Patch pumps, and closed-loop experience in Europe

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Not a patch pump
Originally: a ‘tubeless’ pump attached via an adhesive patch
Insulin ‘patch pumps’

Has become a generic term for next-generation insulin infusion pumps
Patient reactions to long-term continuous subcutaneous insulin infusion


• What advice would you have for us on the future use of the pump?

• Top responses:
  – Smaller or lighter pump
  – Improve attachment to body
  – Improve cannula insertion and design
Generic features of patch pumps: some or all of these features

- Smaller, more discrete
- Easier to use, learn
- Some or all components may be disposable
- Usually attached to body with adhesive patch
- Some are simpler
- Usually integrated cannula (‘tubeless’)
- Some have wireless remote control
- Some with touch-screen on remote control or pump
- Some more suitable for type 2 DM
- Some have mobile connectivity (the ‘cloud’ etc)
Some patch or next-generation pumps

- Omnipod (Insulet)
- Cellnovo
- CeQur PaQ
- Finesse (Calibra) – not really a pump
- JewelPump (Debiotech)
- Medtronic patch pump
- Solo (Roche)
- Spring Hybrid (D-Medical)
- t-slim (Tandem Diabetes Care) – not really patch
- V-Go (Valeritas)
Disclaimer
OmniPod

- First patch pump - launched 2005 (USA)
- Slow to reach Europe (2010 in UK and Germany)
- Two components:
  - Pod – single-use, 3-day disposable pump/reservoir, integrated cannula with automatic insertion, attached with adhesive patch
  - Personal data manager – hand-held remote control of Pod, integrated BG meter
- Smaller pod (Eros) and new PDM on the way
Solo Pump (Roche)

- Acquired by Roche from Medingo
- FDA approved
- Not yet released
- 90-day use
- Four components:
  - Cradle/patch attachment with inserter-cannula
  - Detachable 2-part minipump (reservoir, pump)
  - Remote controller
V-Go (Valeritas)

- Intended for Type 2 DM
- FDA approved, CE mark
- Non-electronic
- Disposable, 1-day use
- Preset basal rates (20, 30, 40 U/day)
- 2-unit manual bolus on demand
- Limited launch from June 2012
CeQur PaQ pump

- Intended for type 2 diabetes
- 3 day use
- 2 parts:
  - Disposable insulin reservoir
  - Re-usable electronic messenger unit
- Up to 7 preset basal basal rates
- On demand push-button 2-unit bolus
- In clinical trials in Austria
- Will be launched in Europe first
JewelPump (Debiotech)

- 2-part pump – reusable electronics and disposable reservoir/pump
- Remote controller with touch screen
- Patch attachment with auto-insert cannula
- In clinical trials in France
t-slim (Tandem Diabetes Care)

- Not patch attached
- Slim, credit card sized
- Color touch screen
- Rechargeable via micro USB port
- Available August 2012?
Cellnovo pump

- 2-part pump:
  - Disposable insulin cartridge
  - Re-usable electronics
  - Activity monitor
- Patch attachment
- Short or long cannula
- Wireless touch screen remote controller with integrated BG meter
- Wireless, automatic and real-time capture of pump and glucose data and transmission to a 'cloud'-based clinical management programme – for access by handset and web
Closing the loop
Strategies for improving control with automatic closed-loop systems

• Closed-loop wearable artificial pancreas
  – Complex, long-term project
  – At least two European AP consortia established

• CSII + CGM with ‘control-to-range’
  – Simpler
  – Available in Europe for ~2 years
Insulin pump with low-glucose suspend

- CGM-linked insulin pump suspends for up to 2 hours if blood glucose falls below set threshold
- May help to prevent severity of hypoglycemia
Paradigm Veo LGS: additional features

• When low glucose threshold reached:
  – Alert sounded
  – Pump basal rate suspended

• Option:
  – Either continue suspend for up to 2 hours or until user cancels
  – Or resume delivery immediately

