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LIST DO REDAKCJI / *LETTER TO THE EDITOR*

Deciphering bioresorbable stent thrombosis: investigating the mechanisms

Badanie mechanizmów prowadzących do zakrzepicy w stencie bioresorbowalnym

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Ουκ εν τω πολλω το ευ αλλα εν τω ευ το πολυ
(Ouk en tō Pollo to aef, but en to aef to poly)
"Not many is the good, but in the good, the many"
Aristotle (384-322 B.C.)

In the first Polish, large-scale, national, 'real world' registry concerning the use of bioresorbable scaffolds, the results were characterised as excellent but in a properly selected group of patients and with appropriate lesion preparation [1]. However, in a recent interesting document compiled by the group of experts on the current knowledge of advantages and limitations of these devices some serious shortcomings were revealed that should be taken into consideration [2].

Similarly, the increased risk of a bioresorbable scaffold or stent thrombosis and other thrombotic events at mid- and long-term follow-up with the use of such devices have been attributed to numerous potential factors, totally 16. They include (alphabetically): acute disruption, device degradation, early discontinuation of dual antiplatelet therapy, edge-related progression, incomplete lesion coverage, late discontinuity (abrupt loss on longitudinal scaffold between two adjacent frames), malposition, neoatherosclerosis, peristrut low-intensity area, poor scaffold expansion, recoil, restenosis, strut thickness, uncovered strut, under-deployment, and very small vessel.

All the above remind us of Aristotle's dictum: "many is not good, but in the good the many", as well as the English proverb "too many cooks spoil the broth".

We are wondering, therefore, why, in all published studies, meta-analyses, reports, editorials, and comments, no attention has been focused on the following pathophysiological associations that we regard as essential aetiological factors, at least in some instances, concerning bioresorbable scaffold safety and efficacy at mid- and long-term follow-up including the much-feared scaffold thrombosis.

The Absorb bioresorbable scaffold is composed of a bioresorbable poly L-lactide (PLLA) skeleton coated with bioresorbable PLLA, four platinum marker beads, by two, at both scaffold ends for visualisation and mTOR inhibitor everolimus. Both polymers are metabolised to lactic acid that finally dissolves into carbon dioxide and water via the Krebs cycle.

These components and metabolites have been associated with pathophysiological consequences leading to thrombosis, as follows: poly L-lactide gel injections have been incriminated for intense inflammatory reaction, especially the low-molecular weight [3], tissue granulomatous reactions [4], hypersensitivity reactions, especially in orthopaedics [5], and papules and nodules infiltrated by multinucleated giant cells with unhydrated birefringent PLLA crystals [6].

Lactic acid itself reduces the surrounding tissue pH, which could trigger inflammatory and foreign body reactions, which stimulate sensory neurons to cause similar pain as in coronary syndromes [7], and induce thrombosis [8].

Carbon dioxide can enhance acidosis, which could cause thrombosis by reducing heparin potency as has been reported in thorax surgery [9].

Everolimus substance has been associated with hypersensitivity pneumonitis, atopic dermatitis, exanthema, and generalised as well as lingual angioedema, occasionally fatally [10]. Finally, platinum anions and taxanes have been associated with hypersensitivity reactions that have been confirmed by skin tests [11].

Other recent meta-analyses [12] have been referred to the recent United States Food and Drug Administration (FDA)

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safety alert for the Absorb BVS (Abbott), but they have not referred to information sheets included in the commercial packages, the special product characteristics, or to the FDA safety alert that clearly states that these devices are contraindicated in patients sensitive to materials used in the device (poly L-lactide, platinum, everolimus), contrast media, aspirin, and antiplatelet agents [13].

Although it is hard to make improvements in anything without understanding in detail its shortcomings at first, we suggest the following: improvement of the current device technology, increased experience in performing the procedure, inventing methods to make the currently used materials inert, discovering new inert materials, and strict adherence to FDA alerts could solve these dangerous shortcomings.

