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ORIGINAL ARTICLE
Arrhythmia/Electrophysiology

Effects of Landiolol, an Ultra-Short-Acting β_1-Selective Blocker, on Electrical Storm Refractory to Class III Antiarrhythmic Drugs

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Background: Occasionally it is difficult to inhibit electrical storm (ES) with standard pharmacological treatment. In the present study the effect of landiolol, an ultra-short-acting β_1-selective blocker, on ES refractory to class III antiarrhythmic drugs was evaluated.

Methods and Results: The study group comprised 42 consecutive patients who developed ES for which intravenous class III antiarrhythmic drugs, such as amiodarone and nifekalant, were ineffective. Landiolol was administered intravenously with an initial dose of 2.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$, which was doubled if it was ineffective, up to a maximum dose of 80 $\mu g \cdot kg^{-1} \cdot min^{-1}$. Landiolol inhibited ES in 33 patients (79%) at a mean dose of 7.5±12.2 $\mu g \cdot kg^{-1} \cdot min^{-1}$. All patients in whom landiolol was ineffective died of arrhythmia. Of the 33 patients in whom landiolol was effective, 25 survived and were discharged (60% of all patients). Landiolol significantly decreased heart rate ($P<0.0001$), but did not affect blood pressure. Landiolol was not discontinued for adverse effects in any of the responders. Age, APACHE II score, and pH of arterial blood gas differed significantly between the responders and nonresponders.

Conclusions: Landiolol is useful as a life-saving drug for class III antiarrhythmic drug-resistant ES. The main mechanism of ES refractory to class III antiarrhythmic drugs could be abnormal automaticity but not reentry. (*Circ J* 2010; **74:** 856–863)

Key Words: Antiarrhythmic drug; β-blocker; Electrical storm; Landiolol; Ventricular tachyarrhythmia

Arrhythmias such as ventricular tachycardia (VT) and ventricular fibrillation (VF) are a major cause of sudden cardiac death, and control of these arrhythmias is important to improve patients' survival.[1] Patients with severe heart diseases, such as acute myocardial infarction and cardiomyopathy, are particularly likely to become resistant to treatment, with a fatal outcome when these arrhythmias occur during the disease course. Guidelines for treatment of severe arrhythmia have been established by the AHA/ACC/ESC and JCS, and cardiopulmonary resuscitation (CPR), electric cardioversion, and antiarrhythmic drugs are performed as standard lifesaving treatment.[2–4] However, in clinical practice, VT/VF occasionally recur even though strict treatment following these guidelines was done.

Frequent occurrence of VT and VF is called an electrical storm (ES)[1,3] and this pathology is the cause of fatal arrhythmia in some patients with severe heart disease. Once ES occurs, control of VT/VF by standard treatment alone is difficult.[5,6] There are various causes of ES, but intravenous injection of class III antiarrhythmic drugs such as amiodarone and nifekalant is used first to inhibit VT/VF in most patients.[7–9] However, ES sometimes shows resistance to these drugs, which is a major problem in emergency medical care. Some clinical studies have demonstrated that β-blockers effectively suppress ES,[10,11] which suggests that enhanced sympathetic nerve activity is involved.[12,13]

In the present study, we evaluated the effect of intravenous injection of landiolol,[14] an ultra-short-acting β_1-selective blocker, as a lifesaving drug for class III antiarrhythmic drug-resistant ES.

Methods

Patient Enrollment

We enrolled 42 consecutive patients (31 men, 11 women; mean age, 65±16 years) admitted to the Acute Critical Care

