Surveillance of Scientific Literature (ARG LIT Service 2020-09)

- **Report Date:** 30.09.2020

New Literature on Argatroban and Related Topics

- **Source:** National Center for Biotechnology Information (NCBI) at the U.S. National Library of Medicine (NLM).

- **Search:** "Argatroban"
  "Heparin-induced Thrombocytopenia"
  "Fondaparinux"

In the following the result of the routine literature search on Argatroban and related topics is given. After selection of action please return to sender.

Mainz, 30.09.2020

What's New for Argatroban and Related Topics in September 2020?

25 September 2020

Full text on file	**Argatroban**

Anticoagulation Strategies in Extracorporeal Circulatory Devices in Adult Populations.

Kato C, Oakes M, Kim M, Desai A, Olson SR, Raghunathan V, Shatzel JJ.

Eur J Haematol. 2020 Sep 18. doi: 10.1111/ejh.13520. Epub ahead of print.

Abstract:Extracorporeal circulatory devices such as hemodialysis and extracorporeal membrane oxygenation can be lifesaving; however, they are also prone to pathologic events including device failure, venous and arterial thrombosis, hemorrhage, and an accelerated risk for atherosclerotic disease due to interactions between blood components and device surfaces of varying biocompatibility. While extracorporeal devices may be used acutely for limited periods of time (e.g., extracorporeal membrane oxygenation, continuous venovenous hemofiltration, therapeutic apheresis), some patients require chronic use of these technologies (e.g., intermittent hemodialysis and left ventricular assist devices). Given the substantial thrombotic risks associated with extracorporeal devices, multiple antiplatelet and anticoagulation strategies - including unfractionated heparin, low-molecular-weight heparin, citrate, direct thrombin inhibitors, and direct oral anticoagulants have been used to mitigate the thrombotic milieu within the patient and device. In the following manuscript, we outline the current data on anticoagulation strategies for commonly used extracorporeal circulatory devices, highlighting the potential benefits and complications involved with each.

Keywords: Dialysis; ECMO; Hemorrhage; Thrombosis; anticoagulation.

PMID: 32946632 Free full text

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25 September 2020

Full text on file	**Argatroban**

Use of Edoxaban for the Treatment of Heparin-Induced Thrombocytopenia.

Kanamoto R, Hiromatsu S, Anegawa T, Sakurai K, Yoshida S, Shintani Y, Otsuka H, Tobinaga S, Tanaka H.

Case Rep Vasc Med. 2020 Sep 7; 2020:2367095. doi: 10.1155/2020/2367095.

Abstract: Heparin-induced thrombocytopenia (HIT) is a life-threatening adverse drug reaction of heparin therapy, which increases a patient's risk of developing venous and/or arterial thromboembolism. HIT should be treated through discontinuation of heparin and administration of nonheparin anticoagulants such as argatroban. For long-term anticoagulation, parenteral nonheparin anticoagulants are generally converted to oral treatment with a vitamin K antagonist such as warfarin. Although administration of warfarin is recommended to overlap with a nonheparin anticoagulant for a minimum of 5 days, overlapping with argatroban and warfarin presents high risks of bleeding. We describe a case of HIT treated with edoxaban. A 78-year-old man underwent surgery for esophageal cancer and was administered heparin perioperatively. After surgery, he was diagnosed with HIT and venous thromboembolism. We immediately stopped heparin and initiated parenteral argatroban. The patient was subsequently started on edoxaban without any overlap between the two drugs. The treatment was successful. The treatment of edoxaban following argatroban for HIT could reduce bleeding complications and shorten the length of hospital stay. To the best of our knowledge, this is the first report of the use of edoxaban for HIT treatment.

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25 September 2020

Full text on file	**HIT II**

Rivaroxaban Treatment for Heparin-Induced Thrombocytopenia: A Case Report and a Review of the Current Experience.

Aon M, Al-Shammari O.

Case Rep Hematol. 2020 Sep 3; 2020:8885256. doi: 10.1155/2020/8885256.

