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Editorial

Heparin induced Thrombocytopenia and its Tomorrow - 8

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EDITORIAL

Heparin Induced Thrombocytopenia (HIT) is an unwanted immunological reaction to the usage of heparin as an anticoagulant yielding thrombosis rather than the positive anticoagulant effects. The patients under heparin usage for several days are prone to HIT and HIT is connected to the risk of life threatening thrombosis by virtue of intravasal platelet aggregation. The destructive effects of HIT constitute thrombocytopenia and the thromboembolic complications risks in veins and arteries. Normally, HIT symptoms are observed within 4 to 15 days after initiation of heparin therapy and platelet count declines to less than half of the initial value [1].

Under heparin therapy, complexes are produced between negatively charged heparin molecule and the positively charged platelet factor 4 (PF4). Some patients react to the stimulus and lead to the production of antibodies against the heparin/PF4 complex. If the antibodies pertain to the IgG class, the patients are victim of developing the clinically destructive HIT. At molecular levels, specific IgG antibodies react with the PF4/heparin complex to form the PF4/ heparin/IgG immune complexes which bind with the FcRIIa receptors on platelets [2]. The outcome is platelet activation, accumulation and decreased platelet counts. The sequences potentially proceed in the form of thrombus formation and embolism due to the interaction with plasmatic pro coagulative stimulation. Therefore the intended positive anticoagulant effect of heparin is reversed into damaging and life threatening. As the thrombosis and reduction in platelet counts are common symptoms in several other diseases, specific assays for HIT diagnostics are prerequisite for adequate treatment [3].

Although functional HIT diagnostics have emerged in clinics department, yet the assays are challenging and need high expertise. Normal HIT diagnosis should not be conducted in laboratories having limited experiences [4], while alternatives are lacking. Safe HIT diagnosis is substantial and essential in the perspectives of the patient's health and cost-effectiveness. A German investigation conducted by Wilke et al [5] divulged that every clinical case of HIT put an average of 9000 Euro of extra costs because of prolonged hospital stay and the costly substitute anticoagulants. Furthermore the alternative anticoagulants for instance argatroban, lepirudin or danaparoid have higher bleeding risks than heparin and are comparatively challenging for monitoring and antagonizing [6]. The recent efforts in the perspectives of HIT diagnostics include the investigations by Hussain et al [7,8], Sachs et al [9], Althaus et al [10], Morel-Kopp et al [11], Solano et al [12], Garritsen et al [13] and Cuker et al [14].

Novel technologies [15] and bio-mimetic approaches [16,17] are a powerful support for the point of care (POC) settings for HIT and relevant studies. For instance, quartz crystal microbalance with dissipation (QCM-D) is an interesting transducer due its unique properties for bio sensing e.g. pharmaceuticals [18,19], clinical investigations etc [20]. The transducer [21,22] has been demonstrated as a proof of principles for HIT [7,8] and haemostatic assays, for instance thromboplastin time (PT) [23,24], activated partial thromboplastin time (aPTT) [25,26], thrombine time (TT) [27], "Prothrombinase induced Clotting Time" (PiCT), [28,29] coagulation disorders [30], and relevant applications [31,32].

