CASE REPORT

Landiolol is effective for the treatment of tachycardia-induced cardiogenic shock in patients during septic shock therapy

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SUMMARY

Septic shock is a life-threatening condition that occurs when the blood pressure drops to a low level after an infection. Atrial fibrillation (AF) is the most common arrhythmia to complicate its course. Beta (β)-blockers are often administered to manage supraventricular tachyarrhythmias observed in patients presenting with sepsis. A 74-year-old woman presenting with sepsis demonstrated AF tachycardia characterised by severe hypotension. She was refractory to conventional therapy including verapamil and digoxin; therefore, treatment using landiolol (an ultrashort-acting β -blocker) was initiated. Her clinical course was followed over 48 hours, and she showed a significant improvement in her heart rate and blood pressure without any adverse effect. Landiolol can rapidly control the accelerated heart rate associated with AF in critically decompensated patients presenting with septic shock.

heart rate (HR) and raised her BP immediately after administration. This information described in our case report is expected to provide physicians with a useful alternative treatment strategy for patients presenting with septic shock and concomitant AF tachycardia.

CASE PRESENTATION

Our patient was a 74-year-old woman, resident of a special elderly care nursing home. She related history of treatment for depression but no history of hypertension, heart failure and/or arrhythmia. She related an episode of fainting during dinner when her BP was observed to be <60 mm Hg and, she was admitted to a primary hospital. Her body temperature was 38°C. She was treated with cefmetazole and dopamine (1.5 μ g/kg/min); however, because of no change in her clinical condition, she was referred to our hospital for intensive care.

BACKGROUND

Septic shock is a serious condition that could be fatal without appropriate medication.¹ A variety of microorganisms (bacteria, fungi, viruses and parasites) can cause the primary infection leading to this condition. Although any part of the body could be affected, the lungs, brain, urinary tract, skin and abdominal organs are common sites of involvement.²

Atrial fibrillation (AF) during sepsis is associated with a high risk of morbidity and mortality.³ AF and concomitant sepsis are associated with poor outcomes owing to increased risks of stroke, cardiac dysfunction and death.

Several papers have reported that beta (β)-blockers are useful to manage supraventricular tachyarrhythmias in patients presenting with sepsis.^{4,5} However, few papers have reported the development of cardiogenic shock secondary to atrial tachycardia in patients being treated for septic shock.

In this report, we report a patient with septic shock in whom initial administration of norepinephrine (NA) effectively raised the patient's blood pressure (BP). However, she showed sudden development of AF leading to a state of haemodynamic collapse. She demonstrated clouding of consciousness with cold clammy skin. She was refractory to treatment using verapamil and digoxin to manage her critical condition. However, landiolol (an ultrashort-acting β -blocker) successfully reduced her

INVESTIGATIONS

On arrival, her BP was 118/57 mm Hg and HR was 111 bpm. An ECG demonstrated a sinus rhythm (SR) and a complete right bundle branch block (figure 1A). Her Sequential Organ Failure Assessment score was 4, and a serum lactate level was 2.2 mmol/L. Arterial blood gas testing showed a partial pressure of arterial oxygen of 60 mm Hg, partial pressure of carbon dioxide of 28 mm Hg and a pH of 7.47 with 1L of nasal oxygen inhalation. A chest X-ray (CXR) showed severe pulmonary oedema, congestion and pleural effusion (figure 1B). Echocardiography demonstrated preserved cardiac contractility calculated by an ejection fraction (EF) of 71%, indicating heart failure with a preserved EF. She was diagnosed as having septic shock secondary to urinary tract infection with acute heart failure. Blood cultures revealed *Escherichia coli*. She was administered NA (0.11 μ g/kg/min) and furosemide (40 mg/day) to treat heart failure and ceftriaxone sodium hydrate for sepsis, and she needed an intensive care unit (ICU) stay. The Acute Physiology and Chronic Health Evaluation II score in this patient was 20. The hospital mortality rate was estimated at 36%.

TREATMENT

During treatment for sepsis using NA and antibiotics, her heart rhythm was changed from SR to AF (figure 2A), her HR suddenly increased to

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Figure 1 ECG and CXR findings on admission. (A) ECG showing a complete right bundle branch block. (B) CXR showing severe pulmonary oedema, congestion and pleural effusion. CXR, chest X-ray; SR, sinus rhythm.

195 bpm and BP dropped to 60/30 mm Hg (figure 3), and she developed clouding of consciousness. She was diagnosed with cardiogenic shock secondary to tachycardia. She was administered verapamil (5 mg) injection during the night shift, leading to a temporary decrease in HR to 135 bpm and an increase in BP to 70/45 mm Hg. However, this effect was not continued and she soon redeveloped haemodynamic collapse. Next, digoxin (0.25 mg) was administered without success.