Abstract: Heparin-induced thrombocytopenia is a life-threatening complication of exposure to heparin. Heparin-induced thrombocytopenia results from an autoantibody directed against platelet factor 4 in complex with heparin. Heparin-induced thrombocytopenia is traditionally treated with bivalirudin, argatroban, danaparoid, or fondaparinux. Recently, direct oral anticoagulants administration to treat heparin-induced thrombocytopenia has been reported. Direct oral anticoagulants do not cause platelet activation in the presence of heparin-platelet factor 4 antibodies, nor do they provoke autoantibody production. Direct oral anticoagulants offer advantages such as consistent and predictable anticoagulation, oral administration with good patient compliance, and a good safety profile. We report a case of heparin-induced thrombocytopenia with deep venous thrombosis successfully treated with rivaroxaban and review the current experience with rivaroxaban for the treatment of heparin-induced thrombocytopenia.

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25 September 2020

Full text not on file	HIT II

Clinical outcomes of cardiac surgery patients undergoing therapeutic plasma exchange for heparin-induced thrombocytopenia.

Moreno-Duarte I, Cooter M, Onwuemene OA, Ghadimi K, Welsby IJ.

Vox Sang. 2020 Sep 23. doi: 10.1111/vox.13008. Epub ahead of print.

Abstract: Background and objectives: Heparin-induced thrombocytopenia (HIT) is an antibody-mediated condition that leads to thrombocytopenia and possible thrombosis. Patients with HIT who require cardiac surgery pose a challenge as high doses of heparin or heparin alternatives are required to permit cardiopulmonary bypass (CPB). Intraoperative therapeutic plasma exchange (TPE) is a valuable adjunct in the management of antibody-mediated syndromes including HIT. The clinical impact of TPE on thromboembolic events, bleeding and mortality after heparin re-exposure is not well established. We hypothesized that TPE with heparin re-exposure will not lead to HIT-related thromboembolic events, bleeding or increased mortality after cardiac surgery with CPB. Materials and methods: We reviewed 330 patients who received perioperative TPE between September 2012 and September 2017. Results: Twentyfour patients received TPE for HIT before anticipated heparin use for CPB. Most patients were males (79%) scheduled for advanced heart failure therapies. Three patients (12·5%) died within 30 days after surgery but none of the deaths were considered HIT-related. Thromboembolic events (TE) occurred in 3 patients within 7 days of surgery; of those, two were possibly HIT-related. Conclusion: Therapeutic plasma exchange with heparin re-exposure was not strongly associated with HIT-related thrombosis/death after cardiac surgery with CPB.

Keywords: cardiac surgery; heparin; plasma exchange; platelet factor 4; thrombocytopenia.

PMID: 32965049

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25 September 2020

Full text on file	HIT II

Systems-based hematology: highlighting successes and next steps.

May JE, Irelan PC, Boedeker K, Cahill E, Fein S, Garcia DA, Hicks LK, Lawson J, Lim MY, Morton CT, Rajasekhar A, Shanbhag S, Zumberg MS, Plovnick RM, Connell NT.

Blood Adv. 2020 Sep 22;4(18):4574-4583. doi: 10.1182/bloodadvances.2020002947.

Abstract: Systems-based hematology is dedicated to improving care delivery for patients with blood disorders. First defined by the American Society of Hematology in 2015, the idea of a systems-based hematologist arose from evolving pressures in the health care system and increasing recognition of opportunities to optimize the quality and cost effectiveness of hematologic care. In this review, we begin with a proposed framework to formalize the discussion of the range of initiatives within systems-based hematology. Classification by 2 criteria, project scope and method of intervention, facilitates comparison between initiatives and supports dialogue for future efforts. Next, we present published examples of successful systems-based initiatives in the field of hematology, including efforts to improve stewardship in the diagnosis and management of complex hematologic disorders (eg, heparin-induced thrombocytopenia and thrombophilias), the development of programs to promote appropriate use of hematologic therapies (eg, blood products, inferior vena cava filters, and anticoagulation), changes in care delivery infrastructure to improve access to hematologic expertise (eg, electronic consultation and disorder-specific care pathways), and others. The range of projects illustrates the broad potential for interventions and highlights different metrics used to quantify improvements in care delivery. We conclude with a discussion about future directions for the field of systems-based hematology, including extension to malignant disorders and the need to define, expand, and support career pathways.

