The effects of esmolol and labetalol on cerebral blood flow velocity during electroconvulsive therapy

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EDITOR:

Electroconvulsive therapy (ECT) has an important role in the treatment of patients with severe depression or schizophrenia. ECT results in an acute cardiovascular response, characterized by tachycardia, hypertension and increase in cerebral artery blood flow velocity (V_{mca}) [1]. For patients at risk of cardiovascular complications, β-adrenergic blocking agents are often administered to prevent or minimize the increase in blood pressure (BP) and heart rate (HR). The aim of this study was to evaluate the effects of two different β-blockers, esmolol and labetalol, on changes in V_{mca} during ECT using transcranial Doppler (TCD).

In a prospective, randomized study, 37 patients undergoing ECT were evaluated. The study was approved by the Stanford Institutional Review Board, and written informed consent was obtained. Anaesthesia was induced with etomidate ($0.25\,mg\,kg^{-1}$) and succinylcholine ($1\,mg\,kg^{-1}$). Monitoring consisted of electrocardiogram, BP (non-invasive) and pulse oximetry. In addition, V_{mca} (Neuroguard, MedaSonics, Fremont, CA, USA) of the left middle cerebral artery was measured, using a 2 MHz ultrasonic wave. Patients without pre-existing hypertension (mean arterial pressure (MAP) < 85 mmHg) received no β-blockers (Group N = 12 patients). Patients with pre-existing hypertension (MAP > 85 mmHg) were, at random, pre-treated with either esmolol (Group E = 13 patients) or labetalol (Group L = 12 patients) intravenously to lower MAP to <85 mmHg. The TCD technician was blinded for the treatment compounds. After induction of anaesthesia, all patients were manually hyperventilated with 100% O_2 for 30 s. ECT was applied when nerve stimulation of the ulnar and radial nerves showed absent twitches, and the patellar reflex was negative. All patients underwent bilateral ECT. V_{mca}, HR and MAP were measured just before induction of anaesthesia (baseline), and at 0.5, 5, 10 and 30 min post-ECT. Data were analysed by one-way analysis of variance on ranks. Dunn's method was used for multiple comparisons. Data are presented as median (range).

Median (range) ages were 41(35–66), 44(38–57) and 55(45–68) yr, weights were 73(67–84), 73(65–85) and 77(68–86) kg and gender ratios (M : F) were 3 : 9, 6 : 7 and 5 : 7 in Groups N, E and L, respectively. In Group N, these were not significantly different. Median total esmolol dose in Group E was 25 (20–30) mg, and median total labetalol dose in Group L was 20 (10–20) mg. MAP increased significantly in all groups during ECT, with no significant difference between the groups. In Groups E and L, HR did not significantly increase after ECT, but in Group N, HR increased significantly ($P < 0.05$) by 20, 24 and 9 beats min^{-1} at 0.5, 5 and 10 min, respectively (Fig. 1). V_{mca} increased in both Group N and E significantly more ($P < 0.05$) than in Group L (Fig. 1) at 0.5 min. At 5 and 10 min, V_{mca} had also increased in Group L, but significantly less ($P < 0.05$) than in Groups N and E. At 30 min, V_{mca} had decreased to baseline values in all groups.

The findings of this study show that pre-treatment with β-adrenergic blocking agents may completely prevent increases in HR during ECT. In addition, labetalol, in contrast with esmolol, attenuates the initial increase in V_{mca} during ECT. This increase in cerebral blood flow is attributed to a combination of increased oxygen demand in the brain and the systemic hyperdynamic response, including hypertension and tachycardia. The changes in V_{mca} observed in this study are in concordance with earlier reports [2]. The haemodynamic effect of ECT is due to a short-lasting parasympathetic discharge followed by a sympathetic response with a duration of approximately 10 min. Because of the potential complications, the observed hypertension and tachycardia are usually treated with antihypertensive and antiarrhythmic agents, particularly in patients at risk for myocardial ischaemia or stroke. Different classes of antihypertensive agents have been advocated. β-Blocking agents like esmolol, labetalol, alprenolol and landiolol are routinely used [1,3,4], but calcium-channel blockers like nicardipine, diltiazem and verapamil are reported to be effective as well [1].

Several authors have focused on the effects of antihypertensive treatment on seizure duration, with conflicting results. Particularly, esmolol is

Correspondence to: Peter J. A. van der Starre, Department of Anesthesia, Stanford University School of Medicine, 300 Pasteur Drive, Room H3580, Stanford, CA 94305, USA. E-mail: pieterva@stanford.edu; Tel: +1 650 725 5848; Fax: +1 650 725 8544