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References

1. Rzeszutko Ł, Siudak Z, Włodarczak A, et al. Use of bioresorbable vascular scaffolds in patients with stable angina and acute coronary syndromes. Polish National Registry. Kardiol Pol. 2014; 72(12): 1394–1399, doi: 10.5603/KP.a2014.0147, indexed in Pubmed: 25001567.
2. Reczuch K, Milewski K, Wąsek W, et al. [Bioresorbable scaffolds in the treatment of coronary artery disease. Expert consensus statement of the Association of Cardiovascular Interventions of the Polish Cardiac Society (ACVI PCS)]. Kardiol Pol. 2017; 75(8): 817–835, doi: 10.5603/KP.2017.0160, indexed in Pubmed: 28819961.
3. Lincoff AM, Furst JG, Ellis SG, et al. Sustained local delivery of dexamethasone by a novel intravascular eluting stent to prevent restenosis in the porcine coronary injury model. J Am Coll Cardiol. 1997; 29(4): 808–816, indexed in Pubmed: 9091528.
4. Alijotas-Reig J, Garcia-Gimenez V, Vilardell-Tarres M. Late-onset immune-mediated adverse effects after poly-L-lactic acid injection in non-HIV patients: clinical findings and long-term follow-up. Dermatology. 2009; 219(4): 303–308, doi: 10.1159/000243804, indexed in Pubmed: 19797889.
5. Mastrokalos DS, Paessler HH. Allergic reaction to biodegradable interference poly-L-lactic acid screws after anterior cruciate ligament reconstruction with bone-patellar tendon-bone graft. Arthroscopy. 2008; 24(6): 732–733, doi: 10.1016/j.arthro.2006.12.029, indexed in Pubmed: 18514119.
6. Janjua TA. Role of massage in preventing formation of papules and nodules after injecting poly-L-lactic acid. JAMA Facial Plast Surg. 2014; 16(6): 457, doi: 10.1001/jamafacial.2014.1173, indexed in Pubmed: 25375414.
7. Immke DC, McCleskey EW. ASIC3: a lactic acid sensor for cardiac pain. Scientific World Journal. 2001; 1: 510–512, doi: 10.1100/tsw.2001.254, indexed in Pubmed: 12805843.
8. Dirkmann D, Hanke AA, Görlinger K, et al. Hypothermia and acidosis synergistically impair coagulation in human whole blood. Anesth Analg. 2008; 106(6): 1627–1632, doi: 10.1213/ane.0b013e31817340ad, indexed in Pubmed: 18499589.
9. Gorter KAM, Stehouwer MC, Van Putte BP, et al. Acidosis induced by carbon dioxide insufflation decreases heparin potency: a risk factor for thrombus formation. Perfusion. 2017; 32(3): 214–219, doi: 10.1177/0267659116677307, indexed in Pubmed: 27789847.
10. Kounis NG, Koniari I, Roumeliotis A, et al. Thrombotic responses to coronary stents, bioresorbable scaffolds and the Kounis hypersensitivity-associated acute thrombotic syndrome. J Thorac Dis. 2017; 9(4): 1155–1164, doi: 10.21037/jtd.2017.03.134, indexed in Pubmed: 28523173.
11. Brault F, Waton J, Poreaux C, et al. [Hypersensitivity to platinum salts and taxanes: The value of skin tests and tolerance induction procedures]. Ann Dermatol Venereol. 2017; 144(11): 685–695, doi: 10.1016/j.annder.2017.05.016, indexed in Pubmed: 28760501.
12. Zhang XL, Zhu QQ, Kang LN, et al. Mid- and long-term outcome comparisons of everolimus-eluting bioresorbable scaffolds versus everolimus-eluting metallic stents: a systematic review and meta-analysis. Ann Intern Med. 2017; 167(9): 642–654, doi: 10.7326/M17-1101, indexed in Pubmed: 29049539.
13. https://www.fda.gov/medicaldevices/productsandmedicalprocedures/deviceapprovalsandclearances/recently-approveddevices/ucm509951.htm. (Accessed 24 November).

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