Drug-Eluting Balloon: An Overview of Clinical Evidences on Safety and Effectiveness

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ABSTRACT

Background: Recent advances in the intravascular diseases have led to the entrance of drug-eluting balloon (DEB) technology. The DEB is a relatively new and easier way to treat vascular stenosis. In this study as part of rapid health technology assessment, we aimed to assess this technology in comparison with drug-eluting stent (DES), uncoated balloon and bare-metal stent in terms of efficacy and safety in common indications by reviewing available clinical evidences.

Methods: In order to evaluate the safety and effectiveness of DEB, a non-systematic review on electronic databases including Cochrane, PubMed, INAHITA, CRD, Scopus, Medline, Trip database, and Google Scholar was conducted by keywords: “balloon angioplasty,” “drug eluting balloon,” “drug eluting stent.”

Results: DEBs could be suggested as a more effective and safe intervention compared with uncoated balloon angioplasty in patients with in-stent restenosis and peripheral vascular disease however there were not adequate evidences supporting the superiority of DEB compared with DES. There were not also adequate evidences comparing DEB with uncoated balloons or DES for decision making about de novo lesion and small vessel arteries.

Conclusion: Conducting an economic evaluation to assess the cost effectiveness of this technology has to be also taken into account for more adequate decision making.

Keywords: Drug-eluting balloon, efficacy, safety, review

1. Introduction

Cardiovascular diseases impose significant burden on societies [1]. In order to manage this and other areas of health care more efficiently, there is an inevitable need for applying an evidence-based policy making approach regarding available and emerging interventions [2].

One of the most progressive and expanding areas in cardiovascular interventional treatments is angioplasty in which balloon angioplasty was one of the first technologies. However, it was faced with some undesirable consequences including: elastic recoil and restenosis by cell proliferation as limiting factors in using this technology. To overcome such constraints, stent technology was developed. Although coronary stenting was able to tackle dissections and elastic recoil and also remove negative remodeling [3,4], risk of stent thrombosis and “neointimal hyperplasia” leading to in-stent restenosis (ISR) remained as major limitations for its use [5].

Addressing the stents’ limitations, drug-eluting stent (DES) was developed as one of the most significant clinical advances in the interventional cardiology which has reduced the incidence of ISR [6,7] and target-lesion revascularization (TLR) [8] however the recurrence rate of ISR is still a limitation [8,9]. This technology could also induce vascular wall inflammation and late thrombosis mainly due to the polymer used in its structure [10] and because of that, dual antiplatelet therapy (aspirin and clopidogrel) is necessary for a long time by this technology. This antiplatelet therapy may put patients on the risk of hemorrhage and vascular complications and need monitoring at the same time [11].

Recent advances in the intravascular diseases have led to the entrance of drug-eluting balloon (DEB) technology. The DEB is a relatively new and easier way to treat vascular stenosis, which was introduced in 2003. DEB is a balloon-like device which enters to the blocked arteries and then will be inflated to release anti-proliferative drugs [12,13]. These balloons would be removed from the vessels when the drug was penetrated to their wall. DEB has been proposed recently as a potential alternative to DES for dealing with stenosis. Paclitaxel is considered as the first medication for DEB because of its rapid uptake and long effects [14,15].

Considering growing demand for using DEB technology in Iran by cardiologists, we aimed to assess this technology in comparison with other available ones including DES in terms of efficacy and safety in all probable indications by reviewing available clinical evidences.

2. Methods

In order to evaluate the safety and effectiveness of DEB in comparison with other available interventions, a non-systematic review of published studies was conducted on electronic databases including Cochrane, PubMed, INAHITA, CRD, Scopus, Medline, Trip database, and Google Scholar by keywords: “balloon angioplasty”, “drug-eluting balloon”, “drug-eluting stent”. All types of clinical trials, systematic reviews and meta-analyses and observational studies between 1990 and 2012 with at least one arm of DEB were included in our study.

3. Results

Totally 10 studies were included in our analysis in which all of them were randomized clinical trial except one that was a prospective registry. The general characteristics of these studies are summarized in table 1. Among these studies, Scheller et al. (2008) [18] is re-analysis of Scheller et al. (2006) [17] with more patients and reporting follow-up results to assess long term efficacy and safety of interventions. The included studies were categorized into following four interventions that DEB had been evaluated in one or more of them.

3.1. Effectiveness and safety evidences of DEB technology in ISR

A1. Cuculi et al. [16] evaluated the effectiveness of DEBs in ISR and de novo lesion. It was a prospective registry study in which 12-month rates of clinically driven TLR as the outcome of interest was reported 5.4% and 4.8% (P = 1.000) in the ISR and de novo lesion group, respectively. The results also indicated that in the ISR and de novo lesion groups of patients with vessel diameter >2.75 mm, the TLR rate was 4.2% and 2.2%, respectively and in the ISR and de novo lesion groups with vessel diameter >2.75 mm, the TLR rate was 9.5% and 6.2%, respectively.
The drug-coated balloon was superior to the DES with respect to the primary end point. This intervention was also associated with fewer adverse clinical events despite shorter period of dual anti-platelet therapy; however, it was not statistically significant.

