Proporsi heparin induced thrombocytopenia (HIT) pada pasien terapi heparin di RSCM = Proportion of heparin induced thrombocytopenia (HIT) in patients with heparin therapy in Cipto Mangunkusumo hospital

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Abstrak

Heparin-induced thrombocytopenia (HIT) adalah salah satu efek samping penggunaan heparin, yang dicurigai bila terdapat penurunan trombosit 50% pada hari ke-5 sampai ke-10 pascaheparinisasi dan dapat disertai komplikasi tromboemboli. Mekanisme HIT melibatkan pembentukan antibodi terhadap kompleks PF4-heparin (anti-PF4). Pemeriksaan diagnostik HIT terdiri dari uji fungsional dan immunoassay. Pemeriksaan immunoassay, yang mendeteksi anti- PF4 dengan metode ELISA memiliki sensitivitas tinggi dan paling sering digunakan untuk deteksi HIT. Angka kejadian HIT sangat bervariasi karena banyak faktor yang mempengaruhi.
Tujuan penelitian ini adalah untuk mengetahui proporsi kejadian HIT dan proporsi pasien yang memiliki anti-PF4 pada pemberian terapi heparin di RSCM. Penelitian ini melibatkan 120 pasien rawat inap yang mendapat drip heparin atas indikasi profilaksis atau pengobatan, dengan dosis minimal 10.000 U/24 jam. Pasien yang memenuhi kriteria masukan dan tolakan dilakukan pencatatan data usia, jenis kelamin, diagnosis klinis, riwayat pemakaian heparin 3 bulan terakhir, dan dosis heparin yang dipakai. Pada hari ke-7 dan ke-10 pascaheparinisasi (H7 dan H10) dilakukan pengambilan darah untuk pemeriksaan hitung trombosit dan anti-PF4. Diagnosis HIT didasarkan atas penurunan hitung trombosit 50% pada H7 atau H10 yang disertai adanya antibodi anti-PF4.
Hasil uji ketelitian within-run dan uji ketepatan pemeriksaan anti-PF4 mendapatkan CV 7,73% dan penyimpangan (d) 2,5-17,4%. Pada 19 dari 120 subjek (15,8%) ditemukan anti-PF4, tetapi kejadian HIT tidak ditemukan. Berdasarkan klasifikasi risiko terjadinya HIT menurut American College of Chest Physician (ACCP), terdapat 46/120 subjek (38,3%) berisiko rendah, 65/120 subjek (54,2%) berisiko tinggi, 8/120 subjek (6,7%) berisiko sangat tinggi, dan 1 orang tidak terklasifikasi. Uji statistik menunjukkan tidak ada hubungan antara temuan anti-PF4 dengan penurunan trombosit 50% (p=0,588). Hal ini diduga karena kurangnya jumlah subjek penelitian yang diperlukan. Antibodi anti-PF4 lebih sering ditemukan pada subjek perempuan dan dengan riwayat heparinisasi.
Proporsi ditemukannya anti-PF4 berturut-turut lebih banyak pada pasien pascabedah vaskular dan ortopedi, trombosis arteri dan vena, kemudian pasien medis yang mendapat profilaksis heparin. Tidak ada perbedaan bermakna proporsi anti-PF4 positif pada subjek dengan atau tanpa riwayat heparinisasi (p=0,293), perbedaan dosis heparin (p=0,141), dan populasi risiko HIT rendah, tinggi, dan sangat tinggi (p=0,662). Empat dari 19 subjek yang memiliki anti-PF4 positif mengalami penurunan trombosit 20-46% pada H7 dan H10.
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Heparin-induced thrombocytopenia (HIT) is an adverse effect of heparin, that suspected when platelet count fall 50% in 5 to 10 days following heparin initiation and may be accompanied with thromboembolic complications. Mechanism of HIT is mediated by the formation of PF4-heparin complex antibody. There are 2 kind of diagnostic test for HIT, functional assay and immunoassay. Immunoassays, that detect anti-PF4

antibody using ELISA method, have high sensitivity and considered the most frequent assay for detecting HIT. The incidence of HIT varies due to many factors.

The aim of this research is to find the proportion of HIT events and also the proportion of anti-PF4-heparin antibody positive in patients with full-dose heparin in Cipto Mangunkusumo hospital. One hundred and twenty participants, who were our hospital in-patients given heparin infusion with minimal dose of 10.000U/24 h for profilactic or treatment indication, participated in this research. Patients met the inclusion and exclusion criteria were noted for age, gender, clinical diagnosis, heparin exposure in the last 3 months, and heparin dose. On day 7 and 10 after heparin initiation, blood sample were collected for platelet count and anti-PF4 antibody assay. Diagnosis of HIT was based on platelet count fall 50% on day 7 or 10 after heparin initiation accompanied with anti-PF4 antibody in the circulation.

Within run precision and accuracy tests for anti-PF4 assay showed a CV of 7,73% and deviations of -2,5 – 17%. Nineteen of 120 subjects (15,8%) had anti-PF4 antibodies, but HIT was not found. Based on the risk classification of HIT from American College of Chest Physician (ACCP), 46 subjects (38,3%) categorized as low risk to HIT, 65 (54,2%) high risk, 8 (6,7%) very high risk, and 1 as unclassified. Statistics showed there was no significant relationship between anti-PF4 antibodies in the circulation with platelet count fall of 50% (p=0,588). This was probably due to inadequate sample size for this study. Anti-PF4 antibodies were detected more frequent in females and subjects with past heparin exposure.

The proportion of positive anti-PF4 antibodies were highest in postoperative vascular or orthopedic surgery patients, followed by arterial or venous thrombosis patients, then medical patients using profilactic dose of heparin. There were no significant difference of positive anti-PF4 antibodies in subjects with vs without past heparin exposure (p=0,293), in subjects using 10.000U/24h vs >10.000U/24h heparin dose (p=0,141), and in subjects with low vs high vs very high risk of HIT (p=0,662). Four of 19 subjects having anti-PF4 antibodies had platelet count fall 20-46% on day 7 and day 10.