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18 September 2020

Full text not on file	Argatroban

Monitoring and Dosing of Argatroban in a Patient With Antiphospholipid Syndrome

Dooling K, Haan B

Hospital Pharmacy. 2020; August 1. doi: 10.1177/0018578720946765

Abstract: Background: This case reports outlines argatroban dosing and necessary dose adjustments in a 56 year-old male with a past medical history of antiphospholipid syndrome and heparin-induced thrombocytopenia. Method: Argatroban was initiated as a fixed dose of 0.5 µg/kg/min with all initial aPTTs above goal. Argatroban was held for a procedure and re-initiated at 0.25 µg/kg/min. The dose was increased or decreased by 25% from the current rate based on supratherapeutic and subtherapeutic aPTTs, respectively. Results: The patient remained on argatroban for 6 total days, while achieving goal aPTT levels with no VTE or bleeding events. Conclusion: Our patient represents the first reported case of monitoring argatroban with aPTTs in an individual with APS.

Keywords anticoagulants, blood, disease management, monitoring drug therapy

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18 September 2020

Full text on file	**Argatroban**

Cytokine adsorption in a patient with severe coronavirus disease 2019 related acute respiratory distress syndrome requiring extracorporeal membrane oxygenation therapy: A case report.

Rieder M, Zahn T, Benk C, Lother A, Bode C, Staudacher D, Duerschmied D, Supady A.

Artif Organs. 2020 Sep 14. doi: 10.1111/aor.13805. Epub ahead of print.

PMID: 32929761 Free full text

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18 September 2020

Full text on file	HIT

Soluble glycoprotein VI is a predictor of major bleeding in patients with suspected heparin-induced thrombocytopenia.

Pishko AM, Andrews RK, Gardiner EE, Lefler DS, Cuker A.

Blood Adv. 2020 Sep 22;4(18):4327-4332. doi: 10.1182/bloodadvances.2020002861.

Abstract: We have shown that patients with suspected heparin-induced thrombocytopenia (HIT) have a high incidence of major bleeding. Recent studies have implicated elevated soluble glycoprotein VI (sGPVI) levels as a potential risk factor for bleeding. We sought to determine if elevated sGPVI plasma levels are associated with major bleeding events in patients with suspected HIT. We used a cohort of 310 hospitalized adult patients with suspected HIT who had a blood sample collected at the time HIT was suspected. Plasma sGPVI levels were measured by using enzyme-linked immunosorbent assay. Patients were excluded who had received a platelet transfusion within 1 day of sample collection because of the high levels of sGPVI in platelet concentrates. We assessed the association of sGPVI (high vs low) with International Society on Thrombosis and Haemostasis major bleeding events by multivariable logistic regression, adjusting for other known risk factors for bleeding. Fifty-four patients were excluded due to recent platelet transfusion, leaving 256 patients for analysis. Eighty-nine (34.8%) patients had a major bleeding event. Median sGPVI levels were significantly elevated in patients with major bleeding events compared with those without major bleeding events (49.09 vs 31.93 ng/mL; P < .001). An sGPVI level >43 ng/mL was independently associated with major bleeding after adjustment for critical illness, sepsis, cardiopulmonary bypass surgery, and degree of thrombocytopenia (adjusted odds ratio, 2.81; 95% confidence interval, 1.51-5.23). Our findings suggest that sGPVI is associated with major bleeding in hospitalized patients with suspected HIT. sGPVI may be a novel biomarker to predict bleeding risk in patients with suspected HIT.

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11 September 2020

Full text on file	**Argatroban**

Intervention in COVID-19 linked hypercoaguable states characterized by circuit thrombosis utilizing a direct thrombin inhibitor.

Seshadri M, Ahamed J, Laurence J.

Thrombosis Update. 2020 Dec;1:100009. doi: 10.1016/j.tru.2020.100009. Epub 2020 Sep 8.

Highlights:

- Circuit thrombosis complicates CRRT in COVID-19 despite standard heparin-based anticoagulation regimens.
- 5 cases of CRRT thrombosis despite heparin-based anticoagulation resolved using a direct thrombin inhibitor, argatroban.
- Changes in fibrinogen levels better reflected response to anticoagulation than did changes in D-dimer levels.
- High fibrinogen levels and decreased anti-thrombin III activity may relate to argatroban superiority in these cases.

