Transition from intravenous insulin to subcutaneous long-acting insulin in critical care patients on enteral or parenteral nutrition

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Abstract

Background and aims: The optimal initial dose of subcutaneous (SC) insulin after intravenous (IV) infusion is controversial, especially in patients receiving continuous enteral nutrition (EN) or total parenteral nutrition (TPN). The aim of this study was to evaluate the strategy used at our hospital intensive care unit (ICU) in patients switched from IV insulin to SC insulin glargine while receiving EN or TPN.

Design and methods: A retrospective analysis was made of 27 patients on EN and 14 on TPN switched from IV infusion insulin to SC insulin. The initial dose of SC insulin was estimated as 50\% of the daily IV insulin requirements, extrapolated from the previous 12 h. A corrective dose of short-acting insulin (lispro) was used when necessary.

Results: Mean blood glucose (BG) level during SC insulin treatment was 136 ± 35 mg/dL in the EN group and 157 ± 37 mg/dL in the TPN group (p=0.01). In the TPN group, mean BG was >180 mg/dL during the first three days after switching, and a 41\% increase in the glargine dose was required to achieve the target BG. In the EN group, mean BG remained <180 mg/dL throughout the days of transition and the dose of glargine remained unchanged.

Conclusions: In the transition from IV to SC insulin therapy, initial insulin glargine dose estimated as 50\% of daily IV insulin requirements is adequate for patients on EN, but inadequate in those given TPN.

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Introducción

La hiperglucemia está asociada con un aumento de la mortalidad y la infección entre los pacientes hospitalizados en la UCI.1,2 El insulina es el agente preferido para el control glucémico en pacientes hospitalizados y, en el setting de la UCI, el insulina es usualmente administrado como infusión continua (IV) para alcanzar los objetivos más seguros.3-8 Cuando la condición del paciente mejoran, hay muchas guías y recomendaciones que sugieren un cambio de IV a insulina SC.5-8

La decisión de transferir el paciente de IV a SC debe ser realizada cuidadosamente, evaluando la situación clínica del paciente, reconociendo los factores que influencian el cambio de la glucemia y el cálculo de la dosificación de la SC insulina.9

En el setting de la UCI, el uso de terapia纠groupname纠10 con isolog de insulina representa una terapia de transferencia de la periferización intravenosa a la subcutánea.1-7,10 Con cuidado de la monitorización de la SC, se puede evitar el riesgo de hipoglucemias. En pacientes recibiendo infusión IV o TPN, la terapia纠groupname纠10 se constituye en una mejor alternativa para manejar la hiperglucemia.6,11,12

La dosificación de la SC insulina usualmente es más alta para mantener la glucemia en el rango del objetivo.9

Pocos estudios han enfocado en el cambio de la glucemia de la IV insulina a la SC insulina.13-16 La dosificación de la SC insulina es incierta (140 mg/dL). Glargina insulina 140 mg/dL fue utilizada y determinada de manera adecuada al obtener el objetivo de la glucemia de la SC insulina.15-18

Este estudio se realizó para evaluar la estrategia usada en los pacientes hospitalizados en la UCI que estaban tomando insulina IV a SC durante el cambio de la glucemia de la IV insulina a la SC. Se intentó para determinar la dosificación adecuada de la SC insulina durante el cambio de la glucemia de la IV a la SC. La glucemia de la SC insulina fue utilizado para mantener los objetivos de glucemia.
analyze the data. Statistical significance was set at two-sided \( p \) value < 0.05.

### Results

The baseline characteristics of patients with EN and TPN are displayed in Table 1.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Enteral nutrition (( N = 27 ))</th>
<th>Total parenteral nutrition (( N = 14 ))</th>
<th>( p )-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>74.29 ± 1.70</td>
<td>73.36 ± 5.46</td>
<td>NS</td>
</tr>
<tr>
<td>Sex (male, %)</td>
<td>75</td>
<td>73.8</td>
<td>NS</td>
</tr>
<tr>
<td>Simplified Acute Physiology Score (SAPS II)</td>
<td>22 ± 16</td>
<td>16 ± 6</td>
<td>NS</td>
</tr>
<tr>
<td>Acute Physiology and Chronic Health Evaluation (APACHE II)</td>
<td>17</td>
<td>58 ± 37</td>
<td>NS</td>
</tr>
<tr>
<td>History of diabetes before hospital admission (%)</td>
<td>22</td>
<td>27.6</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes treatment (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diet</td>
<td>16</td>
<td>50</td>
<td>–</td>
</tr>
<tr>
<td>Oral agents</td>
<td>50</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Insulin</td>
<td>34</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Days in ICU</td>
<td>20.5 ± 11</td>
<td>22.9 ± 8</td>
<td>NS</td>
</tr>
<tr>
<td>Days with artificial nutrition(^a)</td>
<td>26.3 ± 7</td>
<td>19.6 ± 8</td>
<td>0.057</td>
</tr>
<tr>
<td>Days in hospital</td>
<td>32.8 ± 22</td>
<td>34.8 ± 16</td>
<td>NS</td>
</tr>
</tbody>
</table>

Data are mean ± standard deviation.

