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Beta-blocking agents during electroconvulsive therapy: a review

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Editor's key points

- The authors reviewed the literature regarding the effects of beta-blockers during electroconvulsive therapy, in particular, their effects on haemodynamics and seizure attenuation.
- Various effects were noted, but a paucity of consistent evidence appears to mandate a prospective study of the subject.

Electroconvulsive therapy (ECT) is associated with at least transient episodes of hypertension and tachycardia. Beta-blocking agents may be indicated to prevent cardiovascular complications and may shorten seizure duration. This review evaluates studies that used beta-blocking agents during ECT to determine which agent has the most favourable outcomes on cardiovascular variables and seizure duration. A Medline database search was made using the combined keywords 'adrenergic beta-antagonists' and 'electroconvulsive therapy'. The search was restricted to double-blind randomized controlled trials and yielded 29 original studies. With the use of esmolol, significant attenuating effects were found on cardiovascular parameters in the first 5 min after stimulation; its shortening effects on seizure duration may be dose-related. With the use of labetalol, findings on cardiovascular effects were inconsistent during the first minutes after stimulation but were significant after 5 min and thereafter; seizure duration was scarcely studied. Landiolol attenuates heart rate but with inconsistent findings regarding arterial pressure (AP); seizure duration was mostly unaffected. Esmolol appears to be effective in reducing the cardiovascular response, although seizure duration may be affected with higher dosages. Landiolol can be considered a suitable alternative, but effects on AP need further investigation. Labetalol has been studied to a lesser extent and may have prolonged cardiovascular effects. The included studies varied in design, methodology, and the amount of exact data provided in the publications. Further study of beta-blocking agents in ECT is clearly necessary.

Keywords: adrenergic beta-antagonists; electroconvulsive therapy; esmolol; labetalol; landiolol

Electroconvulsive therapy (ECT) is considered a highly effective treatment for severe depression, especially in life-threatening cases or when other methods of treatment have failed.[1 2] However, both the stimulus and the induced seizure cause a parasympathetic and sympathetic reaction, respectively.

The first reaction is mediated through stimulation of the vagus nerve and ends when the actual seizure starts, usually within seconds. The second, amplified by the release of catecholamines, may last several minutes. Heart rate (HR) and arterial pressure (AP) increase dramatically and coronary ischaemia may develop in patients at risk.[3 4]

Pre-treatment screening helps to identify patients at risk of cardiovascular complications during ECT. In these patients it may be necessary to actively attenuate the cardiovascular response during ECT[5] and, to this end, many agents have been studied.[6–11] However, these agents either lacked efficiency or have a biological half-life that exceeds the time of one ECT treatment session.

More recently, beta-blocking agents with a short half-life were studied. However, side-effects such as decrease in seizure duration, prolonged cardiovascular depression, and excessive hypotension have been reported.[12]

Seizure duration has long been used as a measure of adequacy of convulsions.[13] The relation between seizure duration and ECT is complex and other parameters have been identified that may also affect treatment outcomes.[14 15] However, if mentioned in the studies reviewed here, (only) seizure duration was consistently used as a measure of treatment adequacy.

This review aims to summarize the results of randomized controlled trials using beta-blocking agents during ECT. The outcome measures were effects on cardiovascular variables and seizure duration.

Methods

A Medline search was performed using the combined keywords 'beta-adrenergic blockers' and 'electroconvulsive therapy' with the article type set to 'randomized controlled trial': this yielded 27 publications.

An additional search was made with the same keywords, but with institution-defined criteria concerning the trial type: this yielded two additional publications.

These 29 publications were screened by at least two authors and were included when cardiovascular parameters, seizure duration, or both were reported.

