The outcome of Beta cell function after early insulin therapy in the recently diagnosed type 2 diabetes (in Egyptian population) our experience in EL-Minia university hospital


Departments of Internal Medicine and * Clinical Pathology. El-Minia University - Egypt
The purpose of this prospective cohort study was to evaluate whether early insulin therapy is more advantageous in achieving long-term optimal glycemic control with improved B cell function than oral drugs in the recently diagnosed type 2 diabetes mellitus.
**Study Design**

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
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<tbody>
<tr>
<td>20 Pts</td>
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</table>

- **Group 1**
  - Premix Insulin 30/70
  - 2 S/C Injections
  - 10U morning, 5U evening

- **Group 2**
  - Bedtime NPH (10UHumalin N) + 3 Premeal regular insulin (5U)

- **Group 3**
  - Sulphonylurea (Glimipride)
  - And/or metformin

For group 1 & 2, the insulin dose was adjusted gradually according to FBG & PPBG as 2-4 units of insulin to achieve FBG less than 110 mg and PPBG less than 180 mg. For group 3, the given dose of oral antidiabetic drugs (OADs) was increased to achieve the best blood glucose level or reaching to the maximum allowed dose. All the three groups were given the same dietary and exercise instructions.
The treatment continued for 3 months till euglycemia was reached. Then, all medications were stopped and the patients were followed up till the end of the year. BMI, FBG, PPG, HbA$_{1c}$, fasting level of insulin, proinsulin, C- peptide, HOMA-IR, HOMA-B, serum cholesterol, triglycerides were estimated.
BMI before ttt | BMI after ttt
---|---
Group 1 | 27.94 | 28.89
Group 2 | 28.04 | 29.17
Group 3 | 28.69 | 29.32
HbA1C after 3 ms
HbA1C after 6 ms
HbA1C after 9 ms
HbA1C after 1 year

Group 1 (Fixed dose insulin ttt)
Group 2 (Intensive ttt)
Group 3 (Orally ttt)
Serum CHL before ttt: Group1 206.3, Group2 220, Group3 219.3
Serum CHL after 3 ms: Group1 208.6, Group2 176.3, Group3 188.2
Serum triglycerides before ttt: Group1 213.9, Group2 210.8, Group3 213.9
Serum triglycerides after 3 ms: Group1 160.3, Group2 166.9, Group3 211.1

- Group1 (Fixed dose insulin ttt)
- Group2 (Intensive ttt)
- Group3 (Orally ttt)
Group 1 (Fixed dose insulin ttt)

Group 2 (Intensive ttt)

Group 3 (Orally ttt)

Fasting c-peptide before ttt

Fasting c-peptide after ttt
Group 1 (Fixed dose insulin)

Group 2 (Intensive)

Group 3 (Orally)

Fasting serum insulin before ttt

Fasting serum insulin after ttt
Fasting serum proinsulin before and after 3 ms:

- Group 1 (Fixed dose insulin): 24.99 before, 41.75 after
- Group 2 (Intensive): 47.9 before, 18.2 after
- Group 3 (Orally): 16.5 before, 29.9 after

Proins/insulin before and after:

- Group 1 (Fixed dose insulin): 40.9 before, 68.3 after
- Group 2 (Intensive): 60.05 before, 16.47 after
- Group 3 (Orally): 25.95 before, 18.19 after
Group 1 (Fixed dose insulin ttt)

Group 2 (Intensive ttt)

Group 3 (Orally ttt)

HOMA-IR before ttt

HOMA-IR after 3 ms
Group 1 (Fixed dose insulin ttt)

HOMA-β before ttt: 24.99
HOMA-β after 3 ms: 93.83

Group 2 (Intensive ttt)

HOMA-β before ttt: 26.7
HOMA-β after 3 ms: 123.4

Group 3 (Orally ttt)

HOMA-β before ttt: 25.35
HOMA-β after 3 ms: 47.91
Markers of β-cell function in remission patients of pre&post ttt (insulin-treated patients)

Group1 (NO 6)
- C-peptide before ttt: 3.03
- C-peptide after ttt: 5.3

Group2 (NO 9)
- C-peptide before ttt: 1.8
- C-peptide after ttt: 3.6

Legend:
- Black: C-peptide before ttt
- Pink: C-peptide after ttt
Markers of β-cell function in remission patients of pre&post ttt (insulin-treated patients)

- Group 1 (NO 6):
  - Serum insulin before ttt: 53.42
  - Serum insulin after ttt: 127.28

- Group 2 (NO 9):
  - Serum insulin before ttt: 62.22
  - Serum insulin after ttt: 125.33
Markers of β-cell function in remission patients of pre&post ttt