Keywords: Thrombotic complications, Fibrinogen, Direct thrombin inhibitor

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11 September 2020

Full text on file	**Argatroban**

Cold agglutinin syndrome as a complication of Covid-19 in two cases.

Jensen CE, Wilson S, Thombare A, Weiss S, Ma A.

Clin Infect Pract. 2020 Oct;7: 100041. doi: 10.1016/j.clinpr.2020.100041. Epub 2020 Sep 9.

Abstract: Background: Cold agglutinins are autoantibodies against RBC antigens, leading to hemolysis at less-than-physiological temperatures through complement fixation. Production can be triggered by infections, resulting in secondary cold agglutinin syndrome (CAS). This syndrome has been classically described in the setting of Mycoplasma pneumoniae infection, as well as with several viral pathogens. Cases: Here, we present two cases of cold agglutinins identified in the context of Covid-19 in critically ill patients treated at our institution. Each case was characterized by little in-vivo hemolysis, but these antibodies complicated laboratory assessment and renal replacement therapy. Management included anticoagulation and warming of dialysis circuit. Conclusions: Despite minimal in-vivo hemolysis, these antibodies are of clinical significance given their implications for laboratory assessment and renal replacement therapy, particularly with the frequency of multi-organ system dysfunction associated with severe Covid-19.

Keywords: Cold agglutinins; Covid-19; Hemolytic anemia.

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11 September 2020

Full text on file	HIT II

SARS-CoV-2 and pulmonary embolism: who stole the platelets?

Tran M, Sheth C, Bhandari R, Cameron SJ, Hornacek D.

Thromb J. 2020 Sep 3;18:16. doi: 10.1186/s12959-020-00229-8.

Abstract: Background: Patients infected with SARS-CoV-2 often develop venous and arterial thrombosis. The high patient mortality is partly attributed to thrombotic events. An emerging trend is the presence of immunological phenomena including antiphospholipid antibodies which may promote thrombosis. The mechanism for these observations is not clear though many patients with SARS-CoV-2 develop thrombocytopenia. Case presentation: We describe a patient with SARS-CoV-2 pneumonitis who presented with intermediate risk pulmonary embolism (PE). Careful attention to his daily platelet count suggested the possibility of immune mediated heparin-induced thrombocytopenia (HIT) which was confirmed by laboratory testing and resolved when anticoagulation was switched to a direct thrombin inhibitor. Conclusions: Since excessive platelet activation and in situ thrombosis occur in HIT, this case underscores the need to consider that thrombocytopenia in patients with SARS-CoV-2-most of whom receive heparinoids-may be unrecognized HIT. A central role for the platelet in the etiology of thrombosis during the COVID-19 pandemic should be explored.

Keywords: COVID-19; HIT; Heparin; Pulmonary embolism; SARS-CoV-2; Thrombosis.

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11 September 2020

Full text not on file	HIT II

Platelet count trends and response to fondaparinux in a cohort of heparin-induced thrombocytopenia suspected patients after pulmonary endarterectomy.

Li JF, Wu LJ, Wen GY, Zhou RR, Liu F, Wang W, Yang SQ, Gong JN, Miao R, Gu S, Liu Y, Yang YH.

J Thromb Thrombolysis. 2020 Sep 7. doi: 10.1007/s11239-020-02260-y. Epub ahead of print.

Abstract: A definitive diagnosis of heparin-induced thrombocytopenia (HIT) is difficult to make, especially in patients undergoing cardiac surgery. In this retrospective cohort study, we assessed the platelet count trends and the response to fondaparinux in a population of patients of suspected HIT after pulmonary endarterectomy (PEA). Patients enrolled in this study were over the age of 18 years, and survived longer than 7 days after PEA between January 1, 2011 and December 31, 2015. HIT likelihood was assessed by the 4 T's score and interpreted by our institutional algorithm. 54 patients were operated, and 49 patients met the inclusion criteria. Six patients met the criteria for suspected HIT and were treated with fondaparinux until the platelet recovered. No significant difference was observed of clinical characteristics between intermediate to high HIT likelihood patients (HIT SUSPECTED) and low HIT likelihood patients (NO HIT SUSPECTED). HIT SUSPECTED patients reached platelet count lowest later (about 5.5 days after PEA), while NO HIT SUSPECTED patients is about 4.0 days after PEA. Percentage of platelet counts decrease (> 50%) was larger than NO HIT SUSPECTED patients (< 50%). There was no difference in mortality or residual pulmonary hypertension between HIT SUSPECTED and NO HIT SUSPECTED patients. Two HIT SUSPECTED patients who used heparin after PEA died, the other four survived by replacing heparin or low molecular weight heparin with fondaparinux. Suspected HIT patients should be surveilled carefully. Platelet counts trends may have some hints in the prevention of HIT. Fondaparinux may be effective for patients with suspected HIT.