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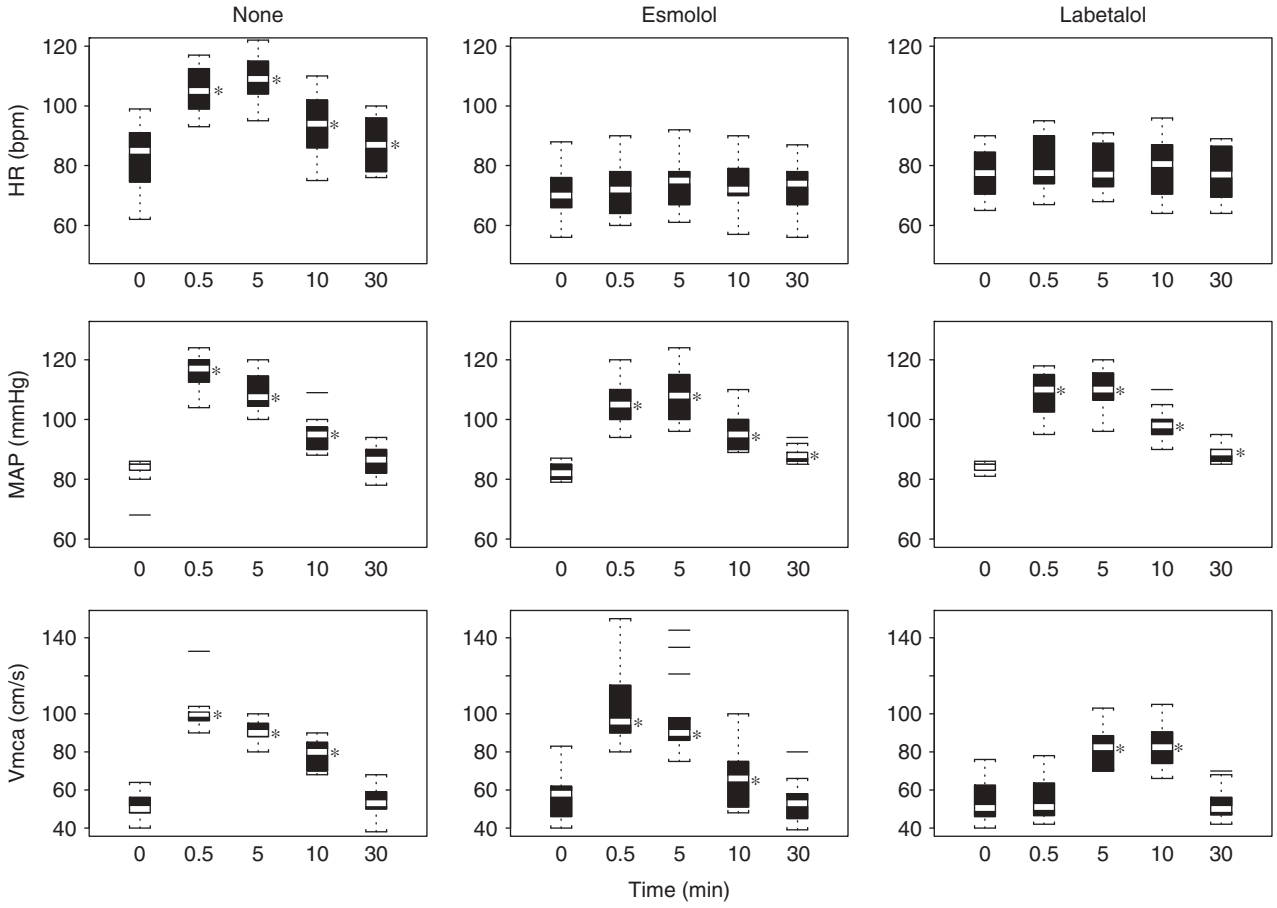

Figure 1.
Box plots of the distribution of heart rate (HR), mean arterial pressure (MAP) and middle cerebral artery blood flow velocity (V_{mca}) during ECT in three groups of patients receiving either no pre-treatment (None) or esmolol or labetalol. The horizontal line in the interior of each box is the median. The height of the box is the interquartile distance, which is the difference between the third quartile and first quartile. The whiskers extend to a distance of 1.5 times the interquartile distance. Horizontal lines indicate outliers. An asterisk indicates a median value statistically different ($P < 0.05$) from baseline (Time 0).

related to shortening of seizure duration in several studies [4], but not in others [5]. Labetalol has been implicated in shortening of seizure duration as well [5]. We did not include seizure duration in the present study since we merely focused on the haemodynamic effects of both agents. None of the patients needed a repeat ECT because of clinically significant short seizure duration.

The methodology of this study implicated the administration of β-adrenergic receptor blockers before ECT, with similar outcome concerning the attenuation of the hyperdynamic response as in earlier studies. We did not observe the reported hypotension post-ECT in the patients receiving labetalol [1]. This may be related to the use of etomidate, since it has minimal cardiovascular depressant effect compared to methohexital or propofol [6].

The changes in V_{mca} observed in the control group in this study are in concordance with earlier reports [2]. The attenuation of the expected increase in V_{mca} during ECT in the patients pre-treated with labetalol could partly be explained by its considerably longer elimination half-life (5.5 h) compared to esmololol (9 min). It could also partly be due to a central effect, since in rats labetalol has been shown to cross the blood–brain barrier resulting in a central inhibition of sympathetic nerve activity [7]. In humans, the effect of labetalol on cerebral blood flow have only been studied in healthy volunteers, showing no influence in clinically relevant doses [8]. This discrepancy can be explained by the difference in study design and conditions. Esmolol did not affect cerebral blood flow in healthy volunteers [9], supporting our findings in the present study.

The prevention of an increase in HR by pre-treatment with β-adrenergic blocking agents is beneficial for patients with a history of coronary artery disease.

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The attenuation of the increase in V_{mca} by labetalol may be advantageous for patients undergoing ECT with a history of cerebral aneurysm or stroke.

A limitation of this study is the relatively small size of the study groups. This is partly due to difficulties obtaining reliable informed consent in patients with a history of major depression. Larger, multicentre studies have to elucidate if our findings could effect seizure duration, the efficacy of ECT and clinical outcome.

P. J. A. van der Starre, H. J. M. Lemmens
A. Chandel, J. G. Brock-Utne
Department of Anesthesia
Stanford University School of Medicine
Stanford, CA, USA

H. B. Solvason
Department of Psychiatry
Stanford University School of Medicine
Stanford, CA, USA

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