**Serum proinsulin before ttt**
- Group1 (NO 6): 20.4
- Group2 (NO 9): 39.55

**Serum proinsulin after ttt**
- Group1 (NO 6): 15.6
- Group2 (NO 9): 18.37

**Proins/insulin before ttt**
- Group1 (NO 6): 38.11
- Group2 (NO 9): 65.77

**Proins/insulin after ttt**
- Group1 (NO 6): 13
- Group2 (NO 9): 14.66
Markers of β-cell function in remission patients of pre&post ttt (insulin-treated patients)

Group1 (NO 6)

Group2 (NO 9)

HOMA-IR before ttt

HOMA-IR after ttt

3.75
4.02

4.62
Markers of ß-cell function in remssion patients of pre&post ttt (insulin-treated patients)

Group1 (NO 6)
- HOMA-ß before ttt: 18.75
- HOMA-ß after ttt: 121.21

Group2 (NO 9)
- HOMA-ß before ttt: 24.64
- HOMA-ß after ttt: 141.42
HbA1C in remission patients of pre&post ttt (insulin-treated patients)

<table>
<thead>
<tr>
<th>HbA1C %</th>
<th>Group 1 (6)</th>
<th>Group 2 (6)</th>
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<tbody>
<tr>
<td>2%</td>
<td>6.6</td>
<td>6.1</td>
</tr>
<tr>
<td>3%</td>
<td>6.6</td>
<td>5.8</td>
</tr>
<tr>
<td>4%</td>
<td>6.5</td>
<td>6.06</td>
</tr>
<tr>
<td>5%</td>
<td>6.5</td>
<td>6.1</td>
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Group1 (NO 6)  Group2 (NO 6)
Evaluation of parameters in succeeded and failed patients in three groups
Succeeded patients

Failed patients

FBS before ttt

FBS after ttt
HbA1C after 3 ms: 6.1, 6.8
HbA1C after 6 ms: 6.2, 7.8
HbA1C after 9 ms: 6.3, 7.9
HbA1C after 1 year: 6.1, 8

- **Succeeded patients**
- **Failed patients**
Mean insulin dose required

- Succeeded patients: 25.9
- Failed patients: 51.1
Succeeded patients

Failed patients

Fasting serum insulin before ttt
Fasting serum insulin after ttt
Fasting c-peptide before ttt

- Succeeded patients: 1.8
- Failed patients: 1.6
Summary and conclusion
• In the present study, the first favorable metabolic effect of insulin therapy was better glycemic control in the insulin treated groups versus orally treated group. There were a statistically significant decrease in FBS and HbA\textsubscript{1c} in the insulin treated groups compared to orally treated group (P=0.04, 0.001 for FBS and 0.001 for HbA\textsubscript{1c} level). HbA\textsubscript{1c} of the group 2(intensively treated group) decreased significantly than that of the group 1(mixed insulin group)(P=0.0001).This better glycemic control continued all through the follow up duration.

• The second favorable metabolic effect of insulin therapy was observed on lipid profile as serum total cholesterol was reduced significantly following insulin therapy(P=0.001) but did not change in the orally treated group. This is consistent with the study of Alvarsson et al., (2003) who demonstrated that the changes in glycemia were mirrored in an improvement of lipid profiles.
• In the present study, we found a significant increase of fasting C-peptide and insulin and HOMA-B and a significant decrease in the proinsulin level and proinsulin/insulin ratio in insulin treated groups (1&2) following insulin therapy versus orally treated group (3). This indicates that parameters of ß-cell function were better preserved in the insulin than in the orally treated patients.
There is evidence that an early intervention with intensive insulin therapy in newly diagnosed type 2 diabetes restores the endogenous insulin secretion, characterized by normoglycemia and no need for hypoglycemic medications. This is because early insulin therapy reduced strain on the β-cell and can potentially induce ‘beta cell rest’, which results in increased insulin secretion and restoration of β-cell function compared with oral hypoglycemic agents (Alvarsson et al., 2003, Weng et al., 2008, Chen et al., 2008). It is also an effective line of therapy that helps in better control of serum cholesterol and triglycerides.
To our knowledge, it may be the first research in Egypt that looks for intensive insulin therapy in newly diagnosed naïve type 2 diabetes mellitus for relatively long time (3 months) with 12 months follow up. Advantages of this study are firstly, comparing the insulin intensively treated patients and patients treated with fixed dose insulin (2 doses: before breakfast and before dinner) with orally treated one, in this way the results were less likely to be influenced by differences in other parameters known and unknown. Secondly, we use several parameters to evaluate if there is improvement of β cell function or not. Further studies on this subject are eagerly awaited; the results of this study need to be confirmed in clinical trials.