REFERENCES

1. Greinacher A, Levy JH. HIT happens: diagnosing and evaluating the patient

- with heparin-induced thrombocytopenia. Anesth Analg. 2008; 107: 356-358. https://goo.gl/hxevKf
- Kelton JG, Sheridan, D, Santos A, Smith J, Steeves K, Smith C. et al. Heparin-induced thrombocytopenia: laboratory studies. Blood. 1988; 72: 925-930. https://goo.gl/qghC9t
- Greinacher A, Juhl D, Strobel U, Wessel A, Lubenow N, Selleng K. et al. Heparin-induced thrombocytopenia: a prospective study on the incidence, platelet-activating capacity and clinical significance of anti platelet factor 4/ heparin antibodies of the IgG, IgM, and IgA classes. J Thromb Haemost. 2007; 5: 1666-1673. https://goo.gl/8jaDJx
- Eichler P, Budde U, Haas S, Kroll H, Loreth RM, Meyer O. et al. First workshop for detection of heparin-induced antibodies: validation of the heparin-induced platelet-activation test (HIPA) in comparison with a PF4/heparin ELISA. Thromb. Haemost. 1999; 81: 625-629. https://goo.gl/KEKdhG
- Wilke T, Tesch S, Scholz A, Kohlmann T, Greinacher A. The costs of heparininduced thrombocytopenia: a patient-based cost of illness analysis. J Thromb Haemost. 2009; 7: 766-773. https://goo.gl/MGQA8d
- Linkins LA, Dans AL, Moores LK, Bona R, Davidson BL, Schulman S. et al. Treatment and prevention of heparin-induced thrombocytopenia: Antithrombotic Therapy and Prevention of Thrombosis, Am. Coll. Ches. Phys. Evid.-B. Clin. Pract. Guidelines. Chest. 2012; 141: 495-530. https://goo.gl/kgLonZ
- Hussain M, Gehring, FK, Sinn S, Northoff H. A straightforward detection of HIT type II via QCM-D. UK J. Pharm. Biosci. 2015; 3: 18-29. https://goo.gl/5DXYvd
- Hussain M, Northoff H, Gehring FK. Detection of HIT antibody dependent platelet aggregation using novel surface imprinting approach. Talanta. 2016; 147: 1-7. https://goo.gl/UV4L23
- Sachs UJ, Hesberg JV, Santoso S, Bein G, Bakchoul T. Evaluation of a new nanoparticle-based lateral-flow immunoassay for the exclusion of heparininduced thrombocytopenia (HIT). Thromb Haemost. 2011; 106: 1197-1202. https://goo.gl/V7AgSc
- Althaus K, Hron G, Strobel U, Abbate R, Rogolino A, Davidson S. et al. Evaluation of automated immunoassays in the diagnosis of heparin induced thrombocytopenia. Thromb Res. 2013: 131: 85-90. https://goo.gl/aHQc2e
- Morel-Kopp MC, Tan CW, Brighton TA, McRae S, Baker R, Tran H. et al. Validation of whole blood impedance aggregometry as a new diagnostic tool for HIT: results of a large Australian study. Thromb Haemost. 2012; 107: 575-583. https://goo.gl/7akH6K
- Solano C, Mutsando H, Self M, Morel-Kopp MC, Mollee P. Using Hit alert flow cytometry to detect heparin-induced thrombocytopenia antibodies in a tertiary care hospital. Blood Coagul Fibrinolysis. 2013; 24: 365-370. https://goo.gl/DrC1o2
- Garritsen, HS, Probst-Kepper M, Legath N, Eberl W, Samaniego S, Woudenberg J. et al. High sensitivity and specificity of a new functional flow cytometry assay for clinically significant heparin-induced thrombocytopenia antibodies. Int J Lab Hematol. 2014; 36: 135-43. https://goo.gl/NBNY8i
- Cuker A, Rux AH, Hinds JL, Cruz MD, Yarovoi SV, Brown IA, et al. Novel diagnostic assays for heparin-induced thrombocytopenia. Blood. 2013; 121: 3727-32. https://goo.gl/fUX4qX
- Hussain M. QCM-D for haemostasis: Current status and future: a review. UK J Pharm Biosci. 2016; 4: 121-132. https://goo.gl/P4F8Xx
- Hussain M, Wackerlig J, Lieberzeit PA. Biomimetic strategies for sensing biological species. Biosensors. 2013; 3: 89-107. https://goo.gl/jqLjUs
- Hussain M. Molecular imprinting as multidisciplinary material science: Today and tomorrow. Int J Adv Mater. Res. 2015; 1: 132-154. https://goo.gl/FAPWKn
- Hussain M, Iqbal N, Lieberzeit PA. Acidic and basic polymers for molecularly imprinted folic acid sensors-QCM studies with thin films and nanoparticles. Sens Act B. 2013; 176: 1090-1095. https://goo.gl/gr6Z8s
- Hussain M, Wendel HP, Gehring FK. Imprinting of pharmaceuticals. Int J Pharma Anal Acta. 2017; 1: 013-014. https://goo.gl/ACVNN9
- Hussain M, Wackerlig J, Lieberzeit PA. Biomimetic strategies for sensing biological species. Biosensors. 2013; 3: 89-107. https://goo.gl/GyA18m
- 21. Müller L, Sinn S, Drechsel H, Ziegler C, Wendel HP, Northoff H. et al.

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- Investigation of prothrombin time in human whole-blood samples with a quartz crystal biosensor. Anal Chem. 2010; 82: 658-663. https://goo.gl/BBYKML
- Sinn S, Müller L, Drechsel H, Wandel M, Northoff H, Ziemer G, et al. Platelet aggregation monitoring with a newly developed quartz crystal microbalance system as an alternative to optical platelet aggregometry. Analyst. 2010; 135: 2930-2938. https://goo.gl/4PJn5H
- 23. Hussain M, Sinn S, Zeilinger M, Northoff H, Lieberzeit PA, Gehring FK. Blood coagulation thromboplastin time measurements on a nanoparticle coated quartz crystal microbalance biosensor in excellent agreement with standard clinical methods. J. Biosens Bioelectron. 2013; 4: 139. https://goo.gl/ebsCY4
- 24. Hussain M. Prothrombin Time (PT) for human plasma on QCM-D technique: A better alternative to 'gold standard. UK J Pharm Biosci. 2015; 3: 01-08. https://goo.gl/4aJU49
- Hussain M. aPTT: 1st recognition for human whole blood on QCM-D technique. UK J Pharm Biosci. 2015; 3: 49-55. https://goo.gl/pSr8CF
- 26. Hussain M, Northoff H, Gehring FK. QCM-D providing new horizon in the

- domain of sensitivity range and information for haemostasis of human plasma. Biosens Bioelectron. 2015; 66: 579-584. https://goo.gl/HV2GTf
- Hussain M. Shortened 'thrombin time' monitoring on QCM-D: A better substitute of 'gold standard'. UK J Pharm Biosci. 2016; 4: 20-26. https://goo.gl/DXuj7T
- 28. Hussain M. PiCT: 1st recognition for human whole blood on QCM-D technique. UK J Pharm Biosci. 2015; 3: 01-08. https://goo.gl/NRGq9m
- Hussain M. A simultaneous monitoring of coagulation time and fibrinogen via PiCT on QCM-D. UK J Pharm Biosci. 2016; 4: 27-25. https://goo.gl/C7TFwh
- Hussain M, Wendel HP, Gehring FK. Coagulation disorders beyond technicalities. Thromb Haemost Res. 2017; 1: 1001. https://goo.gl/5gJ1uG
- 31. Hussain M. 'Argatroban' monitoring in human plasma: aPTT and PiCT studies on QCM-D vs 'gold standard'. UK J Pharm Biosci. 2015; 3: 42-48. https://goo.gl/RqbkfL
- 32. Hussain M. Ultra-sensitive detection of heparin via aPTT using plastic antibodies on QCM-D platform. RSC Adv. 2015; 5: 54963-54970. https://goo.gl/csR1TG