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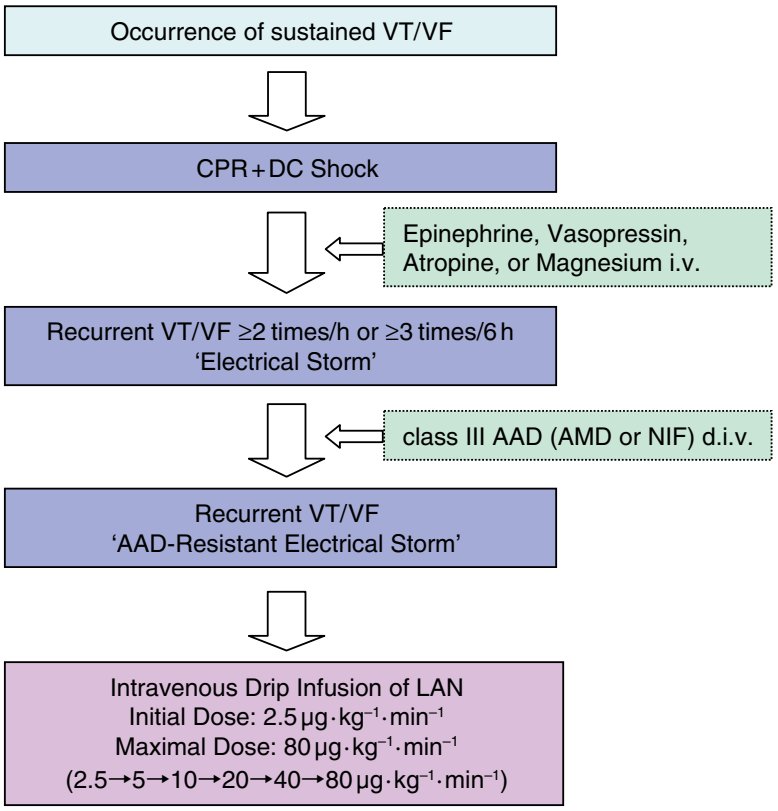

Figure 1. Study protocol. VT, ventricular tachycardia; VF, ventricular fibrillation; CPR, cardiopulmonary resuscitation; DC, direct current; LAN, landiolol.

Center of Kyorin University Hospital between October 2006 and September 2009 in whom ES occurred and was difficult to treat following established guidelines[2–4] using CPR, electric cardioversion, and antiarrhythmic drugs. ES was defined as occurrence of sustained VT/VF twice or more per hour or 3 times or more over 6 h. Conditions in which the QRS configuration could be identified on ECG were defined as VT and those with no apparent QRS configuration were defined as VF. Class III antiarrhythmic drugs were administered to all patients and judged to be ineffective before initiation of landiolol treatment.

The exclusion criteria were cardiac arrest at the time of arrival, administration of antiarrhythmic drugs before arrival, renal failure (serum creatinine >2.0 mg/dl), and the occurrence of hemodynamically stable VT. In patients with acute myocardial infarction, revascularization therapy, such as percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery, was performed in the acute phase. Age, sex, underlying heart disease, left ventricular ejection fraction (LVEF) using the modified Simpson method on echocardiography, Killip classification, APACHE II score[15] (a prognostic index of disease severity), arterial blood gas analyses (pH and alveolar-arterial oxygen pressure difference [A–aDO_2]), complications (hypertension, hyperlipidemia, and diabetes), use of class III antiarrhythmic drugs and general anesthetics, and use of assisted circulation devices (intra-aortic balloon pumping [IABP] and percutaneous cardiopulmonary support [PCPS]) were evaluated before and after landiolol administration.

The study was performed after approval by the Kyorin University Ethics Committee for Medical Studies.

Study Protocol

The study protocol is shown in Figure 1. When lethal sustained VT/VF with collapsing hemodynamics occurred, CPR was first performed using electric cardioversion (direct current [DC] shock) to stop VT/VF. DC shock was applied at 200–360J with a monophasic defibrillator, and at 100–150J with a biphasic defibrillator. Drugs, such as epinephrine, vasopressin, atropine, and magnesium, were used as needed. When VT/VF recurred, class III antiarrhythmic drugs were administered intravenously. With recurrence of sustained VT/VF, landiolol was administered under a diagnosis of antiarrhythmic drug-resistant ES.

Because landiolol was administered to patients with very unstable hemodynamics caused by frequent occurrence of VT/VF, administration was initiated at a very low dose of 2.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$; the normal starting and maintenance doses are 60–125 and 10–40 $\mu g \cdot kg^{-1} \cdot min^{-1}$, respectively.[16] Bradycardia and hypotension are likely to occur as adverse effects because landiolol is a β-blocker, and thus the ECG and blood pressure were monitored during drug administration. Because intravenously administered landiolol is an ultra-short-acting drug with a very short blood half-life (4 min),[17] the effect was assessed 10 min after administration. If it was insufficient, the dose was elevated using a doubling protocol (2.5→5→10 $\mu g \cdot kg^{-1} \cdot min^{-1}$) while monitoring heart rate and blood pressure, up to a maximum dose of 80 $\mu g \cdot kg^{-1} \cdot min^{-1}$. The effect of landiolol was assessed after each dose elevation. Other treatment was maintained during assessment of the antiarrhythmic effect of landiolol.