\(^a\) Outside ICU included.

The baseline characteristics of patients with EN and TPN are displayed in Table 1. There were no significant differences between EN and PN groups in sex distribution, mean age, percentage of patients with previous diabetes (22.2% vs. 28.6%), severity of illness at ICU admission defined by APACHE II (22 ± 16 vs. 16 ± 6) or SAPS II (46 ± 17 vs. 58 ± 37) scores. The distribution of the most common admission diagnoses was also similar in both groups.

Mean BG during IV insulin treatment (113 ± 2 vs. 112 ± 2 mg/dL) was similar between groups. The average insulin drip rate in the 12 h prior to conversion to SC insulin was 2.0 U/h in the EN group and 2.8 U/h in the TPN group.

The initial glargine dose (23 ± 12 vs. 33 ± 15 IU, \( p < 0.05 \)) was significantly higher in patients with TPN.

During SC insulin treatment, the mean BG was 136 ± 35 mg/dL vs. 157 ± 37 mg/dL in EN and TPN, respectively, \( p = 0.01 \). TPN was associated with a transient higher mean glucose in the first 3 days after the switch to glargine (Fig. 1), being > 180 mg/dL in 35–50% of patients, whereas, the mean BG remained <180 mg/dL in the EN group. In patients receiving TPN, glargine dose needed to be increased by 41%, whereas in EN group in the transition period the dose of glargine was increased only about 5% (Fig. 1). Two episodes of blood glucose > 40 mg/dL occurred in the EN group due to protocol violations.

### Discussion

In the present study we observed that basal-correction insulin therapy with insulin analogs was effective and safe in ICU patients receiving continuous EN or TPN. Estimating the initial glargine dose as 50% of the daily insulin requirements, extrapolated from the average IV insulin infused in the previous 12 h, was suitable for patients with continuous EN, but insufficient for patients with TPN.

Use of basal-prandial-correction therapy with insulin analogs constitutes a suitable regimen for inpatient management of hyperglycemia.\(^{10,18} \) Patients receiving continue EN or TPN require basal insulin therapy plus a correction dose every 4–6 h, but they do not need prandial doses since nutrients are delivered continuously. Our study confirms and extends reports that support the use of long-acting insulin glargine in patients with EN or TPN.\(^{12,17,19} \)

Switching from continuous IV insulin infusion to SC therapy is a complex matter that requires evaluation of the patient’s condition, nutritional treatment and recent insulin dosage. In the present study, transition to a SC insulin regimen was undertaken once the critical illness had resolved, all patients received EN or TPN and insulin requirements were stable.

To avoid rebound hyperglycemia after transition from IV to SC insulin require adequate estimation of subcutaneous insulin dose, and sufficient duration of overlap of the insulin infusion with the subcutaneous insulin.\(^{11} \) Planned transition requires that the first dose of SC insulin is administered at least 1 h for short-acting SC insulin and ideally 3–4 h for long-acting SC insulin, prior to discontinuation of the infusion. Initial SC insulin requirements are usually extrapolated from the average infusion rate measured during a stable period of continuous IV insulin infusion and several dose algorithms has been proposed. However, there are no conclusive data about the optimal conversion factor to calculate the initial subcutaneous insulin dose.\(^{11,14,16,20} \) Our findings show that conversion to glargine at a dose based on the previous 12 h insulin requirements maintains the average BG targets, without need to increase glargine insulin dose in patients with EN. Nevertheless, in patients with TPN, a significant increase in glargine was needed, particularly in the first three days after the switch.

The higher dose of insulin needed in the TPN group can be explained by the higher hyperglycemic potential of TPN.\(^{21,22} \) Although data are scarce regarding the influence of the feeding route on insulin secretion, the higher insulin
requirements with TPN could be due, at least in part, to the lack of stimulation of the incretin system that determines lower beta-cell response to intravenous glucose and facilitates glucagon release. In critically ill patients, hyperglycemia may also reflect the increase in insulin resistance.

Limitations of the present study are related to retrospective design, sample size, the inclusion of patients with and without DM, and that it was conducted at a single tertiary care center. However, it reflects the application of a management protocol for hyperglycemia in the usual clinical practice, patients are likely to be representative of the admitted to a medical-surgical ICU and our findings could help fill the gap in the literature on the transition from IV to SC insulin in patients with continuous artificial nutrition. Nevertheless, it would be helpful to conduct similar studies comparing different protocols at other institutions to obtain results that have greater generalizability.

On the basis of our findings, for patients receiving EN we recommend an initial SC insulin glargine dose equal to 50% of the overall daily insulin requirements extrapolated from the infusion rate 12 h before transition. Future studies could be conducted to determine the optimal dose of initial SC insulin in PN.

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**Conflict of interest**

APP has participated as a consultant for, or has received lecture fees or travel reimbursement from Sanofi-Aventis, Esteva, GSK, Almirall, Novo Nordisk, Eli Lilly, MSD, Boehringer Ingelheim, Novartis, Menarini, Janssen and Astra Zeneca. None of the other authors have any conflict of interest.

**References**