AS. In a prospective, single-blind, multicenter, randomized trial (PEPCAD-DES study), paclitaxel coated balloon angioplasty and uncoated balloon angioplasty was compared with each other in DES restenosis located in a native coronary artery [20]. The late lumen loss as the primary outcome indicated superiority of DEB versus uncoated balloons (0.43 ± 0.61 mm vs. 1.03 ± 0.77 mm [P = 0.001]). Restenosis rate was also significantly reduced from 58.1% to 17.2% (P < 0.001) by DEB.

### 3.2. Effectiveness and safety evidences of using DEB in peripheral vascular disease (PVD)

#### B1. In THUNDER study conducted by Tepe et al. [21], effectiveness of uncoated balloon catheter, paclitaxel-coated balloon and uncoated balloon with paclitaxel dissolved in contrast medium were compared in 154 patients with stenosis or occlusion of femoropopliteal artery. In this multicenter study which had been conducted on 154 patients, late lumen loss after 6 months was considered as a primary outcome, and the secondary outcome was TLR. In term of late lumen loss, the difference between patients treated with paclitaxel DEBs and uncoated balloon group was 1.30 (95% CI 0.65-1.95, P < 0.001). In term of TLR at 24 months, the percent difference between paclitaxel DEB group and simple balloon group was 37 (95% CI 21-54, P < 0.001).

In term of safety, during the intervention, Tepe study has reported three serious complications (6%) in the DEB group, and two serious complications in the simple balloon group was 37 (95% CI 21-54, P < 0.001) by DEB.

### 3.3. Drug-eluting balloon in iliofemoral artery disease (IFAD)

#### B2. In the FemPac study [22], 87 patients with femoropopliteal peripheral artery disease were randomly assigned to two groups of DEB...
and conventional uncoated balloons. After 6 months, late lumen loss in the DEB group was significantly lower than simple balloon group (0.5 ± 1.1 vs. 7.5 ± 1.1 mm; P = 0.031). The percentage of binary restenosis was also significantly lower in paclitaxel coated balloon groups compared with uncoated balloon (19% vs. 47%; P = 0.035). TLR rate in the DEB group was 7% and in the conventional balloon group was 33% (P = 0.0024).

B3. In an international, multicenter, randomized, single-blind study [23] to evaluate the angiographic and clinical outcomes of T-stenting technique in three groups of DEB plus bare-metal stent (BMS), BMS, and DES, 117 patients with coronary bifurcation lesions were classified into three groups. Late luminal loss after 6 months as the primary outcome was not statistically significant different between combination of DEB and bare-metal stent (BMS) with BMS. Also in secondary outcomes including binary restenosis after 6 months and major cardiac events after 12 months, including death, myocardial infarction, and target vessel revascularization no statistically significant difference was observed between these two groups.

The results indicate that pre-treatment with DEBs by provisional T-stenting technique has no superiority to BMS, but angiographic results of DESs comparison with BMS are significantly different.

3.3. Effectiveness and safety evidences of DEB in small vessel arteries

One study has been published in this field [24]. In this study (PICCOLETO study), 57 patients with small coronary artery disease were enrolled. Both DEB and DES technology with paclitaxel were evaluated. This study has been finished early, due to a high priority of one arm over the other. The incidence of stenosis was 43.6% in the DEB group and 24.3% in the DES group (P = 0.029). The angiographic restenosis rate in DEB and DES was 10.3% and 32.1%, respectively (P = 0.043). Major cardiovascular events were reported 35.7% in DEBs and 13.8% in DES group (P = 0.054).

3.4. Effectiveness and safety evidences of DEB in de novo lesions

In a prospective, single-blind multicenter randomized clinical trial [25], 120 patients with a de novo lesion in a native coronary artery were randomly assigned to treatment with paclitaxel-coated balloon plus endothelial progenitor cell capturing (EPC) stent or EPC stent alone. In-stent late lumen loss as the primary outcome in DEB plus EPC group was 0.34 ± 0.45 mm versus 0.88 ± 0.48 mm (P < 0.001) in EPC alone group. The re-stenosis rate was also lower in DEB plus EPC group (23.2% to 5.1% (P = 0.006)). This study concluded paclitaxel-coated balloon plus EPC stent implantation as superior to EPC stent implantation alone for treatment of de novo coronary artery disease.

4. Discussion

In this study, the clinical evidences on safety and efficacy of DEB were reviewed as part of a rapid health technology assessment. Considering this review result, DEBs could be suggested as more or similar effective and safe intervention (regarding different studies and outcomes) compared with uncoated balloon angioplasty in patients with ISR and PVD however there were not enough evidences supporting the superiority of DEB compared with DES. There is not also enough evidences for making decision about using DEB in small vessel restenosis and de novo lesions. Conducting an economic evaluation to assess the cost effectiveness of this technology has to be also taken into account for more adequate decision making.

5. Conclusion

Considering this review result, DEBs could be suggested as more or similar effective and safe intervention (regarding different studies and outcomes) compared with uncoated balloon angioplasty in patients with ISR and PVD however there were not enough evidences supporting the superiority of DEB compared with DES. There is not also enough evidences for making decision about using DEB in small vessel restenosis and de novo lesions. Conducting an economic evaluation to assess the cost effectiveness of this technology has to be also taken into account for more adequate decision making.

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