Assessment of Landiolol Therapy

When severe bradycardia or hypertension observed in pa-

Table 1. Baseline Characteristics of Patients (n=42) Treated With Landiolol

Age (years)	65±16
Sex (M/F)	31/11
Baseline heart disease	
Acute MI	21 (50%)
PCI/CABG	19/1
Previous MI	4 (10%)
Idiopathic dilated cardiomyopathy	5 (12%)
Hypertrophic cardiomyopathy	2 (5%)
Secondary cardiomyopathy	8 (19%)
Idiopathic VT/VF	2 (5%)
LVEF (%)	39±15
Killip class III and IV	21 (50%)
APACHE II score	19±10
Arterial blood gas analysis	
pH	7.3±0.2
A-aDO_2 (torr)	192±166
Hypertension	32 (76%)
Hypercholesterolemia	20 (48%)
Diabetes	18 (43%)
No. of DC shocks	5±13
Class III antiarrhythmic drugs	42 (100%)
Amiodarone	33 (79%)
Nifekalant	9 (21%)
General anesthetic	37 (88%)
Assisted circulation devise	
IABP	14 (33%)
PCPS	3 (7%)

Data are n (%) unless otherwise shown.
MI, myocardial infarction; PCI, percutaneous catheter intervention; CABG, coronary artery bypass graft; VT, ventricular tachycardia; VF, ventricular fibrillation; LVEF, left ventricular ejection fraction; APACHE, acute physiology and chronic health evaluation; A-aDO_2, alveolar-arterial oxygen pressure difference; DC, direct current; IABP, intra-aortic balloon pumping; PCPS, percutaneous cardiopulmonary support.

tients in which landiolol was judged effective for VT/VF, a temporal pacemaker or catecholamines were used as needed. If continuation of landiolol was difficult even with this treatment, administration was discontinued. The acute and chronic effects of landiolol were evaluated based on inhibition of ES, and survival and discharge from hospital, respectively. Inhibition of ES was judged to have occurred if sustained VT/VF completely resolved for 12 h after the start of administering the maintenance dose of landiolol. In patients in whom landiolol was effective, concomitant administration of carvedilol or bisoprolol (oral β-blockers) was immediately initiated at doses of 2.5 and 1.25 mg/day, respectively. The dose of landiolol was slowly reduced as the dose of oral β-blocker was increased.

Statistical Analysis

All statistical analyses were performed using SPSS version 15.0 for Windows (Chicago, IL, USA). Values are presented as means±standard deviation. Data were compared using an unpaired Student's t-test. All comparisons were 2-sided and $P<0.05$ was regarded as significant.

Results

Clinical Background

The underlying heart disease was acute myocardial infarction in 21 patients, ischemic cardiomyopathy in 4, idiopathic dilated cardiomyopathy in 5, hypertrophic cardiomyopathy in 2, secondary non-ischemic cardiomyopathy in 8, and idiopathic VT/VF in 2. Ischemic heart disease was present in 60% of the patients (Table 1). The mean LVEF was 39±15% (20–70%) and the Killip classification was class I in 20 patients (24%), II in 1 (2%), III in 2 (5%), and IV in 19 (45%). The mean APACHE II score was 19±10. As regards arterial blood gas analyses, pH and A–aDO_2 were 7.3±0.2 and 192±166 torr, respectively. Hypertension was noted in 32 patients (76%), hyperlipidemia in 20 (48%), and diabetes in 18 (43%). The mean number of DC shocks applied before landiolol administration was 5±13. Temporal pacing was performed