Keywords: Chronic thromboembolic pulmonary hypertension; Fondaparinux; Platelet count; Pulmonary endarterectomy; Thrombocytopenia.

PMID: 32894400

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11 September 2020

Full text not on file	HIT II

A prospective, blinded study of a PF4-dependent assay for HIT diagnosis.

Samuelson Bannow BT, Warad D, Jones C, Pechauer S, Curtis BR, Bougie DW, Sharma R, Grill D, Redman M, Khalighi PR, Leger R, Pruthi RK, Chen D, Sabath D, Aster RH, Garcia D, Padmanabhan A.

Blood. 2020 Sep 8:blood.2020008195. doi: 10.1182/blood.2020008195. Epub ahead of print.

Abstract: Heparin-induced thrombocytopenia (HIT) is a life-threatening, pro-thrombotic, antibody-mediated disorder. To maximize the likelihood of recovery, early and accurate diagnosis is critical. Widely available HIT assays such as the Platelet Factor 4-Heparin ELISAs lack specificity, and the "gold standard" C14-labeled serotonin release assay (SRA) is of limited value for early patient management due to availability only through reference laboratories. Recent studies demonstrate that "pathogenic" HIT antibodies selectively activate PF4-treated platelets and that a technically simpler assay, the PF4-dependent P-selectin Expression Assay (PEA), may provide an option for rapid and conclusive results. Four hundred and nine consecutive adults suspected of HIT were classified as disease-positive, -negative or -indeterminate based upon predefined criteria that combined 4Ts scores and HIT ELISA results. Patients deemed "HIT-indeterminate" were considered disease-negative in the primary analysis and disease-positive in a sensitivity analysis. The ability of PEA and SRA to identify patients judged to have HIT was compared using receiver operating characteristic curve statistics. Using these predefined criteria, the diagnostic accuracy of PEA was high (Area under the curve [AUC] of 0.94; 0.87-1.0, 95% CI) and similar to that of SRA (0.91; 0.82-1.0, 95% CI). In sensitivity analysis, the AUCs of PEA and SRA were also similar at 0.88 (0.78-0.98, 95% CI) and 0.86 (0.77-0.96, 95% CI), respectively. The PEA, a technically simple non-radioactive assay that uses ~20-fold fewer platelets compared to the SRA had high accuracy for diagnosing HIT. Widespread use of the PEA may facilitate timely and more effective management of patients with suspected HIT.

PMID: 32898858

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04 September 2020

Full text on file	Argatroban

Thrombin Inhibition by Argatroban: Potential Therapeutic Benefits in COVID-19.

Aliter KF, Al-Horani RA.

Cardiovasc Drugs Ther. 2020 Sep 1. doi: 10.1007/s10557-020-07066-x. Epub ahead of print.

Abstract: Thrombin is a trypsin-like serine protease with multiple physiological functions. Its role in coagulation and thrombosis is well-established. Nevertheless, thrombin also plays a major role in inflammation by activating protease-activated receptors. In addition, thrombin is also involved in angiogenesis, fibrosis, and viral infections. Considering the pathogenesis of COVID-19 pandemic, thrombin inhibitors may exert multiple potential therapeutic benefits including antithrombotic, anti-inflammatory, and antiviral activities. In this review, we describe the clinical features of COVID-19, the thrombin's roles in various pathologies, and the potential of argatroban in COVID-19 patients. Argatroban is a synthetic, small molecule, direct, competitive, and selective inhibitor of thrombin. It is approved to parenterally prevent and/or treat heparin-induced thrombocytopenia in addition to other thrombotic conditions. Argatroban also possesses anti-inflammatory and antiviral activities and has a well-established pharmacokinetics profile. It also appears to lack a significant risk of drug-drug interactions with therapeutics currently being evaluated for COVID-19. Thus, argatroban presents a substantial promise in treating severe cases of COVID-19; however, this promise is yet to be established in randomized, controlled clinical trials.

