Ribavirin in treatment of Crimean-Congo Hemorrhagic Fever (CCHF): An international multicenter retrospective analysis

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OBJECTIVES

➤CCHF is a fatal viral hemorrhagic illness transmitted by ticks with no proven antiviral treatment.

➤While ribavirin has been proposed as a potential therapy, results of previous studies are not conclusive.

➤This multi-centric study is aimed to evaluate the efficacy of Ribavirin in treatment of CCHF.

METHODS

➤In a multi-center, non-interventional, retrospective observational study, 543 Turkish and Iranian hospitalized CCHF patients were evaluated (2011-2015).

➤Patients' demographic, epidemiological, clinical characteristics, laboratory data, treatment and outcome variables were compared between patients who received ribavirin and supportive therapy and those who only received supportive therapy.

➤Data analysis was performed by SPSS 16.0.

➤Significance was set at p<0.05.

RESULTS

➤Data for 543 patients from 7 centers were reviewed (Table 1).

➤Ribavirin was administered to 198 patients (36.5%) who were mainly younger than 65 years old (85%) and male (%65.2).

➤Leukocyte count on admission was significantly higher in ribavirin group (P=0.023). PT and aPTT on admission were significantly higher in the ribavirin group (p=0.047 and 0.006, respectively), while bleeding was not significantly different (0.246).

➤Platelets, Hemoglobin, liver enzymes, INR, CPK, LDH and D-Dimer levels on admission were not significantly different between groups.

➤Ribavirin group had a significantly longer duration of hospitalization (7.4±3.3 vs. 7.3±5.6, P=0.042).

➤Overall, 44 patients died of CCHF (8%).

➤Mortality was observed in 15 patients who received ribavirin (7.6%) and in 29 (8.4%) patients in the non-ribavirin group. (P=0.733).

➤Nine patients died within the first 3 days (3 received ribavirin).

➤Time from hospitalization to death was 6.4±5.9 days in the ribavirin vs. 5.3±2.7 days in non-ribavirin group (p=0.867).

➤During hospitalization, platelet counts were significantly lower in the ribavirin group (P>0.05)(Figure), while leukocyte and hemoglobin counts were not significantly different (Table 2).

➤Ribavirin group significantly needed more plasma transfusions (43.4% vs. 29.3%) (P=0.001).

➤Need for platelet and erythrocyte transfusions were similar among two groups while in thrombocytopenic patients, ribavirin patients needed more frequent platelet transfusions (P=0.013).

Table 1: Comparing admission data for CCHF patients with Ribavirin (Group A) and without Ribavirin (Group B) treatment (Significant P-value<0.05). Abbreviations; AST (aspartate transaminase), ALT (alanine transaminase, CPK (creatine phosphokinase), LDH (lactate dehydrogenase), PTT (partial thromboplastin time), aPTT (activated partial thromboplastin time), INR (international normalized ratio)

Variables	Group A (n= 198)	Group B (n= 345)	P-value
Age (years± SD)	47.0± 15.4	50.6± 16.7	0.009
≥Age, 65, n (%)	29 (14.6)	75 (21.7)	0.043
Male gender, n (%)	129 (%65.2)	185 (%53.6)	0.009
Endemic region, n (%)	184 (93%)	317 (92%)	0.258
History of Animal contact, n (%)	131 (66%)	242 (70%)	0.594
Tick bite, n (%)	124 (63%)	236 (68%)	0.170
Fever, n (%)	160 (81%)	264 (76.5%)	0.224
Bleeding, n (%)	51 (%25.8)	105 (%30.4)	0.246
Hospitalization time (days± SD)	7.4± 3.3	7.3± 5.6	0.042
Platelet count	67,000± 50270	69,700± 48610	0.340
Platelet count<50,000, n (%)	95 (48%)	142 (41%)	0.123
Leukocyte count	3,397± 2886	2,872± 2627	0.023
Leukocyte count <1500	36 (18%)	65 (19%)	0.849
Hemoglobin	13.6± 2.1	13.8± 1.9	0.427
ALT	165± 332	136± 204	0.829
AST	377± 842	282± 442	0.758
CPK	885± 1535	846± 1913	0.203
LDH	799± 946	752	0.692
PT	13.9± 3.3	13.4± 2.9	0.047
aPTT	42.5± 20.1	38.9± 22.1	0.006
INR	1.16± 0.4	1.12± 0.4	0.274
D-Dimer	7.2± 13.9	7.1± 10.7	0.624
Mortality	15 (%7.6)	29 (%8.4)	0.733

Table 2: Comparing Platelet, Leukocyte and Hemoglobin (Hb.) counts on days 1, 3, 5, and 7 in patients receiving or not receiving Ribavirin treatment

Variables		1st day	3rd day	5th day	7th day
Platelet count	Ribavirin (n)	+n=198 -n=345	+n=183 -n=317	+n=167 -n=260	+n=113 -n=173
	+	67,000±15 0270	58,284± 41932	64,958± 39286	88,898± 78380
	-	69,700±4 8610	66,857± 39342	78,195± 47426	100,079 ±63088
	P-Value	0.340	0.004	0.008	0.014
Platele t	+	95 (48.0%)	89 (48.6%)	66 (39.5%)	38 (33.6%)
	<50,0 00	142 (41.2%)	111 (35.0%)	72 (27.7%)	33 (19.1%)
	P-Value	0.123	0.003	0.011	0.005
Leuko cyte count	+	3,397±2, 886	3,013±1, 995	3,745±3 087	4,494±5 988
	-	2,872±2, 627	3,262±3 510	3,670±2 351	4,848±4 857
	P-Value	0.023	0.532	0.971	0.011
Leuko cyte <1.50 0	+	36	29 (15.8%)	9 (5.4%)	2 (1.8%)
	-	65	43 (13.6%)	18 (6.9%)	2 (1.2%)
	P-Value	0.023	0.484	0.666	0.649
Hb.	+	13.6±2.1	13.2±2.1	12.9±2.3	12.6±2.3
	-	13.8±1.9	13.0±2.1	12.7±2.2	12.7±2.2
	P-Value	0.849	0.246	0.646	0.596
Hb.< 10	+	13	16	18	16
	-	14	21	24	20
	P-Value	0.196	0.383	0.600	0.517

Figure: Platelet count by days in ribavirin receiving patients
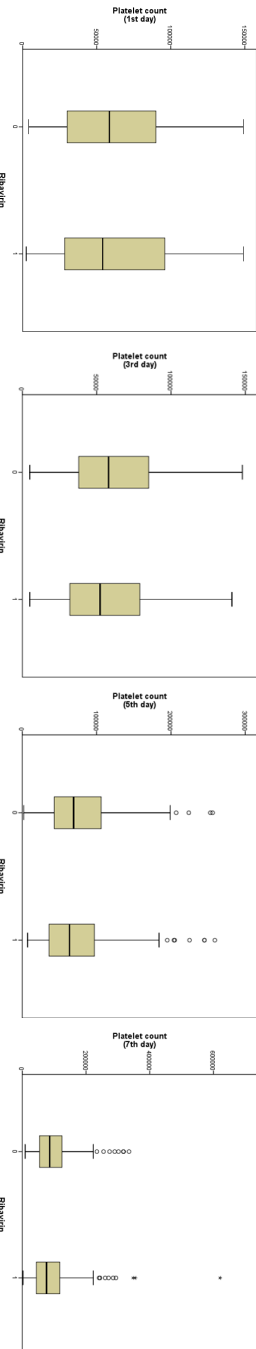
CONCLUSION

➤Our findings suggest that ribavirin use did not significantly improve outcome in CCHF patient.