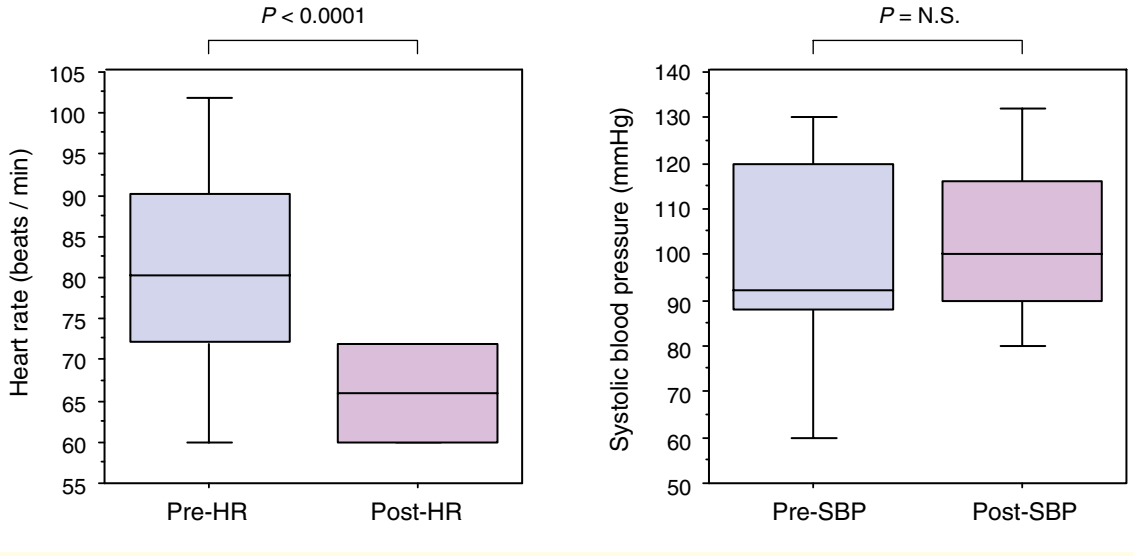

Figure 2. Comparisons of HR and SBP during sinus rhythm pre- and post-administration of landiolol. HR, heart rate; SBP, systolic blood pressure.

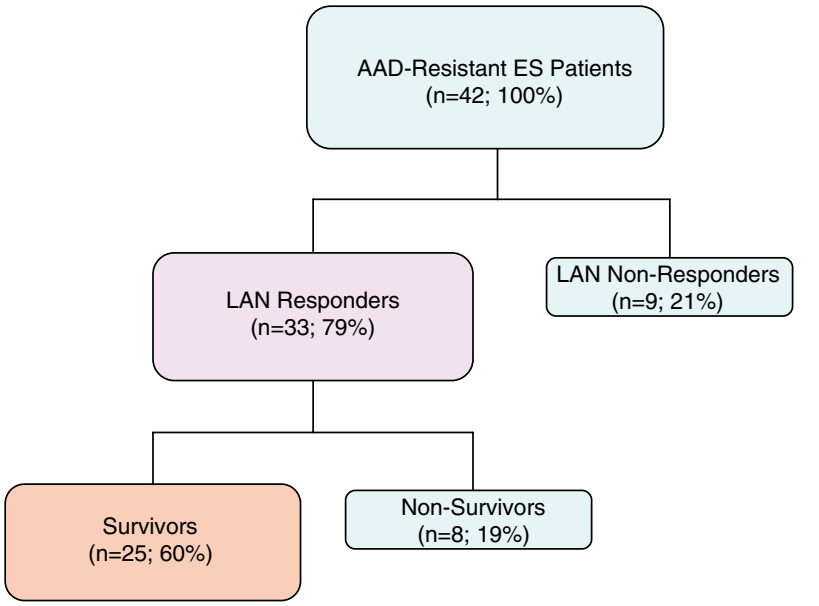

Figure 3. Antiarrhythmic and prognostic effects of landiolol (LAN) in patients with electrical storm (ES).

in 1 patient (2%). IABP and PCPS for assisted circulation were used in 14 patients (33%) and 3 patients (7%), respectively.

Either of intravenous amiodarone or nifekalant was administered as a class Ⅲ antiarrhythmic drug before landiolol administration in all patients; 33 (79%) received amiodarone and 9 (21%) received nifekalant. A general anesthetic (propofol or midazolam) was administered to 37 patients (88%) to induce deep sedation. Tracheal intubation was performed and respiration was managed using a ventilator in all patients treated with general anesthetics.

Effects of Landiolol on ES

Landiolol-induced changes in heart rate and blood pressure are shown in **Figure 2**. Landiolol significantly reduced the heart rate (P<0.0001). Temporal pacing was performed for bradycardia in 1 patient (2%), but landiolol was not discontinued in this patient. No significant changes were noted in blood pressure, but the catecholamine dose was increased in 3 patients (7%). Landiolol inhibited ES in 33 patients (79%) and was ineffective in 9 (21%) (**Figure 3**). In this study, other class Ⅲ antiarrhythmic drugs were not used when landiolol was ineffective. All patients in whom landiolol was ineffective died of arrhythmia. The clinical findings of patients who were or were not responsive to landiolol are compared **Table 2**. There were significant differences in age, APACHE Ⅱ score, and pH of arterial blood between these groups, with younger age (P=0.04), lower APACHE Ⅱ score (P=0.03), and higher pH of arterial blood (P=0.01) for the responders. More of the responders were treated with amiodarone (85%), but the difference was not significant regarding use of class Ⅲ antiarrhythmic drugs.

