An affordable Fc-receptor blockade method to treat patients with chronic refractory autoimmune thrombocytopenic purpura

Twenty-one patients with chronic refractory autoimmune thrombocytopenic purpura were treated with ex vivo anti-D opsonized autologous red cells. Eighteen patients had an increase in their platelet count. Nine of 14 individuals with an early response had a subsequent drop in the platelet count. When last evaluated 71% patients were thrombocytopenia-free.

There are various therapeutic approaches to the management of patients with autoimmune thrombocytopenic purpura (ATP): corticosteroids, splenectomy, Fc receptor (FcR) blockade, immunosuppressive agents, etc.[1-3] The FcR blockade can be accomplished by intravenous (IV) immunoglobulin G (IV-IgG),[2] IV anti-RhO-(D) IgG (anti-D)[2] or ex vivo anti-D opsonized autologous red blood cells (RBC).[4,5] For more than a decade we have been treating patients with chronic refractory ATP with ex-vivo opsonized autologous RBC;[5] we here report the results of a group of 21 individuals so treated. Patients: All RhO (D) positive consecutive patients with chronic refractory ATP studied and treated in the Centro de Hematología y Medicina Interna de Puebla since 1987 were prospectively entered in the study. Ten had received immunosuppressive agents and eight had been splenectomized; a normal bone marrow aspirate was a requisite. Table 1 shows some of the salient data of these individuals. Treatment: A venous blood sample of 5 mL was obtained in sterile tubes containing EDTA-K3.[5] Three milliliters of saline solution with 100 µg of anti-RhO (D)-IgG (Cutter) were placed in a sterile flask and 2 mL of the patient's packed RBC were added. The mixture was incubated with gentle rotation at 25°C for 1 hr and then the whole mixture was given slowly in a single IV dose. This procedure was repeated every other day to a total of five administrations. The patients who did not have an early response were given a single intramuscular dose of 250 µg of anti-RhO (D)-IgG. Response criteria: a partial response (PR) was defined as a platelet increase of at least 50×10^9/L and a complete response (CR) as an increase to a level above 150×10^9/L. Early response (ER) was defined as a response by 24 hr after the last dose of opsonized red blood cells, whereas a late response (LR) was defined from the last platelet count obtained prior to another therapeutic intervention. Twenty-one patients were prospectively included in the study. Eighteen (86%) had an increase in their platelet count; fourteen (66%) had an ER. In 10 cases, the increase was more than 50×10^9/L platelets and in 8 a CR was achieved. Late responses were observed in four patients, whereas three patients (14%) did not respond at all. Nine of the 14 individuals who achieved an ER had a subsequent drop in the platelet count; however, only three had a drop below 50×10^9/L. Three patients who relapsed underwent a subsequent splenectomy and two achieved sustained CR. When last censored, of the 21 patients, 15 (71%) had a platelet count above 50×10^9/L, whereas 13 (62%) had a platelet count above 100×10^9/L. The 84-month thrombocytopenia-free (over 50×10^9/L platelets) status of the whole group is 54%. Fifteen patients displayed abnormally low levels of free haptoglobins as evidence of hemolysis, but the hemogobin level did not drop by more than 0.5 g/dL in any patient. Two patients had fever after receiving the first dose of anti-D coated autologous RBC. There were no instances of hemoglobinuria or raised creatinine levels and there were no other adverse effects of the treatment. In the 7 patients who did not have an ER, the IV treatment was followed by the intramuscular delivery of anti-RhO (D)-IgG, whereas in one individual (#15) two courses of anti-D opsonized RBC were delivered, 4 weeks apart.

In the treatment of patients with refractory ATP, the usual dose of IV-IgG is 2 g/kg[2] and that of IV anti-D: 50 µg/kg,[2] whereas 100-500 µg per patient are usually enough to accomplish a full treatment with IV anti-D opsonized red blood cells (4, 5). Accordingly, we can calculate that the approximate costs of these treatments, in a 60 Kg adult in our country (Mexico), are: IV-Ig; 8400 USD (Grifols) or 30000 USD (Sandoz); IV-anti-D, 3200 USD (Cangene-Nabi); and anti-D opsonized erythrocytes, 170 USD (Cutter). These figures indicate that treatment with ex vivo anti-D coated RBC is 50-150 times cheaper than treatment with IV-IgG. The results obtained with this treatment so far are satisfactory and similar to those which we[5] and others[4] had previously published using ex vivo anti-D coated RBC, and to the ones of other methods to achieve Fc receptor blockade.[6] These data suggest that ex vivo anti-D opsonized RBC may represent be a substantially cheaper method for accomplishing Fc-receptor blockade as part of the treatment of patients with chronic refractory ATP.

Table 1. Salient data of the patients treated with *ex-vivo* anti-D opsonized autologous red blood cells. Data on platelet counts are from before the treatment (prior), immediately after the treatment (end) and the last evaluation (last), months after the treatment (time, mo).

Number	Age	Sex	Splenectomy	Platelets ($\times10^9$/L) Prior	End	Last	Time (mo.)
1	2	M	(-)	11	3	3	1
2	3	F	(-)	13	8	6	2
3	31	F	(-)	53	150	91	2
4	18	F	(-)	4	58	10	2
5	51	F	(-)	30	180	80	3
6	55	M	(-)	69	151	199	3
7	41	F	(+)	27	167	364	4
8	8	M	(-)	87	206	131	5
9	11	M	(+)	63	99	174	6
10	38	F	(+)	38	225	170	8
11	38	F	(-)	11	11	4	8
12	8	F	(+)	35	30	164	21
13	69	F	(-)	76	150	62	24
14	13	F	(-)	114	88	186	24
15	25	F	(+)	10	263	150	24
16	48	F	(+)	19	51	20	36
17	58	F	(+)	5	53	195	40
18	61	F	(-)	36	57	16	42
19	44	M	(-)	123	122	206	48
20	2	F	(-)	18	16	395	72
21	10	F	(+)	21	149	556	84

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