ketamine antidepressant actions in Electroconvulsive Therapy of Treatment-Resistant Depression

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BACKGROUND

Major depressive disorder affects approximately 5% of the population with nearly 1-third of patients failing to achieve remission, despite adequate pharmacological treatment [1]. Although electroconvulsive therapy (ECT) is the gold standard approach for treatment resistant depression (TRD), a considerable fraction of patients also show a delayed improvement or appear to be resistant to ECT. One of the most promising rapid-acting antidepressants is ketamine, a noncompetitive N-methyl-D-Aspartate receptor antagonist that can be used as an anesthetic during ECT to augment antidepressant efficacy [2].

Data on ECTs using ketamine are both scarce and conflicting, which lead the American Psychiatric Association to call for further studies [3].

An experimental, non-randomized clinical trial with consecutive sampling of TRD patient (persistent HAM-D ≥ 23) was conducted. Patients who were initially assigned to 6 ECT sessions using thiopental anesthesia (Std ECT) but showed a very limited symptomatic relief were included in the study. Patients in Group 1 maintained treatment with Std ECT whereas patients in Group 2 were treated with further 6 ECT sessions using ketamine anesthesia (Ket ECT).

INCLUSION CRITERIA AND STUDY DESIGN

Inclusion Criteria:

- 1) ≥ 3 -trials of antidepressants (TRD) and persistent HAM-D ≥ 23 + Psychotic and/or Catatonic symptoms;
- 2) Patients treated with 6 Std ECTs with very limited or no improvement in HAM-D score and maintenance of Psychotic and/or Catatonic symptoms were assigned to be included in Group 1 or Group 2.

Study Design:

METHODOLOGY

Contraindications for ECT were assessed by anamnesis and complementary analytic and imagological testing. Depression was assessed using the Hamilton Depression Scale (HAM-D, 17-item version) and Psychotic Depression Assessment Scale (PDAS) 24 hours before performing Std ECT, 24 hours after the 6th Std ECT and 48 hours after the last ECT session (Figure 1). Prescribed psychiatric medications were not discontinued.

ECT treatment was performed using a Thymatron System IV machine. Bilateral electrode placement was used and the stimulation parameters determined by the attending psychiatrist according to age-based methods and titrated in order to elicit seizures of a minimum of 25 seconds. ECT was conducted at a frequency of 2 sessions/week. Standard ECT sessions were conducted using standard anesthesia with thiopental. Patients enrolled for ECT sessions with ketamine, were treated with 5mg of haloperidol EV 30 min before the procedure. Perioperative management of hemodynamics and postanesthetic status were under discretion of the anesthesiologist.

CONCLUSION

Currently, there is conflicting data supporting the relevance of ketamine and the potentially synergistic effect of ketamine and ECTs for the treatment of TRD patients. In this context, we have carried out the current experimental clinical trial that showed no significant reduction in the mean HAM-D and PDAS scores for Group 1 but a significant reduction of the HAM-D score of $38,8 \pm 2,4$ to $13,4 \pm 10,55$ ($p < 0,01$) and of the mean PDAS score of $34,2 \pm 4,9$ to $11,4 \pm 8,5$ ($P < 0,01$). Our results provide further evidence of superimposed effect of ketamine on ECT which is likely to be important not only for TRD but particularly relevant for the subset of patients with TRD who appear to be resistant to ECT using standard methodology.

I hereby declare no potential conflicts of interest regarding the data presented in the current Poster.

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RESULTS

Patients	Score at 24h before 1 st Std ECT											Score at 24h after the 6 th Std ECT										
	A	B	C	D	E	F	G	H	I	J	A	B	C	D	E	F	G	H	I	J		
HAM-D																						
HAM-D score	39	38	41	36	40	38	40	40	35	41	39	34	40	33	30	37	40	38	35	41		
PDAS																						
HAM-D 6 item	19	20	19	18	19	21	20	19	18	21	19	18	18	17	15	21	20	19	18	21		
BPRS 5 item	13	15	15	10	15	13	17	11	11	20	13	14	14	10	16	13	17	11	11	20		
PDAS Score	32	35	34	28	34	34	37	30	29	41	32	32	32	27	31	34	37	30	29	41		

Grupo 1

Patients	Score at 72h after the 12 th Std ECT				
	A	B	C	D	E
HAM-D					
HAM-D score	37	32	35	33	25
PDAS					
HAM-D 6 item	17	18	17	17	14
BPRS 5 item	11	12	13	9	14
PDAS Score	28	30	30	26	28

Grupo 2

Patients	Score at 72h after the 6 th Ket ECT				
	F	G	H	I	J
HAM-D					
HAM-D score	19	1	4	26	17
PDAS					
HAM-D 6 item	10	0	2	10	10
BPRS 5 item	4	1	2	8	10
PDAS Score	14	1	4	18	20

HAM-D

PDAS