• If no response after 2 min, insulin suspended for 2 hours and screen displays ‘I have diabetes, call for emergency’
Duration of nocturnal hypoglycemia in highest quartile of hypoglycemia at baseline reduced by 96% by a LGS insulin pump

Choudhary P et al. Diabetes Care 2011; 34 2023-5
Low glucose suspend events

- 86% of subjects experienced an LGS event

Average number of LGS events/week = 1.9
Two-hour LGS events

- Full 2-hr LGS events = 12% of total
  - 75% of these occurred at night

- Patient responded to alarm and elected to continue for 2 hr = 8% of total

- Patient did not respond to alarm, LGS continued for 2 hr = 4% of total
### Low glucose suspend times

<table>
<thead>
<tr>
<th>Suspend time (min)</th>
<th>Percent events (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-10</td>
<td>55</td>
</tr>
<tr>
<td>10-59</td>
<td>26</td>
</tr>
<tr>
<td>60-119</td>
<td>7</td>
</tr>
<tr>
<td>120</td>
<td>12</td>
</tr>
</tbody>
</table>
LGS events by time of day

<table>
<thead>
<tr>
<th>Day</th>
<th>Night</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 am - 12 MN</td>
<td>12 MN - 8 am</td>
</tr>
</tbody>
</table>

76%          | 24%           |
Quartile Trend: Pre and Post LGS

- **Pre LGS (-1 hr)**
- **LGS (0-2 hr)**
- **Post LGS (+1 hr)**
- **Post LGS (+1.5 hr)**
- **Post LGS (+2 hr)**

<table>
<thead>
<tr>
<th>Glucose (mmol/L)</th>
<th>Pre LGS -1 hr</th>
<th>LGS 0-2 hr</th>
<th>Post LGS +1 hr</th>
<th>Post LGS +1.5 hr</th>
<th>Post LGS +2 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.5 mM</td>
<td>81 mg/dl</td>
<td>2.8 mM</td>
<td>5.7 mM</td>
<td>6.5 mM</td>
<td>6 mM</td>
</tr>
<tr>
<td>20 mmol/l (360 mg/dl)</td>
<td></td>
<td></td>
<td>10 mmol/l (180 mg/dl)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **10 mmol/l (180 mg/dl)**
- **20 mmol/l (360 mg/dl)**
Computer download: 2-hr nocturnal LGS (age 43 yr, female)
**Veo data in European users**

Agrawal P et al. ADA 2012

7,810 Veo users in Europe
Data from 398,902 pt-days downloaded from CareLink
LGS on and off days compared

Duration of hypoglycemia reduced

Sensor glucose values (mg/dl)

Duration of hypoglycemia (min)

P < 0.001 for all

LGS on days
LGS off days

<50
<60
<70
<80
Sensor glucose before and after LGS
Agrawal P et al ADA 2012

![Graph showing sensor glucose levels before and after LGS over time.](image-url)
Patients likely to benefit from LGS pumps

• Those with a continued high rate of hypoglycemia and/or hypoglycemia unawareness on optimised CSII
  – Variable subcutaneous insulin absorption
  – Gastroparesis
  – Unpredictable responses to exercise
  – Mismatch of insulin and food at meals
  – Renal impairment

• Those with excessive fear of hypoglycemia (often maintain high HbA1c to avoid hypoglycemia)
At least two European artificial pancreas consortia
Artificial pancreas (AP) at home

- EC-funded, 4-year project
- 10.5 million Euros
- Aims:
  - Improve CL algorithms
  - Construct and validate single- and dual-port AP
- 12 partners, 7 European countries

www.apathome.eu
Partners

• Universities with AP experience:
  – Amsterdam
  – Cambridge
  – Graz
  – Montpellier
  – Padua
  – Ecole Polytechnique Fédérale Lausanne

• Industrial partners/clinical research institutes: Profil Institute, Sensile, STMicroelectronics, Triteq, 4a engineering

