrenergic response to surgery. This effect occurs at doses higher than 2 mg kg⁻¹, such as in our study. Given at lower doses (1 mg kg⁻¹), clonidine inhibits β cells of the pancreas and limits insulin secretion, which can accentuate the hyperglycaemic response induced by surgery. As the opposite effects of clonidine on blood glucose are dose-related, and as the dose of clonidine administered to our patients was higher than 2 mg kg⁻¹, the risk that clonidine could have affected blood glucose in opposite directions in the two groups is low. We cannot exclude the possibility that the limitation of blood glucose increase by clonidine was lower in our diabetic group of patients, as they had higher body weights and received the same dose of clonidine as non-diabetic patients. However, it remains that we observed a good correlation between blood glucose increase and HbA (1c), a variable that can be considered as independent to the dose of clonidine.

In conclusion, we found that, after a bolus of 10 mg dexamethasone, blood glucose concentration profile, although parallel, was significantly higher in type 2 diabetic than in non-diabetic patients undergoing routine abdominal surgery and peaked 120 min after injection. BMI and preoperative HbA (1c) were determinant factors of perioperative blood glucose concentration. Paying attention to these factors is important to detect patients at higher risk of experiencing elevated blood glucose levels that are known to be associated with worsened outcomes after major surgery or in patients at risk of ischaemia. After dexamethasone administration, tight monitoring of blood glucose and correction of hyperglycaemia in those patients should be recommended.

References

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