OUTCOME AND FOLLOW-UP

Given her serious haemodynamic instability, landiolol was continuously administered at an initial dose of 1 µg/kg/min, which was gradually increased to 3.3 µg/kg/min. Following this dosage, her HR decreased to 120 bpm and BP increased to 80/48 mm Hg (figure 3), and she showed a clearing of her previously observed disturbed consciousness. Landiolol was switched to bisoprolol transdermal patch (2 mg) 8 hours after initiation of treatment, and digoxin (0.25 mg) was reinjected. Her AF converted to SR 10 hours after the onset of AF (figure 2B; HR was 90 bpm and BP was 128/72 mm Hg.) Soon, doses of landiolol and NA could be gradually reduced and eventually discontinued with resolution of her pulmonary oedema, congestion and pleural effusion (figure 3).

DISCUSSION

AF and concomitant sepsis are associated with increased morbidity and mortality. New onset AF is causally linked to poor outcomes in patients who were critically ill and diagnosed with sepsis.^{3 6} β-blocker therapy may control HR and reduce the deleterious effects of β-adrenergic stimulation in patients diagnosed with septic shock. Esmolol is a short-acting β-blocker (elimination half-life of approximately 9 min).⁷ Previous reports have shown that compared with standard treatment regimens, it can achieve a reduction in HR to target level without an increase in adverse outcomes.⁸ Recent reports have shown that β-blockers are associated with superior survival rates compared with calcium channel blockers, digoxin and amiodarone when used for the treatment of AF and concomitant sepsis.⁴

Landiolol is an intravenously administered, ultrashort-acting β-blocker with an elimination half-life of 3–4 min.⁹ This new drug is commercially available in Europe this year and is expected to be approved soon in the USA. It has been approved in Japan to treat patients demonstrating intraoperative and postoperative tachyarrhythmias, as well as AF associated with a reduced EF.^{10 11} Clinical trials have revealed that it is generally well tolerated with a relatively low risk of associated hypotension and bradycardia, although routine monitoring of cardiac function is essential during administration of landiolol. Thus, it is safer to be used in an ICU setting.

In our patient, initial treatment with NA for the management of septic shock was effective to maintain BP. However, supraventricular tachyarrhythmia secondary to AF caused cardiogenic shock. Verapamil was temporarily effective in this critical situation but did not demonstrate a sustained effect. Continuous intravenous administration of landiolol rapidly reduced HR and reversed the patient's haemodynamic instability. Previous reports have described that the systolic and diastolic pressures in patients treated using landiolol were 113±34 and 60±17 mm Hg, respectively.⁵ It should be noted however that in these patients tachyarrhythmia had not precipitated shock and haemodynamic instability. Moreover, landiolol administration was not shown to have affected BP in this previous report. In our patient, the patient's BP was initially 60/30 mm Hg because of tachycardia and was significantly increased following administration of landiolol.

Figure 2 ECG obtained during treatment. (A) AF tachycardia occurred during treatment. The patient's HR was observed to be 195 bpm. (B) Sinus conversion after administration of landiolol showing reduction in HR to 90 bpm. AF, atrial fibrillation; HR, heart rate.

Figure 3 The patient's clinical course observed during treatment. AF: atrial fibrillation; BP, blood pressure; HR, heart rate; ICU, intensive care unit; SR, sinus rhythm; γ , $\mu\text{g/kg/min}$.

Based on the results of the J-Land Study, rate control using an intravenous infusion of landiolol at 1–10 $\mu\text{g/kg/min}$ is a useful option for the management of patients with left ventricular dysfunction (EF 25%–50%) who demonstrate a rapid ventricular response during AF.¹⁰ EF was not applicable in our study because the patient showed acute heart failure with a preserved EF, however, an ultrashort-acting β -blocker is a useful treatment option in patients presenting with shock. Although it is not effective for treatment of AF, this drug is associated with minimum adverse effects because of a very short elimination half-life.

Furthermore, it could effectively achieve sinus conversion when used in combination with other medicines including bisoprolol. Bisoprolol, commonly available also as a transdermal patch in Japan, is indicated for the management of hypertension. However, bisoprolol fumarate tablets are used for the management of patients with AF tachycardia. In Japan, initial treatment using landiolol is often switched to a transdermal patch of bisoprolol because the latter is relatively easy to manage. In cases where use of the patch leads to an excessive, unexpected drop in BP and HR, the transdermal patch is easy to remove with a rapid reversal of the vital parameters. Moreover, medication adherence is better with use of a transdermal patch than it is with use of tablets, particularly in elderly patients who might have difficulty with oral administration. Information is that this treatment strategy using landiolol could benefit clinicians to treat patients presenting with AF tachycardia and concomitant shock.

Landiolol rapidly and effectively controls the elevated HRs associated with AF in critically decompensated patients with concomitant septic shock. Cardioselective, ultrashort-acting drugs such as landiolol, which are associated with a lesser risk of adverse effects, could be useful treatment strategies available to physicians for effective haemodynamic management in cases such as ours.

Learning points

- Atrial fibrillation (AF) during sepsis is associated with a high risk of morbidity and mortality.
- Landiolol is a cardioselective and ultrashort-acting drug.
- Landiolol can rapidly control the accelerated heart rate associated with AF in critically decompensated patients presenting with septic shock.

Contributors YA: wrote this manuscript and involved in the patient's care. TS and SY: involved in the patient's care. SH: organised the patient's care.

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