Keywords: Argatroban; COVID-19; Coagulopathy; Inflammation; SARS-CoV-2.

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04 September 2020

Full text on file	**Argatroban**

Spontaneous heparin induced thrombocytopenia (HIT) following curettage and bone graft of femur in a patient with monostotic fibrous dysplasia.

Swarup S, Kopel J, Yendala R, Thirumala S, Quick DP.

Thromb Res. 2020 Aug 8;196:75-77. doi: 10.1016/j.thromres.2020.08.009. Epub ahead of print.

PMID: 32853979 Free full text

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04 September 2020

Full text not on file	HIT II

Incidence of heparin-induced thrombocytopenia in patients with 2019 coronavirus disease.

Lozano R, Franco ME.

Med Clin (Barc). 2020 Jul 28:S0025-7753(20)30494-2. English, Spanish. doi: 10.1016/j.medcli.2020.05.041. Epub ahead of print.

PMID: 32883507

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04 September 2020

Full text on file	HIT

Heparin Induced Thrombocytopenia for the Perioperative and Critical Care Clinician.

Moreno-Duarte I, Ghadimi K

Curr Anesthesiol Rep. 2020 August 29. doi: 10.1007/s40140-020-00405-6. Epub ahead of print.

Abstract: Purpose of Review: This review will illustrate the importance of heparin-induced thrombocytopenia in the intraoperative and critical care settings. Recent Findings: Heparin-induced thrombocytopenia (HIT) occurs more frequently in surgical patients compared with medical patients due to the inflammatory release of platelet factor 4 and perioperative heparin exposure. Recognition of this disease requires a high index of suspicion. Diagnostic tools and therapeutic strategies have been expanded and refined in recent years. Summary: HIT is a condition where antibodies against the heparin/platelet factor 4 complex interact with platelet receptors to promote platelet activation, aggregation, and thrombus formation. Our review will focus on intraoperative and postoperative considerations related to HIT to help the clinician better manage this rare but often devastating hypercoagulable disease process.

Keywords: Heparin; Thrombocytopenia; Surgery; Limb ischemia; Thrombosis

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04 September 2020

Full text not on file	HIT II

Therapeutic plasma exchange and intravenous immune globulin in the treatment of heparin-induced thrombocytopenia: A systematic review.

Onuoha C, Barton KD, Wong ECC, Raval JS, Rollins-Raval MA, Ipe TS, Kiss JE, Boral LI, Adamksi J, Zantek ND, Onwuemene OA.

Transfusion. 2020 Aug 19. doi: 10.1111/trf.16018. Epub ahead of print.

Abstract: Background: Immunomodulatory strategies in heparin-induced thrombocytopenia (HIT) include the use of intravenous immune globulin (IVIG) and therapeutic plasma exchange (TPE). The optimal application of these therapies is unknown and outcomes data are limited. We investigated treatment categories and laboratory and clinical outcomes of IVIG and/or TPE in HIT with a systematic literature review. Study design and methods: We searched MEDLINE, Embase, and Web of Science through December 2019 for studies combining controlled vocabulary and keywords related to thrombocytopenia, heparin, TPE, and IVIG. The primary outcome was treatment indication. Secondary outcomes were platelet recovery, HIT laboratory parameters, heparin re-exposure, and post-treatment course. Case-level data were analyzed by qualitative synthesis. Results: After 4241 references were screened, we identified 60 studies with four main categories of IVIG and/or TPE use as follows: (a) treatment of refractory HIT (n = 35; 31%); (b) initial therapy (n = 45; 40%); (c) cardiopulmonary bypass surgery (CPB; n = 30; 27%); and (d) other (n = 2; 2%). IVIG was most commonly used for the treatment of refractory HIT while TPE was primarily used to facilitate heparin exposure during CPB. Both IVIG and TPE were equally used as initial therapy. Heparin re-exposure occurred without thrombotic event in 29 TPE-treated patients and three IVIG-treated patients. Conclusion: In patients with HIT, both TPE and IVIG are used for initial therapy or treatment of refractory HIT. However, TPE is more commonly used in patients undergoing CPB. Prospective studies may help clarify which treatment is indicated in HIT population subsets.

