The Paper that Changed my Practice

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AIMS

• To describe metabolic changes
• To lower mortality (approx 20%)
• To improve therapeutic regimen
INITIAL INSULIN REGIMEN 1971-72

• Based on Plasma Ketostix

• Range:

from 120 units IV + 180 units IM
to 30 units IV + 50 units IM

Alberti & Hockaday, 1972
FIRST RANDOMIZED COMPARISON OF INSULIN DOSES: Smith & Martin 1954

Initial dose of 80, 160 or 240 units IV

~ no difference
Sonksen PH et al.

Growth hormone and cortisol responses to insulin infusion in patients with diabetes mellitus.

Lancet 1972
Stepped insulin infusion 1.3-11 units/hr

- Healthy volunteers
- 9 patients with “moderate” diabetes
- 3 DKA, I HONK
Fig. 5—Serum-G.H. and plasma-glucose responses to the standard infusion protocol in four patients with severe diabetes (coma or pre-coma).
# INSULIN LEVELS WITH ORIGINAL OXFORD REGIMEN

<table>
<thead>
<tr>
<th>Time</th>
<th>mU/l</th>
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<tbody>
<tr>
<td>&quot;Baseline&quot;</td>
<td>7 (0–20)</td>
</tr>
<tr>
<td>1 hr</td>
<td>744 (36–3200)</td>
</tr>
<tr>
<td>5 hrs</td>
<td>425 (30–2400)</td>
</tr>
<tr>
<td>24 hrs</td>
<td>50 (8–211)</td>
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</tbody>
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PHASE 1

FIG. 11. Computer simulation of serum insulin concentrations after intravenous insulin. The calculations were based on an insulin half-life of 4 min in blood. •—•, 200 units soluble insulin given at 0 and 2 hr; o--o, 100 units soluble insulin given at 0 and 2 hr.

Alberti, Postgrad Med Journal 1973
PHASE 2

• IV INSULIN 6 units/m delivered by pump

• Pump problems
PHASE 3

Intramuscular insulin
Fig. 12. Computer simulation of serum insulin concentration after intramuscular insulin. The plot represents predicted serum insulin values after giving 10 units intramuscular insulin hourly. D, mean measured serum insulin for 3 new diabetic patients given this regime.

Alberti, Postgrad Med Journal 1973
Fig. 1—Insulin therapy and change in plasma-glucose and blood-ketone-body concentrations in 14 ketoacidotic patients.
Values are given as mean fall (±S.E.M.) from time 0.
Fig. 2—Mean plasma-glucose and blood-ketone-body concentrations in 14 ketoacidotic patients after treatment with low doses of I.M. insulin.

Alberti, Hockaday & Turner, Lancet 1973
FIG. 3—Mean (± 1 S.E. of mean) plasma free fatty acids (F.F.A.) and glycerol and serum insulin concentrations during insulin infusion. Numbers of patients are given in parentheses.
## LOW DOSE INSULIN THERAPY FOR DIABETIC KETOACIDOSIS

<table>
<thead>
<tr>
<th></th>
<th>IM</th>
<th>IV</th>
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<tbody>
<tr>
<td><strong>n</strong></td>
<td>184</td>
<td>170</td>
</tr>
<tr>
<td>Loading dose (u)</td>
<td>15</td>
<td>3</td>
</tr>
<tr>
<td>Hourly dose</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Rate of fall of PG (mg%/m)</td>
<td>80</td>
<td>95</td>
</tr>
<tr>
<td>Hypokalaemia %</td>
<td>1</td>
<td>0.6</td>
</tr>
<tr>
<td>Hypoglycaemia %</td>
<td>1</td>
<td>0.6</td>
</tr>
<tr>
<td>Deaths %</td>
<td>6</td>
<td>2</td>
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</table>
EARLIEST USE OF LOW DOSE INSULIN

• Katsch 1946

• Repeated IM & SC injections of 4–10 units insulin - every 15–60 mins

• 118 units in 12 hrs

• 166 units in 24 hrs
CONCLUSIONS (1)

Route of Insulin

• IV infusion ~ preferable
• IM insulin ~ safest
• SC insulin ~ too slow, poor absorption
CONCLUSIONS (2)

Importance of serendipity
CONCLUSIONS (3)

Initial treatment of DKA

- REHYDRATION more important than insulin!