The mean dose of landiolol was 7.5±12.2 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (2.5–80 $\mu g \cdot kg^{-1} \cdot min^{-1}$). ES was inhibited at the starting dose (2.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$) in 1 patient (3%) and only at the highest dose (80 $\mu g \cdot kg^{-1} \cdot min^{-1}$) in 1 patient (3%). The most frequent effective dose was 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$, which was effective in 28 patients (85%).

The ECG records during the course for the patient in whom inhibition of ES was only achieved at the highest dose are shown in **Figure 4**. This patient was a 78-year-old woman with acute myocardial infarction. Urgent coronary angiography was performed and the proximal region of the anterior descending branch of the left coronary artery was found to be completely obstructed. PCI of this region was performed and revascularization succeeded. However, VF suddenly occurred on the 2nd hospital day and was stopped by DC shock, but then recurred repeatedly and was refractory to intravenous amiodarone. Following our study protocol outlined earlier, intravenous drip infusion of landiolol was initiated at 2.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and increased by doubling while monitoring the blood pressure and ECG until an effect was obtained. VF completely disappeared at the highest dose (80 $\mu g \cdot kg^{-1} \cdot min^{-1}$) and ES was vanished.

Carvedilol was given to 21 patients (64%) and bisoprolol to 12 (36%), with administration of the oral β-blocker initiated immediately after landiolol was judged to be effective. The maintenance doses of carvedilol and bisoprolol were 2.5–10 mg and 1.25–5 mg, respectively. The mean duration of landiolol treatment was 29±31 h (12–116 h) and treatment was completed within 5 days in all patients.

Prognosis of Patients Who Responded to Landiolol Therapy

Of the 33 patients in whom landiolol was effective for ES, 25 survived and were discharged (60% of all patients), but the other 8 patients died. The main causes of death were multiple organ failure, severe heart failure, and severe infection such as pneumonia. The clinical findings of the survivors (n=25) are compared with those of the non-survivors (n=17, including the 9 patients who died of arrhythmia in the acute phase) in **Table 3**. Significant differences were found between the 2 groups for age, incidence of acute myocardial infarction, Killip classification, APACHE Ⅱ score, pH of arterial blood, history of hypertension, and use of IABP.

Of the 25 survivors, 24 (57% of all patients) could walk by themselves at discharge. The remaining patient (2%) transferred to another facility for rehabilitation. The mean hospital stay for the survivors was 30±38 days.

Table 2. Comparison of the Clinical Features of the Patients Who Were or Were Not Responsive to Landiolol in All States and Each State After Use of Amiodarone or Nifekalant

	All (post-AMD+post-NIF) states			Post-AMD state			Post-NIF state		
	Responders to LAN (n=33)	Non-responders to LAN (n=9)	P value	Responders to LAN (n=28)	Non-responders to LAN (n=5)	P value	Responders to LAN (n=5)	Non-responders to LAN (n=4)	P value
Age (years)	62±16	74±12	0.04	62±17	69±11	NS	63±11	81±10	0.04
Sex (M/F)	25/8	6/3	NS	21/7	4/1	NS	4/1	2/2	NS
Baseline heart disease									
Acute MI	16 (48%)	5 (56%)	NS	13 (46%)	1 (20%)	NS	3 (60%)	4 (100%)	NS
PCI/CABG	15/1	4/0		12/1	1/0		3/0	3/0	
Previous MI	4 (12%)	1 (11%)	NS	3 (11%)	1 (20%)	NS	1 (20%)	0 (0%)	NS
Idiopathic dilated cardiomyopathy	5 (15%)	0 (0%)	NS	5 (18%)	0 (0%)	NS	0 (0%)	0 (0%)	–
Hypertrophic cardiomyopathy	1 (3%)	1 (11%)	NS	1 (4%)	1 (20%)	NS	0 (0%)	0 (0%)	–
Secondary cardiomyopathy	7 (21%)	2 (22%)	NS	7 (25%)	2 (40%)	NS	0 (0%)	0 (0%)	–
Idiopathic VT/VF	2 (6%)	0 (0%)	NS	1 (4%)	0 (0%)	NS	1 (20%)	0 (0%)	NS
LVEF (%)	38±15	42±15	NS	38±15	43±9	NS	38±13	29±9	NS
Killip class III and IV	15 (45%)	6 (67%)	NS	13 (46%)	2 (40%)	NS	2 (40%)	4 (100%)	NS
APACHE II score	17±9	26±12	0.03	17±9	19±11	NS	18±12	34±9	NS
Arterial blood gas analysis									
pH	7.3±0.1	7.1±0.2	0.01	7.3±0.1	7.2±0.2	NS	7.3±0.2	7.0±0.1	0.04
A-aDO_2	175±157	254±193	NS	174±155	138±147	NS	182±186	400±141	NS
Hypertension	24 (73%)	8 (89%)	NS	20 (71%)	4 (80%)	NS	4 (80%)	4 (100%)	NS
Hypercholesterolemia	16 (48%)	4 (44%)	NS	13 (46%)	2 (40%)	NS	3 (60%)	2 (50%)	NS
Diabetes	15 (45%)	3 (33%)	NS	12 (43%)	1 (20%)	NS	3 (60%)	2 (50%)	NS
No. of DC shocks	6±17	3±2	NS	7±18	3±2	NS	4±2	4±2	NS
Use of temporary pacing	1 (3%)	0 (0%)	–	1 (4%)	0 (0%)	–	0 (0%)	0 (0%)	–
Use of catecholamines	3 (9%)	0 (0%)	–	3 (11%)	0 (0%)	–	0 (0%)	0 (0%)	–
General anesthetic	28 (85%)	9 (100%)	NS	23 (82%)	5 (100%)	NS	5 (100%)	4 (100%)	NS
Assisted circulation devise									
IABP	12 (36%)	2 (22%)	NS	11 (39%)	0 (0%)	NS	1 (20%)	2 (50%)	NS
PCPS	2 (6%)	1 (11%)	NS	2 (7%)	0 (0%)	–	0 (0%)	1 (25%)	–