PMID: 32812222

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04 September 2020

Full text on file	HIT

Current Perspectives on Diagnostic Assays and Anti-PF4 Antibodies for the Diagnosis of Heparin-Induced Thrombocytopenia.

Sahu KK, Jindal V, Anderson J, Siddiqui AD, Jaiyesimi IA.

J Blood Med. 2020 Aug 17; 11:267-277. doi: 10.2147/JBM.S232648.

Abstract: Heparin-induced thrombocytopenia (HIT) is a recognized clinical entity in patients receiving unfractionated heparin and low-molecular weight heparin. Currently, diagnosing HIT includes the combination of a physician's clinical suspicion based on a clinical scoring system and a series of laboratory tests. In the present article, we discuss challenges in suspecting and diagnosing HIT in consideration of the turnaround time of available tests and recent advances in techniques and methodologies of newer immunoassays and functional assays.

Keywords: HIPA test; functional assay; heparin-induced thrombocytopenia; immunoassay; laboratory diagnosis; platelet factor 4; platelets; serotonin-release assay.

PMID: 32884385 Free full text

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04 September 2020

Full text on file	HIT

Platelet-Derived Microparticles Bearing PF4 and Anti-GAGS Immunoglobulins in Patients with Sepsis.

Sartori MT, Zurlo C, Bon M, Bertomoro A, Bendo R, Bertozzi I, Radu CM, Campello E, Simioni P, Fabris F.

Diagnostics (Basel). 2020 Aug 24;10(9): E627. doi: 10.3390/diagnostics10090627.

Abstract: PF4 is a megakaryocyte-derived cationic chemokine that plays a part in innate immunity through its activity on the macrophages. In bacterial sepsis, PF4 binds to glycosaminoglycans (GAGs) on the surface of aerobic bacteria, giving rise to an antigenic complex that induces the early formation of anti-PF4 IgG-IgA-IgM. This triggers the immune response in patients receiving heparin therapy who develop heparin-induced thrombocytopenia (HIT). These antibodies have also been identified in patients with chronic Gram-negative infections. Given the complexity of this innate immune response network, our study on 45 patients with sepsis focused on the immune response mediated by platelet PF4. We analyzed the role of IgG-IgA-IgM against PF4-GAGs, and the presence of specific PF4-bearing platelet microparticles (PMPs). Anti-GAGs/PF4 IgG-IgA-IgM levels were significantly higher in septic patients than in control groups (healthy controls or acute patients without sepsis, $p < 0.001$). PF4-bearing PMP levels were only significantly higher in septic patients ($p < 0.001$). The occurrence of IgG-IgA-IgM against PF4-GAGs and PF4+ PMPs correlated with an improvement in patients' sepsis. In conclusion, we demonstrated that, in the course of bacterial sepsis, platelet activation leads to the formation of specific PF4-bearing PMPs. These specific microparticles bind to polyanionic sequences on the surface of aerobic bacteria, giving rise to an antigenic complex that induces the early formation of IgG-IgA-IgM against PF4-GAGs as an innate immune response to infection.

Keywords: anti-heparin/PF4 antibody; platelet; platelet microparticles; sepsis.

PMID: 32846949 Free full text

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04 September 2020

Full text not on file	HIT II

Ticagrelor: falsch negative Funktionstests bei heparininduzierter Thrombozytopenie

N.N.

Transfusionsmedizin - Immunhämatologie · Hämotherapie · Transplantationsimmunologie · Zelltherapie 2020; 10(03): 134. DOI: 10.1055/a-1193-5617

Abstract: Ticagrelor ist ein Inhibitor des ADP-Rezeptors P2Y12, der als Mittel der Wahl zur Vorbeugung von atherothrombotischen Ereignissen bei Patienten mit einem akuten Koronarsyndrom eingesetzt wird. Im Gegensatz zu irreversiblen Inhibitoren wie beispielsweise Aspirin bindet Ticagrelor reversibel an den ADP-Rezeptor, das Medikament liegt in hohen Konzentrationen im Plasma vor.

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