• Coordinators: Lutz Heinemann and Hans deVries
AP@home aims

- Compare and optimise AP algorithms (MPC vs. PID)
- Improve CGM performance with new algorithms
- Investigate improved insulin absorption (new formulations, SC site heating, routes etc)

- Develop two-port AP using existing CGM and pumps with improved algorithms as above

- Develop single-port AP (CGM and insulin delivery at same site)
  - Glucose-responsive hydrogel membrane controls insulin delivery in microneedles
  - Insulin cannulae with integrated glucose sensors
DREAM (Diabetes Wireless Artificial Pancreas Consortium)

• Pediatric Diabetes Centers:
  – Israel (Moshe Phillip)
  – Slovenia (Tadej Battelino)
  – Germany (Thomas Danne)

MD-logic artificial pancreas (fuzzy logic-based algorithm using individual patient characteristics, insulin requirements etc)
Recently, overnight closed-loop control at home reported in outpatients
What next for the artificial pancreas, sensors and pumps?

A personal view
What are the bottlenecks in closed-loop insulin delivery?

- Glucose sensor
  - More stable, reliable glucose sensing
  - Non-invasive glucose sensing

- Algorithm
  - More rapid insulin absorption needed
  - More predictable insulin absorption needed

- Insulin pump

- Insulin

New technology needed:
Improving CGM

Fluorescence-based glucose sensors and smart tattoos
Bacterial glucose-binding protein

Marked change in conformation on glucose binding
Labelled with fluorophore at binding site
Fluorescence intensity and lifetime increase on glucose binding
Fibre-optic fluorescence lifetime-based glucose sensor

Fluorescence lifetime is stable
Not affected by electrochemical interferences in tissues

Saxl et al Analyst 2011; 136: 968-972
‘Smart tattoos’ for non-invasive glucose sensing

1. Inject nano- or microsensors SC or intradermally
2. Illuminate with light to excite fluorescence
3. Record glucose-dependent fluorescence changes
Layer-by-layer encapsulation of sensors in nano-engineered membranes

Sensing protein adsorbed to CaCO₃

Alternating layers of poly-lysine and poly-glutamic acid or heparin assembled ‘layer-by-layer’

Template dissolution with EDTA

CaCO₃ → CaCO₃ → CaCO₃ → Protein

Saxl et al Biosens Bioelectron 2009
Fluorescence lifetime imaging microscopy (FLIM) of microsensors

- Glucose
- Intensity
- Fraction of long lifetime closed form of GBP
- Pixel histogram each image

The future of diabetes devices: the burden of too much technology
The burden of diabetes: so much to consider

- What affects my diabetes and what I need to know:
  - Blood glucose, HbA1c
  - Food
  - Activity
  - Insulin
  - Illness
  - Stress level

- What I need to carry:
  - Insulin pump
  - Blood glucose meter
  - CGM
  - Computer
  - Internet access
  - Mobile phone
  - Instruction manuals

Too much information! Too many devices!
The burden of diabetes

• Who needs to know about my diabetes?
  – The hospital doctors
  – The general practitioner
  – The diabetes nurses
  – The dietitian
  – The family
  – Maybe school
  – The pharmacy
  – The pump supplier

Too many people!
We need to **connect** the patient, pump, sensor, doctor, nurse, dietitian, educator, hospital, school, computer, telephone

Is mobile healthcare the answer?
Connected and shared information via ‘cloud’ computing and the web
Mobile healthcare for connectivity

- CGM
- Activity
- Food
- Insulin pump

Cloud
- Software/
- Algorithms
- Data interpretation
- Software updates

Variable access
- Patient
- Parent
- Doctor
- Nurse, dietitian
- School
- Manufacturer

Remote controller
Cell phone
Web
Summary

• Several patch and next-generation insulin pumps are under development

• Low-glucose insulin suspend pumps have been in safe and effective clinical practice in Europe for 2 years and are known to reduce hypoglycemia

• At least two European AP consortia are in operation

• Improved fluorescence based glucose sensors are being developed

• Mobile healthcare may reduce the burden of diabetes technology