Drug Eluting Balloons for PAD

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19/06/2009 at 12:15 during 4mn
Session: Session 5 - BTK Angioplasty : Beyond critical limb ischemia in the Main auditorium

No Financial Relationships to Disclose
Background

+ Drug-coated balloons were first investigated in the 1990s, but were not pursued at that time due to difficulties in transferring the drug from the balloon into the tissue quickly enough. Once an additive allowing the tissue to quickly absorb the drug was developed did the field evolve.

+ The concept behind the drug coated balloon technology is based on the assumption that delivering a rapid release of drugs into the arterial tissue is more effective than the gradual release of drugs, as seen with drug-eluting stents.
Why Drug Coated Balloons?

Advantages:

- First is ease of use: in the periphery, especially below the knees, balloon angioplasty has been a stalwart in the traditional method of treating atherosclerotic lesions.
  - You are in the vessel treating with PTA, why not DEB (drug eluting balloon)
- Second is cost: balloon catheters have traditionally been less expensive than stents.
Markets for DEB

- The coronary market
- Small vessel disease below the knee
- In-stent restenosis for coronary and periphery.
Key Questions: Animal Coronary Studies

- Does the Drug get Absorbed?
Animal Data: Drug Elution

- No paclitaxel was found in the peripheral blood at any time point.

- Short exposure of the coronary artery to paclitaxel with a coated balloon is sufficient for the attainment of an adequate tissue concentration of paclitaxel, which is known to be efficient in inhibiting neointimal growth.

Animal Studies: Encouraging

- Drug-eluting stents have shown promising antirestenotic effects in clinical trials. Non-stent-based local delivery of antiproliferative drugs may offer additional flexibility and also reach vessel areas beyond the immediate stent coverage.

- CONCLUSIONS: Paclitaxel balloon coating is safe, and it effectively inhibits restenosis after coronary angioplasty with stent implantation in the porcine model. The degree of reduction in neointimal formation was comparable to that achieved with drug-eluting stents.

Key Questions: Animal Coronary Studies

- What about bare stent with or without DEB and with or without Contrast and Paclitaxel?
Animal Studies: DEB with Stents

- Paclitaxel was either dissolved in a nonionic contrast medium or coated on balloons. Stents were crimped on the coated balloons. Effectiveness was tested in 22 pigs. Two coronary stents were placed in each pig.


- **Control** (Bare Stent, Uncoated Balloon)
- **Bare Stent, Uncoated Balloon, Paclixel Contrast**
- **Bare Stent, Pac Balloon, plain contrast**
- **Sirolimus Stent, noncoated balloon, plain contrast**

\[ P < .001 \]
Key Questions: Animal Coronary Studies

- Does a DEB Carrying a conventional stent better than a non-DEB?
Animal Studies: Delivery Stents on DEB versus Standard Balloons

- Fifty-six stainless steel stents were implanted in the left anterior descending and circumflex coronary arteries of 28 domestic pigs.

- Stents were mounted on conventional uncoated and paclitaxel-coated angioplasty balloon catheters.

DEB in the SFA: Early Human Studies

- Does it work?
DEB in Human Femoropopliteal Disease

Randomly assigned 154 patients with stenosis or occlusion of a femoropopliteal artery to treatment with standard balloon catheters coated with paclitaxel, uncoated balloons with paclitaxel dissolved in the contrast medium, or uncoated balloons without paclitaxel (control).

Players

- EuroCor/Opto Circuits
- Lutonix
- Bayer (Medrad/Schering Plough)
- B. Braun Melsungen
- Aachen Resonance
- Genesis Technologies
- DSM Biomedical
- Invatec (In.Pact Admiral Cook Inc.)
- Cook Inc.
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Data: Bayer/Medrad Results

- Tepe et al

- Bayer (Medrad) paclitaxel-coated balloons with paclitaxel in 48 patients, another 52 patients who were injected with a high-dose of paclitaxel mixed with contrast medium, and another 54 control patients

<table>
<thead>
<tr>
<th>Patients Requiring Additional Surgery Post-Procedure</th>
<th>6 Mos</th>
<th>24 Mos</th>
</tr>
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<tbody>
<tr>
<td>Control</td>
<td>37%</td>
<td>52%</td>
</tr>
<tr>
<td>Paclitaxel/Contrast</td>
<td>29%</td>
<td>40%</td>
</tr>
<tr>
<td>Drug Coated Balloon</td>
<td>4%</td>
<td>15%</td>
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</tbody>
</table>
Bayer/Medrad/Schering AG licensed the Paccocath® technology in 2005.

The company co-sponsored the THUNDER (Local Taxan with Short Time exposure for Reduction of Restenosis in Distal Arteries) clinical trial in 2004 to assess the efficacy of the DEB technology for preventing restenosis in the superficial femoral and popliteal arteries.

