Platelets 2

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USE OF ROMIPLOSTIM IN PATIENTS WITH CHRONIC IDIOPATHIC THROMBOCYTOPENIC PURPURA (CITP) DURING PERI-OPERATIVE PERIOD

R Ramakrishna[1,*], W Alexander[1], K Sarathy[1]
[1]Southern Haematology and Cancer Research Institute, Wollongong, Australia

Background: Conventional treatments for managing cITP in the peri-operative period include corticosteroids or IVIG and immunosuppressive therapies. Each of these therapies has its own drawbacks.[1-3]Romiplostim, a thrombopoiesis stimulating peptibody is currently indicated for use weekly for long-term management of patients with prolonged very low platelet counts (<20/nL) or low platelet counts with bleeding (20-30/nL). Cessation of therapy after periods >10 weeks can be associated with marked, unremitting rebound thrombocytopenia[4]. Its use in the peri-operative period is not well established. Patients who are refractory to steroids and IVIG can be a challenge to manage peri-operatively. Safety data on use of thrombopoietin agonists is limited with little or no published data exists on short-term use, such as during the peri-operative period.
Aims: The aim of this cohort study was to evaluate the safety and effectiveness of Romiplostim in managing the bleeding risk of cITP patients peri-operatively.
Methods: Patients with cITP requiring surgery who had proven refractory to IVIG and steroids were trialled on Romiplostim to determine its effectiveness at managing their bleeding risk peri-operatively. Patients were given up to three doses starting 2 weeks prior to their surgery with a starting dose of 3µg/kg. Platelet counts were monitored and subsequent doses were adjusted as necessary.
Results: Thirteen surgical procedures were performed after using this protocol and none of the patients treated with this protocol experienced any bleeding complications peri-operatively (Table 1). One patient experienced mild headaches associated with Romiplostim usage which resolved once therapy was ceased. One patient experienced mild rebound thrombocytopenia which resolved to baseline spontaneously after 4 weeks. One patient had a delayed response to treatment. One patient achieved sub-optimal response but no surgical complications. Possible platelet dysfunction did not appear to contribute to any bleeding complications.

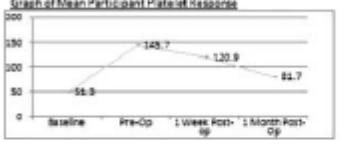
Table 1.

Summary of Results

Demographics	Type of Surgery	Baseline Plts	Pre-Op Plts	1 Week Post-Op Plts	1 Month Post-Op Plts	Platelet Function	Complications
Female/ 65 years old	Mitral valve replacement	65	130	174	146	Abnormal	Nil
Male/ 65 years old	Mitral valve replacement	35	100	70	40	Abnormal	Nil
Male/ 52 years old	Liver biopsy	32	114	80	45	Abnormal	Headache
Male/ 56 years old	Thyroidectomy	35	145	164	97	Abnormal	Nil
Male/ 52 years old	Aortic valve replacement	68	219	128	166	Abnormal	Nil
Female/ 48 years old	Mucocsectomy	39	112	139	86	Normal	Nil
Male 69 years old	Coronary artery bypass graft	51	104	52	37	N/A	Nil
Male/ 56 years old	Cystoscopy and prostate enucleation	75	207	200	114	Abnormal	Nil
Male/ 45 years old	Thyroidectomy and neck dissection	64	410	42	62	Normal	Rebound thrombocytopenia
Male/ 75 years old	Spinal surgery	62	104	247	73	Abnormal	Nil
Female/ 59 years old	Colonoscopy/ gastroscopy	54	50	154	51	N/A	Had a delayed response to therapy.
Female/ 58 years old	Liver Biopsy	47	104	102	89	N/A	Nil
Male/ 64 years old	Colon Polypectomy	39	70	40	36	Abnormal	Platelet count only 70 pre-op, surgeon happy to go ahead.

Abbreviations used: Plts = platelet count (nL)

Graph of Mean Participant Platelet Response



Summary and Conclusions: Romiplostim so far appears to be effective in managing bleeding risk in the peri-operative period. It eliminates the need for platelet transfusions or immunoglobulin infusions, saving this resource. In addition, it is relatively convenient for patients when compared to intravenous therapies, in terms of time required, invasiveness and incidence and severity of adverse events. The platelet response is maintained beyond one month in some cases, and rebound thrombocytopenia does not appear to be a concern in our experience. Our data supports use of Romiplostim as a safe and effective therapy for management of bleeding risk for patients with cITP, during the peri-operative period.