Abbreviations see in Table 1.

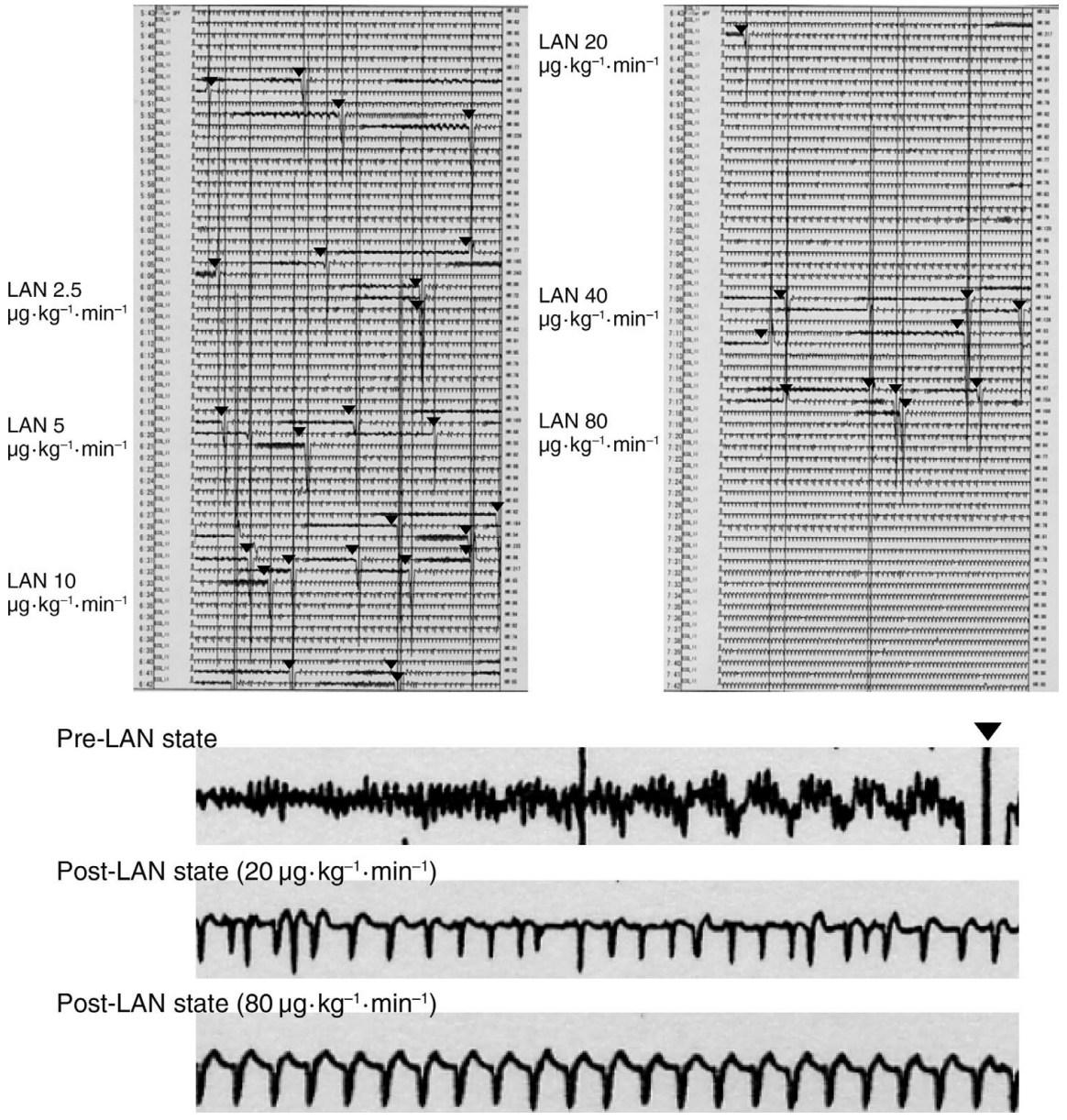

Figure 4. Compressed and actual ECG recordings during intravenous drip infusion of landiolol for electrical storm (ES). Note the number of direct current shocks (▼) required for terminating ventricular fibrillation. Landiolol (LAN) was increased up to a maximum dose of 80 μg·kg^{-1}·min^{-1}, and then ES vanished from the ECG.

Discussion

ES in patients with severe heart disease such as acute myocardial infarction is likely to be aggravated and may not be inhibited by treatment with class III antiarrhythmic drugs alone. Enhanced sympathetic nerve activity is thought to be associated with the development and persistence of ES,[12,13] and β-blockers and surgical stellate ganglion block (sympathetic ganglion) are useful for reducing this nerve activity.[10,11,18] Deep sedation induced by general anesthetics[18,19] and catheter ablation[20] have also been shown to be effective, indicating the variety of treatments that have been attempted for ES.

In this study, intravenous injection of landiolol, an ultra-short-acting β_1-selective β-blocker, inhibited class III antiarrhythmic drug-resistant ES in 80% of the subjects. Three β-blockers for intravenous injection are available in Japan: landiolol, esmolol, and propranolol. Landiolol has a shorter plasma half-life (4 min) than the other two drugs (esmolol: 9 min; propranolol: 2 h) and higher heart (β_1) selectivity (β_1/β_2: landiolol, 277; esmolol, 20; propranolol, 0.6).[14,17] These properties suggest that adverse respiratory effects, such as bronchial asthma, are less likely to develop and persist with landiolol, which may make it more suitable for emergency medical care.

