

Combination of veno-arterial extracorporeal membrane oxygenation and hypothermia for out-of-hospital cardiac arrest due to *Taxus* intoxication

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ABSTRACT

A young woman presented with cardiac arrest following ingestion of yew tree leaves of the *Taxus baccata* species. The toxin in yew tree leaves has negative inotropic and dromotropic effects. The patient had a cardiac rhythm that alternated between pulseless electrical activity with a prolonged QRS interval and ventricular fibrillation. When standard resuscitation therapy including digoxin immune Fab was ineffective, a combination of extracorporeal membrane oxygenation (ECMO) and hypothermia was initiated. The total duration of low flow/no flow was 82 minutes prior to the initiation of ECMO. After 36 hours of ECMO (including 12 hours of electrical asystole), the patient's electrocardiogram had normalized and the left ventricular ejection fraction was 50%. At this time, dobutamine and the ECMO were stopped. The patient had a full neurologic recovery and was discharged from the intensive care unit after 5 days and from the hospital 1 week later.

RÉSUMÉ

Une jeune femme est arrivée à l'hôpital en état d'arrêt cardiaque à la suite de la prise de feuilles d'arbre de l'espèce *Taxus baccata*. La toxine contenue dans les feuilles d'if produit des effets inotropes et dromotropes négatifs. Le rythme cardiaque alternait entre une activité électrique sans pulsation, accompagnée d'un prolongement de l'intervalle QRS, et la fibrillation ventriculaire. Lorsqu'il s'est avéré que le traitement habituel de réanimation, composé de fragments d'anticorps spécifiques à la digoxine (Fab) d'origine ovine était inefficace, une intervention associant l'oxygénation extracorporelle (ECMO) et l'hypothermie a été entreprise. Il s'est écoulé, en tout, 82 minutes d'absence de débit sanguin ou de faible débit sanguin avant l'amorçage de l'ECMO. Après 36 heures de traitement par l'ECMO (dont 12 heures en état d'asystolie électrique), l'électrocardiogramme était redevenu

normal, et la fraction d'éjection du ventricule gauche s'élevait à 50%. Le traitement par la dobutamine et l'ECMO ont alors été interrompus. La patiente a connu un rétablissement neurologique complet; elle est sortie du service des soins intensifs au bout de 5 jours et a obtenu son congé de l'hôpital 1 semaine plus tard.

Keywords: cardiac arrest, extracorporeal membrane oxygenation, intoxication, therapeutic hypothermia

Ingestion of leaves from the common yew tree (*Taxus* spp, Taxaceae), a known poison, is associated with adverse myocardial effects, for which there are limited therapeutic options. We present the case of a patient with intoxication causing severe arrhythmia and cardiac arrest and discuss the successful management of this patient with combined use of venoarterial extracorporeal membrane oxygenation (ECMO) and therapeutic hypothermia.

CASE REPORT

A 19-year-old female patient intentionally ingested *Taxus baccata* leaves and rapidly developed signs of profound weakness associated with abdominal cramps. When the ambulance arrived, she had ventricular tachycardia with a weak pulse and severe hypotension, which rapidly evolved into ventricular fibrillation. Cardiopulmonary resuscitation (CPR), including several countershocks and injections of epinephrine and amiodarone, was carried out for 25 minutes. The heart rhythm alternated between pulseless electrical activity

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with a prolonged QRS interval and ventricular fibrillation (Figure 1).

The patient was brought to our tertiary university hospital with ongoing mechanical CPR (Lucas, Medtronic SA, Brussels, Belgium). During transport, there were brief periods during which the circulation resumed and chest compressions could be discontinued. On arrival at hospital, the patient had a low mean arterial pressure and transesophageal echocardiography showed a left ventricular ejection fraction of about 10%. The patient was rapidly given 240 mg of digoxin immune Fab, resulting in a small and transient narrowing of the QRS complex on the electrocardiogram, but she remained in cardiogenic shock with an ejection fraction of about 10%. Dobutamine and norepinephrine infusions were started at 20 and 0.3 µg/kg/min, respectively, without any increase in heart contractility. Ventricular fibrillation recurred, followed by asystole, and CPR was resumed. Hypothermia was initiated using a transnasal evaporative cooling device (Rhinochill, Benechill Inc., CA), and venoarterial ECMO was implanted during CPR using femorofemoral heparin-coated cannulation (22 Fr arterial cannula and 24 Fr venous cannula, Edwards Lifesciences, Irvine, CA). The perfusionist, present only at the time of implantation, set the initial centrifugal blood pump (Revolution blood pump, Sorin, Milan, Italy) at a blood flow of 4 L/min. The ECMO circuit was primed with 700 mL of Plasma-Lyte solution (Baxter Healthcare Corporation, Deerfield, IL). The patient's leg was perfused using an antegrade single-lumen 8 Fr catheter (Arrow Inc, Reading, PA) to prevent limb ischemia. A heat exchanger was used on the ECMO circuit to maintain body temperature at 33°C (91.4°F) for 24 hours. Circulation was finally restored with ECMO 37 minutes after hospital arrival and 82 minutes after the original loss of spontaneous circulation. Norepinephrine and dobutamine infusions were then discontinued.

Cardiac activity resumed after 12 hours of electrical asystole. Because global myocardial hypokinesia persisted on transesophageal echocardiography, dobutamine was reintroduced at 20 µg/kg/min. Twenty-four hours after

ECMO implantation, the patient was warmed at 1°C/h to normothermia, and sedation was withdrawn. After 36 hours, the electrocardiogram had normalized and the ejection fraction had increased to about 50%. The dobutamine and the ECMO were stopped.

