EVIDENCE BASED USE OF ERYTRHOPOIETIN IN PATIENTS WITH AUTOIMMUNE HEMOLYTIC ANEMIA: A MULTICENTER INTERNATIONAL STUDY

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Contributions

ABSTRACT

Abstract

Abstract: S900

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Background

Autoimmune hemolytic anemia (AIHA) is clinically heterogeneous, from chronic compensated to abrupt hemolysis. Together with the rate of antibody mediated erythrocyte destruction, bone marrow reticulocyte compensation is a recently recognized determinant of outcome. Erythropoietin (EPO) has been anecdotally used in AIHA to ameliorate bone marrow response, but only one systematic series has been published and predictors of response are not known

Aims

To evaluate EPO efficacy and its predictors in a cohort of AIHA patients

Methods

Data on primary and secondary AIHA cases who had received EPO either alone or concomitantly to other therapies were retrospectively collected using a preformed survey. Efficacy was evaluated at 15 and 30 days, and then at 3,6 and 12 months; Hb response was considered partial (PR, >2 g/dL Hb increase or >10g/dL) or complete (CR, >12g/dL) and hemolytic markers (LDH, reticulocytes) were registered

Results

29 AIHA cases followed from June 2007 to February 2019 at 7 centers in Italy, France, Norway, Austria, and UK were included in the study. Main AIHA types (warm, cold, mixed, and DAT negative) were present, and 3 cases were secondary to a lymphoproliferative disorder (not active and without specific treatment at the moment of the study). Patients' characteristics are shown in table 1: at diagnosis 74% of cases presented with severe anemia and 95% displayed inadequate reticulocytosis (i.e. bone marrow responsiveness index<121). Bone marrow evaluation at diagnosis (N=16) showed hypercellularity with dyserythropoiesis in 7 cases, and reticulin fibrosis in 3; a lymphoid infiltrate was found in 13

patients (T-cell in 4, B-cell in 7, mixed in 2), greater than 10% in the 3 secondary cases only. All patients had received at least one previous therapy, and the majority (69%) started EPO because of non-response to ongoing treatment (steroids 15, immunosuppressor 4, sutimlimab 1). Six patients had received rituximab during the 3 months before EPO start (median 1 month, range 0-5). At EPO initiation, 21% of cases displayed severe anemia, 73% had inadequate reticulocytosis, and 89% (of 18 tested) showed inappropriately low endogenous EPO levels. Patients were treated for a median of 7 months and responses were observed in about 70% of cases at month+1 and +3 (table1), with a median Hb and reticulocyte increase of 21.5 (2-48) g/L ($p<0.001$) and 25(0-220)x10^9/L at month+1; and 29 (0-66) g/L ($p<0.001$) and 49 (0-195)x10^9/L at month+3, respectively. Notably, 64% of patients responded as soon as at day+15; this finding supports an activity of EPO although recent or concomitant treatments may have contributed. At last follow up, 13 cases had discontinued EPO: 6 for long standing CR and 7 because of NR (3 with hemolytic flares). We observed an association of response to EPO and primary AIHA (73 vs 33% in secondary), inadequate reticulocytosis (76 vs 50% with adequate reticulocytosis), and not-warm (85 vs 50% in warm cases) not transfusion dependent cases (76 vs 50% transfusion dependent), although the small number did not allow statistical significance

Table 1

Age years, median(range)	68 (35-92)
M/F	16/13
CAD, N(%)	12 (41.4)
WAIHA IgG, N(%)	5 (17.2)
WAIHA IgG+C, N(%)	9 (31)
MIXED, N(%)	2 (7)
DAT neg, N(%)	1 (3.4)
Haematologic parameters at diagnosis	
Hb g/L, median(range)	73 (41-118)
LDH U/L, median (range)	468 (193-6000)
Ret x109/L, median(range)	122 (57-310)
BMRI, median(range)	69 (35-193)
EPO, median(range) N=15	35 (8-670)
Previous therapy lines	
steroids, N(%)	22 (76)
rituximab, N(%)	19 (66)
splenectomy, N(%)	2 (7)
immunosuppressor, N(%)	13 (45)
time from diagnosis to EPO days, median (range)	1740 (209-1760)
time on EPO days, median (range)	209 (21-2464)
Haematologic parameters at EPO initiation	
Hb g/L, median(range)	87 (62-109)
LDH U/L, median (range)	338 (193-1030)
Ret x109/L, median(range)	117 (34-310)
BMRI, median(range)	85 (30-222)
EPO, median (range) N=17	27 (9.3-620)
Concomitant therapy, N(%)	20 (69)
Response rates, ORR (%), CR/PR	
day+15, N=29	18(64), 3/15
day+30, N=23	16(69), 4/12
month+3, N=24	17(71), 9/8
month+6, N=15	9(60), 9/0

Conclusion

Use of EPO is effective in about 70% of AIHA patients unresponsive to ongoing/previous treatments, particularly in cases with inadequate reticulocytosis. Although preliminary, these data advise EPO use to stimulate bone marrow compensatory response

Session topic: 28. Enzymopathies, membranopathies and other anemias

Keyword(s): Autoimmune hemolytic anemia (AIHA), Bone marrow failure, Erythropoietin

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