Occurrence of severe bradycardia and rapid hypotension

Table 3. Comparison of the Clinical Features of Survivors and Non-Survivors

	Survivors (n=25)	Non-survivors (n=17)	P value
Age	60±16	72±11	0.01
Sex (M/F)	19/6	12/5	NS
Baseline heart disease			
Acute MI	8 (32%)	13 (76%)	0.01
PCI/CABG	6/1	13/0	
Previous MI	2 (8%)	1 (6%)	NS
Idiopathic dilated cardiomyopathy	5 (20%)	0 (0%)	–
Hypertrophic cardiomyopathy	1 (4%)	1 (6%)	NS
Secondary cardiomyopathy	7 (28%)	2 (12%)	NS
Idiopathic VT/VF	2 (8%)	0 (0%)	–
LVEF (%)	40±16	37±13	NS
Killip class (I/II/III/IV)	16/1/0/8	4/0/2/11	0.02
APACHE II score	15±9	24±11	0.01
Arterial blood gas analysis			
pH	7.3±0.1	7.2±0.2	0.007
A-aDO_2	167±157	228±178	NS
Hypertension	16 (64%)	16 (94%)	0.03
Hypercholesterolemia	9 (36%)	11 (65%)	NS
Diabetes	8 (32%)	10 (59%)	NS
No. of DC shocks	3±2	10±23	NS
Use of temporary pacing	1 (4%)	0 (0%)	–
Use of catecholamines	1 (4%)	2 (12%)	NS
Class III antiarrhythmic drugs			
Amiodarone	22 (88%)	11 (65%)	NS
Nifekalant	3 (12%)	6 (35%)	NS
General anesthetic	20 (80%)	17 (100%)	NS
Assisted circulation device			
ABP	5 (20%)	9 (53%)	0.04
PCPS	0 (0%)	3 (18%)	–

Abbreviations see in Table 1.

are of concern because landiolol is a β-blocker, but these effects can largely be avoided by starting administration at a low dose, as performed in this study. A tendency for bradycardia to occur during landiolol administration can be managed with temporal pacing, and hypotension can be treated with catecholamines, allowing continuation of landiolol. Temporal pacing was performed in 1 patient (2%) and the catecholamine dose was increased in 3 (7%) in this study. These countermeasures enabled continuation of landiolol, with subsequent inhibition of ES and avoidance of death from arrhythmia.