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CIRCULATING FOLLICULAR HELPER T CELLS IN CHILDREN WITH IMMUNE THROMBOCYTOPENIC PURPURA

E Parodi[1,*], M Lanza[1], E Ricotti[2], F Ferro[2], D Montin[3], M Giraudo[4], U Ramenghi[1]
[1]Pediatric Department, University of Torino, Hematology Unit, Pediatric Department, [2]Lab of Hematology, Regina Margherita Children Hospital, [3]Department of Immunology, [4]Department of Mathematics, University of Torino, Torino, Italy

Background: Immune Thrombocytopenic Purpura (ITP) is an autoimmune disorder characterised by low platelet count and mucocutaneous bleeding. Immunological tolerance among T cells is of paramount importance for the control of autoimmune antibody specificities. Recent studies examined the T-cell repertoire in patients with ITP and found differences compared with healthy individuals, lending further credence to T cells being at the heart of the pathogenesis of the disease. T follicular helper cells (TFH) are the effector T helper that regulates the steP-wise development of antigen-specific B cell immunity *in vivo*. It is likely that TFH cells provide inappropriate helper signals to self-reactive B cells in cases of antibody-mediated autoimmune diseases. Recent studies raised the possibility that dysregulated TFH cell activity may contribute to SLE in humans.
Aims: The aim of the study is to analyze the TFH cells in children with ITP.
Methods: Thirty-one pediatric ITP patients, 15 males and 16 females, with a median age of 5 years (range 1-15), were enrolled in the study. In13, TFH analysis was performed at diagnosis, prior to any drug treatment (acute ITP). Eighteen patients were enrolled in the chronic phase of the disease (ITP lasting for more than 12 months); at the time of sample collection, patients were at least one month off-treatment. Twelve healthy children were enrolled as control group.T cells were analyzed by flow cytometry from peripheral blood mononuclear cells (MNC). Immunofluorescence was performed using the following monoclonal antibodies (Becton Dikinson): FITC anti-CD45RO, PE anti-CXCR5, Per-CP anti-CD3, APC anti- CD4. Cells were analyzed by using aBD FACS Canto II equipment and were gated for lymphocytes on the basis of their forward scatter and side scatter profile. A minimum of 10,000 events of the MNC fraction was collected. Statystical analysis was performed with the Wilcoxon's rank sum test and the t-student test. Spearman's rank correlation test was used for correlation analysis.
Results: The median percentage of circulating TFH cells resulted significantly lower in acute ITP patients than in chronic ITP patients (4,23*versus*8,60; P=0.0001) and in acute ITP patients than in controls (4,23*versus*7,79; P=0.0004). No significant correlations were detected between TFH cells and platelet count, between TFH cells and gender, and between TFH cells and anamnestic data (family history for autoimmune disease, recent history for infection or vaccination).
Summary and Conclusions: Our results suggest that dysregulated TFH may have a prognostic value in ITP.

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A MULTICENTER OBSERVATIONAL STUDY FOR EARLY DIAGNOSIS OF GAUCHER DISEASE IN PATIENTS WITH SPLENOMEGALY AND/OR THROMBOCYTOPENIA

I Motta[1,*], M Stroppiano[2], W Barcellini[1], E Poggiali[1], A Dragani[3], G Gaidano[4], F Merli[5], M Cappellini[1]
[1]Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milano, [2]Istituto Gaslini, Genova, [3]Ospedale Civile Spirito Santo, Pescara, [4]Ospedale Maggiore Della Carita', Novara, [5]AO S. Maria Nuova, Reggio Emilia, Italy

Background: Gaucher disease (GD) is an autosomal recessive lysosomal storage disorder resulting from deficiency of beta-glucosidase and the accumulation of glucocerebroside in the reticuloendothelial cells. Prevalence of GD is elevated in Ashkenazi Jewish population (1/450-1/1000), and rare in the non-Ashkenazi (1/40000-1/60000). GD is a multisystemic disease; cytopenias and splenomegaly are frequently the presenting symptoms leading to hematological evaluation. Data from the Gaucher Registry 2008 show that splenomegaly and thrombocytopenia are present at diagnosis in more than 5000 patients (respectively 86% and 60%). Because of the non-specific presenting symptoms, diagnostic delays are frequent, leading to severe complications including hematological malignancies.Enzyme replacement therapy is available and-