FDA Perspective on Closed-Loop Studies

Practical Ways to Achieve Targets in Diabetes Care

July 19, 2014
Keystone, CO

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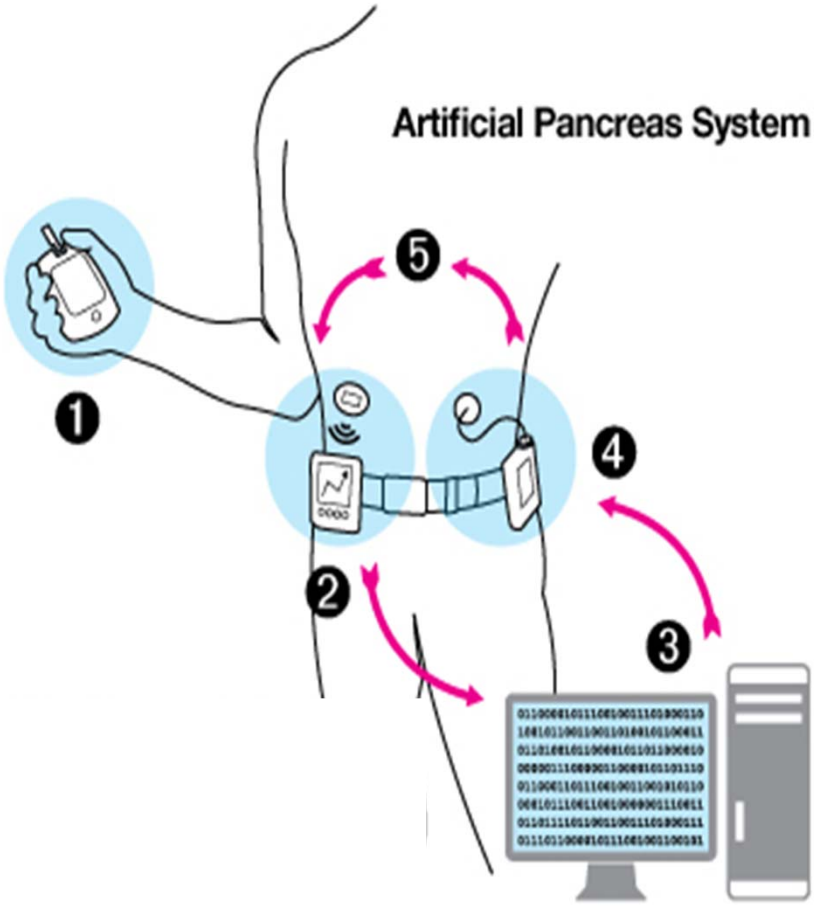
What is an Artificial Pancreas (AP)?



Artificial Pancreas

- Many still struggle to maintain good glycemic control
- Hypoglycemic unaware individuals at risk
- Risk of nighttime hypoglycemia
- Better quality of life needed

- FDA believes that development of an Artificial Pancreas will improve outcomes for people with diabetes

- Challenges:
  - Device limitations – pump imprecision, sensor inaccuracy/unreliability
  - Biology – complicated
  - Inter-individual variability – one size fits all possible? Smart algorithms?

- Good news - Brilliant people working on these problems….

Background

- Where we were 10 years ago
- CGM approval/improvement
- Open loop studies / Algorithm development
- Compensating for CGM/pump failures
- Gradually increasing confidence in algorithms

Current Status

- AP Clinical studies – much progress!
  - Clinic – close monitoring, oversight
  - Camp – stresses the system
  - Outpatient/Hotel – managed supervision
  - Home – flexible, can be monitored, use of companions

Current Status

- Medtronic MiniMed 530G Threshold Suspend System Approved in October 2013
- First step toward an AP
- Suspends insulin delivery when CGM value reaches a set threshold (e.g., 60 - 90 mg/dL)

Opportunities – Device Consolidation

- Challenges for patients
  - Difficult being a patient with diabetes
  - Medical devices help, but can also contribute to frustrations and non-compliant therapy
  - Must carry - Cell phone, pump, meter, CGM receiver, insulin pens, strips, etc…

- Potential solutions
  - Efforts to consolidate devices onto fewer platforms (e.g., meter, CGM, pump receiver in one)
  - Requires good coordination between companies in many instances

- FDA is creating and communicating policies to encourage device company collaboration

Opportunities – Mobile Apps

- To facilitate device consolidation, mobile platforms are key
  - Nearly everyone now carries a cell phone
  - enable functions to allow for medical device interaction from that platform

- Challenges include
  - Security, hacking – specialized communication protocols essential
  - Android vs. Apple OS

- FDA is working closely with industry on requirements/process for market entry, upgrades, etc.
  - Guidance on Mobile Medical Apps – provides more clarity and transparency

- Promises to be more convenient for patients and better for AP development

Opportunities – Component AP Systems

- Traditional pathway = one company sells whole AP device (sensor, pump, algorithm)
- Alternate pathway = different companies sell the components of an AP (e.g., algorithm on app that communicates with pump and sensor)
- More choices/access
- Working on Policies to Foster this Innovation:
  - Who is responsible? (for adverse events, etc.)
  - Impact of Device modifications/generations

Opportunities - Commercialization

- Investigators beginning to think more about commercialization
- Previous focus on algorithm development/tweaking
- Much more attention on how to translate their discoveries/innovations into real medical devices
- Very significant and exciting change in tone!

Common Misconceptions

- An AP does not have to develop/approve in a measured progression
  - Some thought FDA would require a slow progression (e.g., threshold suspend, predictive suspend, treat-to-range, full AP)
  - No reason not to try to develop the fully closed loop device if the technology is ready!
- Remote monitoring can be a good safety mitigation in studies, but is not always required
  - There are many ways to mitigate the risk in clinical studies
  - Appropriate tools depend on study design

Common Misconceptions

- Clinical studies in children is allowed
  - Some have thought FDA will not allow AP investigations in children
  - Often can design studies to incorporate pediatric patients
  - Have been many pediatric trials already
  - Investigators should consider device differences between populations
    - e.g., DexCom G4 approved in pediatrics, but studies show the sensor much less accurate in children than adults (particularly in the hypo range)
    - Study mitigations and algorithms may need to account for device performance differences
- HbA1c is not the only endpoint FDA will accept for AP studies
  - Some have thought only HbA1c is accepted
  - Endpoint should be what makes sense for the claims being tested

Common Misconceptions

- Enacting safety mitigations for studies does not mean that these mitigations have to be part of the final system
  - Some have thought that if remote monitoring is used to mitigate risks in a clinical study that it will also be needed once the device in approved
  - Study mitigations are for the safety of study participants and are not part of the device itself
- Artificial Pancreas devices do not have to be perfect with zero risk to be beneficial
  - Approval decision is a benefit/risk decision
  - Approval Decision made in the context of the significant risks people with diabetes face every day due to their disease

Where do we go next?

- Continue to work with Investigators and Companies who are developing these devices to encourage their development
- Continue to learn from patients and healthcare providers about the needs and desires of this community
- Continue to develop policies that promote rather than prohibit AP availability

It will happen, and sooner than you think!

Thank you!

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