ES complicated by ischemic heart disease was present in 60% of the patients in the study. ES (ie, VT/VF) is more likely to occur in patients with ischemic heart disease because enhanced sympathetic nerve activity aggravates ischemic heart disease-associated VT/VF[12,13] and increases the electrical instability of the heart, thereby accelerating development of arrhythmia.[21,22] The oral β_1-blocker, metoprolol, inhibits ventricular arrhythmia in patients with acute myocardial infarction.[23,24] Enhanced sympathetic nerve activity may also be involved in the development of VT/VF in chronic ischemic heart disease.[25,26] Thus, β-blockers could be effective in the acute phase and for inhibiting VT/VF in the chronic phase (ie, prevention of sudden cardiac death). Carvedilol and bisoprolol are used as oral β-blockers in patients in whom landiolol is effective. Carvedilol is a multi-acting β-blocker that blocks β_2 and α receptors, in addition to the β_1 receptor, whereas bisoprolol is a pure β_1-blocker. The superior β_1 selectivity of bisoprolol may make it more appropriate as an oral β-blocker for patients in whom landiolol inhibits ES, given the similar β_1 selectivity of landiolol.

With respect to class III antiarrhythmic drugs for intravenous injection, amiodarone is a multichannel blocker that is used in Western countries, whereas nifekalant is a pure IKr channel blocker that is used in Japan, in addition to amiodarone. The mechanism of action of class III antiarrhythmic drugs is inhibition of reentry by prolonging the refractory period. Nifekalant is a faster-acting drug compared with amiodarone and causes no adverse effects associated with cardiac function, such as hypotension. Nifekalant may cause torsade de pointes through prolongation of the QT interval, but we did not observe this effect in any patients, probably because the duration of administration was short.

In patients with ES that is refractory to amiodarone or nifekalant, there are 2 strategies for inhibiting ES. The first strategy is to use another class III antiarrhythmic drug, because the antiarrhythmic actions of amiodarone and nifekalant are not the same. The second strategy is to use β-blockers. It may be better to switch to landiolol rather than to another class III antiarrhythmic drug, because landiolol has a quite different action. The mechanism of VT/VF in patients in whom amiodarone or nifekalant is ineffective appears to be abnormal automaticity, rather than reentry. Landiolol may suppress triggers related to abnormal automaticity. When amiodarone

or nifekalant is ineffective, intravenous β-blockers such as landiolol should be considered immediately as the second choice of treatment. The subsequent effect of landiolol may be monitored by clinical indices reflecting disease severity, such as the APACHE II score and pH of arterial blood, as shown in this study. These indices may also serve as indications for initiation of landiolol in patients with severe disease.

Study Limitations

Landiolol inhibited class III antiarrhythmic drug-resistant ES with high efficacy. However, it is unclear when landiolol should be used as the first choice for suppressing ES. The efficacy of landiolol may be low if it is used before the antiarrhythmic drug(s). In this study, amiodarone was more used than nifekalant as an initial class III antiarrhythmic drug. Because amiodarone has a longer plasma half-life, the high efficacy of landiolol may be a multiplier effect with amiodarone. Therefore, the main mechanism of VT/VF is reentry and the first choice of treatment is a class III antiarrhythmic drug. When such a drug is ineffective, the underlying mechanism could be abnormal automaticity and in that situation, landiolol is recommended for inhibiting VT/VF. In this study, only landiolol was used as a β-blocker, and it is unclear whether the effects of landiolol are superior to those of esmolol and propranolol. However, the duration of action of landiolol is shorter than that of esmolol and propranolol,[17] and the β_1-selectivity is high,[14] which make landiolol favorable for use in emergency medical care.

Conclusions

There are various causes of ES and different treatments may be needed for individual patients. Class III antiarrhythmic drugs are the main therapy, but when these are ineffective VT/VF may have developed by a mechanism other than reentry. Enhanced sympathetic nerve activity may be the major factor. Because landiolol is an ultra-short-acting intravenous injection with superior cardiac selectivity, it can be readily used in emergency medical care and should be considered for patients with ES that is refractory to antiarrhythmic drugs.

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