Trial results concluded that the Paccocath® DEB technology showed a significant reduction in late lumen loss and target-lesion revascularization compared to standard PTA.
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Several trials have confirmed:

- A low dosage of $3 \mu g$ per mm$^2$ balloon surface results in effective treatment outcomes.
- No adverse events or additional effects detected at higher dosages.
- **Conclusion:** In.Pact Admiral offers a wide therapeutic window with a high safety margin.
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B Braun: Coronary Data

- **B. Braun** drug-eluting balloon catheter features a matrix coating that is fully bioabsorbable and polymer-free.

- PEPCAD I (the first study to investigate the use of drug-eluting balloons in native lesions in Germany), the SeQuent Please patients (n=120) showed a **5.5% binary restenosis rate and 6.1% MACE after six months**. The researchers noted that previously published rates for DES in small vessel disease were 31.2% restenosis and 18.9% MACE.

- In the ongoing PEPCAD II trial, SeQuent Please is being compared to another manufacturer’s DES in 131 patients.

- Drug eluting balloons experienced only **3.7 percent restenosis and 4.8 percent MACE**, as compared to patients with DES, wherein restenosis was 20.8 percent with 22.0 percent MACE rate.
DEB: Is It Worth It?

  - Probably beneficial for periphery
  - Nothing better to offer.
- Coronary and re-stent issues:
  - Again more data needed
It All Comes Down to DATA

Pre-Clinical and Clinical Trials

2. Speck U et al. Radiology 2006; 240: 56-64
DEB: Is It Worth It?

- More Research needed.
  - Multi-country, multiple sites, randomized needed
- What will the 3-5 year data bring?
- Will governments/insurance co. pay for the increased cost?
Thank you
Bottom Lines

- **Unanswered Questions:**
  - Are DEB more effective than Conventional Stents?
  - Are they more effective than drug eluting stents?
  - Do DEB work in the SFA and Periphery?
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  German company **EuroCor**, a subsidiary of Opto Circuits (India), has developed the DIOR (Dilation of Restenosis) paclitaxel-eluting balloon catheter designed for treatment of coronary in-stent restenosis.

  The company notes that the greatest benefits are achieved with three months of antiplatelet therapy.

  DIOR is treated like a typical PTCA catheter, is inflated to the lesion site up to 60 seconds for full drug release, and may be inflated several times. A first inflation of 20 seconds leads to 35% drug release; a second inflation of 20 seconds releases another 35% of paclitaxel.
Players

Elutax paclitaxel-eluting balloon for coronary arteries (de novo, small vessels, in-stent restenosis) and small vessels below the knee.

The structural coating of Elutax is such that the drug is encased on the surface of the balloon and 20% of the total drug is released from the balloon after each inflation.

- Aachen Resonance
Players

- EuroCor/Opto Circuits

The devices use an older tubular (nitinol) mesh braid.

According to Genesis, the drug coating on the balloon and/or mesh braid will cover more area than with stents and the drug on the braid will be deposited into microfractures or crevasses adjacent to the vessel wall.

- Genesis Technologies
Bottom Lines

- Are DEB more effective than conventional angioplasty? Probably.
Schering AG (now part of Bayer AG) and B. Braun Melsungen AG appeared first on the scene by co-licensing Scheller et al’s DEB coating technology and process.
Will Governments Reimburse DEB?

- US did not reimburse cutting balloon technology
- How much European data required to help launch US trials
EuroCor Data

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- Companies which have developed drug-coated balloon catheters include:
  - EuroCor/Opto Circuits
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  - Possis Medical
  - B. Braun Melsungen
  - Aachen Resonance
  - Genesis Technologies
  - DSM Biomedical (in partnership with Caliber Therapeutics).
  - Invatec (In.Pact Admiral 0.035” system)
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Animal Studies in SFA

- Neointimal proliferation and stenosis were induced by overstretch and stenting of 40 peripheral arteries in 20 pigs. Paclitaxel was administered locally during PTA using coated balloons (n = 20) or dissolved in contrast medium (n = 10). Conventional balloons and contrast medium were used in a control group (n = 10). Reangiography with quantitative analysis was performed after 5 weeks.

- RESULTS: On reangiography diameter stenosis and late lumen loss were significantly reduced by both methods of local drug delivery compared with control group; minimal luminal diameter was significantly larger in the treatment groups.

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Stent Re-Stenosis

- One-quarter of DESs can result in restenosis. Conventional stent-in-stent drug-delivery techniques used in restenosis may result in arterial stiffness.
- DEB offers a novel technique for drug delivery to the in-stent lesion, which minimizes arterial stiffening and provides homogenous drug delivery to 100% of the in-stent coronary lesion. Furthermore when treated with DEB, in-stent coronary lesions remain accessible for re-intervention and show reduced repeat in-stent restenosis versus conventional stent-in-stent interventions.