Results

The search yielded a total of 29 articles. Of these, the following nine articles were excluded from this review. One study explored the response of schizophrenia to the addition of a beta-adrenergic blocking agent, without the use of ECT.[16] One study explored the response of major depressive disorder to the addition of pindolol to ECT: pindolol has a long biological half-life that exceeds the duration of one ECT-treatment session; therefore, we did not consider this study suitable for our review.[17] One study explored the effects of beta-adrenergic blockers on neuroendocrine hormones and another investigated the effects of ECT on neuroendocrine hormones after administration of a beta-blocking agent;[18 19] one reported on the effect of esmolol on a processed EEG registration in healthy male patients who did not undergo ECT;[20] one explored the effects of nicardipine in different dosages, both with and without labetalol 10 mg and another study with nicardipine used labetalol as an outcome criterion;[21 22] one was written in Chinese and one was excluded because of concomitant use of nifedipine.[23 24]

Of the remaining 20 papers, 9 described one or multiple comparisons between esmolol and placebo;[25–33] 4 publications studied both esmolol and labetalol;[34–37] 1 publication studied esmolol and landiolol;[38] 2 publications studied labetalol only;[39 40] and 4 publications described one or more comparisons between landiolol and placebo.[12 41–43]

ECT typically involves multiple treatment-sessions: this allows a cross-over study-design, in which patients serve as their own controls. Many studies adopted this strategy.

In two publications, patients received 1–3 randomized pairs of treatment alternating placebo and intervention:[29 33] their total number of treatment interventions was averaged.

Dosages studied are denoted in milligrams per kilogram: if this was not specified in the article, then dosages were calculated for each trial.

Table 1 Pre- and post-ECT values for significant differences in HR (bpm) in the included studies of esmolol. *n*, number of patients; TI, number of treatment interventions per patient; [a]average number of TI; [c]calculated; [e]estimated; ns, no significant difference compared with placebo; *roughly extrapolated from graphic representation in original study; [†]in the original study, per cent changes compared with baseline values are represented in the figures. After extrapolation, actual values were estimated. Significant differences indicate difference in per cent change. [‡]Mean value of each patient's average of three measurements immediately after stimulus

Study	Dosage (mg kg^{-1})	*n*	TI	Pre-ECT	Post-ECT (min)				
					1	2	3	5	9
Howie and colleagues[25]	Placebo	20	4	84	110*	92*	85*	86*	90*
	3.9[c]	20	4	84	85*	75*	72*	76*	83*
Howie and colleagues[26]	Placebo	20	2	82*	100*	88*	85*	89*	89*
	1.3[c]	20	2	78*	87*	ns			
	2.1[c]	20	2	77*	87*	ns			
	2.9[c]	20	2	83*	84*	ns			
Kovac and colleagues[27]	Placebo	17	1	Significant data not provided					
	4.3[c]	17	1						
Kovac and colleagues[28]	Placebo	12	1	85	114*,†	98*,†	97*,†	96*,†	98*,†
	1.4[c]	12	1	87	86*,†	89*,†	89*,†	ns	
	2.8[c]	12	1	89	85*,†	85*,†	85*,†	91*,†	93*,†
McCall and colleagues[29]	Placebo	18	1.6[a]	–	–				
	2.7[c]	18	1.6[a]	–	–				
O'Connor and colleagues[30]	Placebo	16	1	73*	100*	89*	85*	82*	85*
	1.0	16	1	77*	78*	73*	ns		
O'Flaherty and colleagues[31]	Placebo	10	3	76*	108*	97*	94*	100*	102*
	2.0	10	3	77*	83*	86*	85*	ns	
Van den Broek and colleagues[32]	Placebo	20	3	79	98[‡]				
	1.3[c]	20	3	79	86[‡]				
Zvara and colleagues[33]	Placebo	19	1.8[a]	85*	103*	104*	111*	98*	99*
	2.9[e]	19	1.9[a]	108*	86*	87*	84*	ns	
Castelli and colleagues[34]	Placebo	18	1	79*	116*	–	86*	80*	–
	1.3	18	1	74*	84*	–	ns		
	4.4	18	1	79*	71*	–	ns		
Shrestha and colleagues[35]	Placebo	30	1	83	94	–	100	86	–
	1.0	30	1	86	86	–	88	ns	
Van der Starre and colleagues[36]	Placebo	12	1	–	–				
	0.3[c]	13	1	–	–				
Weinger and colleagues[37]	Placebo	10	1	73*	120*	–	75*	–	–
	1.0	10	1	Significant data not provided					
Saito and colleagues[38]	Placebo	12	1	83*	113*	102*	95*	86*	–
	1.0	12	1	81*	90*	ns			