The patient's subsequent course was uneventful, and she made a full neurologic recovery. The patient revealed that she had taken the *Taxus baccata* leaves to draw attention to herself, and family therapy was started. She was discharged from the hospital after 12 days.

DISCUSSION

This report presents a case of cardiogenic shock complicated by cardiac arrest secondary to intoxication by leaves from the common yew tree (*Taxus* spp, Taxaceae), which have been used as a poison for centuries. Catuvolcus, the king of the Eubrones, famously committed suicide using yew leaves, and the hunting arrows of Celts were coated with a yew preparation. The toxicity of the yew is the result of a mixture of taxine alkaloids, principally taxine A and taxine B. Taxines have minor effects on smooth muscle cells, including those of the gastrointestinal tract. The main toxic effect is myocardial, with negative inotropic and dromotropic effects resulting in a decrease in excitability and conduction velocity.¹ The mechanism of action seems to be via inhibition of sodium and calcium membrane currents, resulting in bradycardia, arrhythmia, and cardiac arrest.^{2,3} Death is usually due to severe arrhythmia.

The first treatment for *Taxus* intoxication was gastric lavage. In 1836, Hurt explained that he had used an emetic substance to treat several children whose younger brother had earlier died after eating yew berries.⁴ Several antiarrhythmic agents have been used for treatment, including lidocaine, but their efficacy is limited.⁵ Administration of sodium bicarbonate has also been proposed, but an animal study failed to demonstrate any beneficial effect.⁶ Temporary

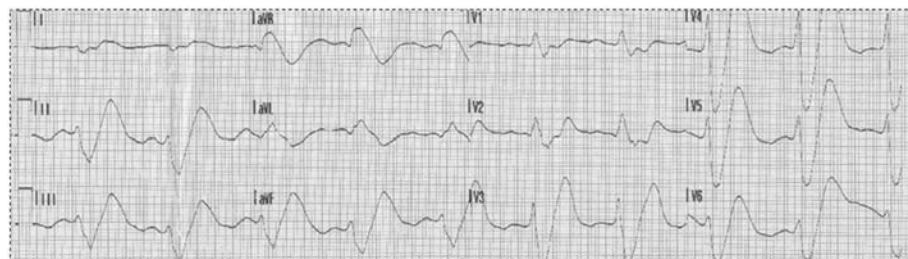


Figure 1. Initial electrocardiogram showing electrical activity with wide QRS.

pacemaker insertion may be proposed in selected cases of bradycardia⁷; however, most patients die from pulseless refractory ventricular fibrillation, which is refractory to any pacing procedure.⁵ The molecular weight of taxine B is too large to be removed by dialysis filter pores, and Dahlqvist and colleagues failed to demonstrate any improvement in a fatal case of intoxication even after 4.5 hours of hemodialysis using a high-flux filter.⁸

The effect of digoxin immune Fab fragments in such patients is controversial. The rationale for use is based on the similarity between the effects of yew and digoxin on myocardial cells and on the amount of cross-reactivity between digoxin and other glycosides, such as taxines. Cummins and colleagues reported no improvement in cardiac rhythm after administration of digoxin immune Fab for human intoxication,⁷ whereas Willaert and colleagues reported a beneficial effect.⁹ In our patient, digoxin immune Fab fragments had some effect on electrical activity with a slight narrowing of the QRS complex, but no significant improvement in contractility, and ultimately a disappointing response.

Because of the limited options available to treat severe yew intoxication, we managed our patient using a combined application of ECMO for CPR (eCPR) and hypothermia during CPR. ECMO has been successfully used to treat cardiac arrest secondary to various drug intoxications, including β -blockers, calcium antagonists, and antiarrhythmic drugs.^{10–12} Indeed, in patients with reversible heart failure or cardiac arrest from poisoning, venoarterial ECMO is now recommended to help maintain an adequate hemodynamic status until cardiac recovery.^{10–13} At our institution, eCPR is considered in all patients less than 65 years old without major comorbidities who have a witnessed cardiac arrest with unsuccessful bystander CPR for less than 30 minutes. Two other cases of ECMO use for the treatment of *Taxus* intoxication have been reported, but none applied ECMO for out-of-hospital cardiac arrest. Panzeri and colleagues described a patient with cardiogenic shock and severe ventricular arrhythmia who was successfully treated by ECMO.¹⁴ Soumagne and colleagues reported a similar case with cardiac failure complicated by in-hospital sustained ventricular fibrillation in whom ECMO was successfully applied for 50 hours.¹⁵ In our case, the use of ECMO was lifesaving despite an out-of-hospital cardiac arrest and a prolonged no-flow/low-flow period.

The originality of our case also resides in the combined application of eCPR and mild therapeutic intra-arrest hypothermia, which was not used in previous reports. Intra-arrest hypothermia has been shown to improve neurologic recovery in animal models, although clinical data remain scarce.¹⁶ Although the total duration of cardiac arrest was more than 1 hour, this young woman made a complete neurologic recovery.

SUMMARY

Taxus poisoning can cause severe myocardial dysfunction, and traditional CPR may be inadequate. We suggest that eCPR, coupled with hypothermia to improve neurologic recovery, should be considered for cardiac arrest secondary to severe poisoning.

Competing interests: None declared.

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