J Anesth (1996) 10:63–65

Journal of
Anesthesia

Clinical reports

Combined use of amrinone and high-dose epinephrine for postoperative low output syndrome (LOS) in pediatric patients

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Key words: Amrinone, Epinephrine, Low output syndrome

Introduction

Low output syndrome (LOS) is one of the serious consequences following open-heart surgery, and high-dose catecholamines and/or mechanical assist devices are required to support failed myocardial function. As one of the pharmacological options to counteract this complication, epinephrine remains the most potent drug to treat LOS, especially in pediatric cases. Since the inotropic effect of epinephrine is dose-dependent, high-dose epinephrine is sometimes necessary in patients with severe pump failure. However, the administration of high-dose epinephrine can interfere with peripheral circulation because of its strong vasoconstricting effects, resulting in severe acidosis and oliguria.

Amrinone has become available as an inotrope and vasodilator with a suggested main mechanism of selective phosphodiesterase III inhibition. Its unique properties include inotropic support combined with pulmonary and systemic vasodilation [1], and this effect is maintained in the presence of exogenous catecholamines including dopamine (DOA), epinephrine and norepinephrine (NE) [2–4]. Therefore, the benefit of using amrinone and other inotropes in combination is the vasodilating action of amrinone to counteract the vasoconstricting effects of the strong inotropes, in addition to its inotropic support.

We report on two pediatric patients who successfully recovered from life-threatening heart failure by the combined use of high-dose epinephrine and amrinone.

Address correspondence to: J. Uehara
Received for publication on December 26, 1994; accepted on April 7, 1995

Case reports

Case 1

A 2-day-old male infant weighing 2.8 kg suffered from total anomalous venous connection (TAPVC) type III. On admission he presented marked pulmonary congestion, and immediate definitive surgery under cardiopulmonary bypass (CPB) was required. Anesthesia was induced and maintained with oxygen, air, and fentanyl ($11\,\mu g\,kg^{-1}$). The radial artery was cannulated percutaneously and a double lumen catheter was inserted into the right subclavian vein percutaneously. The tip of the catheter was guided manually into the left atrium (LA) through the atrial septum under direct vision during total CPB and used for monitoring left atrial pressure (LAP). During 77 min of total CPB, the vertebral vein, which was found to be draining into the hepatic vein was ligated, and the pulmonary vein was found to be anastomosed to the LA. After the uneventful repair of these defects, weaning from CPB was started while systemic blood pressure (sBP) was maintained over 50 mmHg with the values of CVP and LA at 8–12 mmHg and 8–10 mmHg, respectively. However, as the sternum was closed, the patient developed a brief episode of severe hypotension (sBP < 30 mmHg) without significant changes in HR (160–170), CVP, LAP, ECG, electrolytes, or arterial blood gases (Table 1). This brief hypotension eventually responded to increased inotropes, including epinephrine ($0.5\,\mu g \cdot kg^{-1} \cdot min^{-1}$), isoproterenol (ISP; $0.05\,\mu g \cdot kg^{-1} \cdot min^{-1}$), DOA ($10\,\mu g \cdot kg^{-1} \cdot min^{-1}$), and dobutamine (DOB; $5\,\mu g \cdot kg^{-1} \cdot min^{-1}$). Two hours after surgery, in ICU the patient gradually became hypotensive again and this time did not respond to increased doses of those catecholamines and volume loading. Although the dose of epinephrine was increased to $1.5\,\mu g \cdot kg^{-1} \cdot min^{-1}$ without any change in the doses of other cathecholamines, he continued to pre-sent cardiogenic circulatory shock (HR > 190, sBP < 40 mmHg, LAP = 16 mmHg, CVP = 13 mmHg) with

Table 1. Changes in the values of arterial blood gas and electrolytes in Case 1

	At the start of weaning from CPB	After sternal closure	6 h after surgery	3 h after amrinone administration
FIO_2	1.0	0.5	0.8	0.8
pH	7.441	7.326	7.233	7.369
$PaCO_2$ (mmHg)	32.9	38.9	38.4	39.1
PaO_2 (mmHg)	483.1	133.7	93.5	137.2
BE	−0.7	−4.4	−9.8	−2.3
Na ($mEq \cdot l^{-1}$)	140	141	136	141
K ($mEq \cdot l^{-1}$)	3.2	3.5	3.6	2.9
Ca ($mEq \cdot l^{-1}$)	1.23	1.27	1.13	0.94

CPB, cardiopulmonary bypass; BE, base excess.

severe metabolic acidosis at 6 h after surgery. The value of base excess (BE) was decreased to −9.8 despite aggressive correction with sodium bicarbonate (52 mEq in 6 h). The bleeding in the closed pericardium was drained effectively and a chest X-ray showed no cardiac tamponade. Myocardial failure was suspected. At this point, administration of amrinone ($1\,mg \cdot kg^{-1}$ in a bolus followed by $20\,\mu g \cdot kg^{-1} \cdot min^{-1}$) was started, and was expected to reduce the afterload and enhance the inotropic effects of epinephrine. After 3 h of amrinone administration, a remarkable hemodynamic improvement (HR > 190, sBP > 60 mmHg, CVP = 11 mmHg, LAP = 11 mmHg, increased urine output) was achieved with better metabolic indices. BE recovered to −2.3 with only light correction with sodium bicarbonate (7 mEq in 3 h). Epinephrine was decreased gradually over 4 days after surgery, and amrinone was discontinued on postoperative day (POD) 12. The patient was discharged on POD 58.

Case 2

A 23-day-old female infant weighing 2.0 kg suffered from type II persistent truncus arteriosus. Her general condition was extremely poor, with severe heart failure when she was admitted to hospital. Emergent surgical correction was indicated and VSD closure, separation of the pulmonary artery from the aorta, and its reconstruction were performed. Anesthesia was induced and maintained with oxygen, air and fentanyl ($50\,\mu g \cdot kg^{-1}$). The left radial artery was cannulated percutaneously and a double lumen catheter was inserted into the right atrium through the atrial appendage under direct vision after pericardiotomy. Correction of the defects was performed uneventfully under 150 min of total CPB. Weaning from CPB was started using amrinone ($10\,\mu g \cdot kg^{-1} \cdot min^{-1}$), prostaglandin E_1 (PGE_1; $0.03\,\mu g \cdot kg^{-1} \cdot min^{-1}$), DOA ($5\,\mu g \cdot kg^{-1} \cdot min^{-1}$) and ISP ($0.03\,\mu g \cdot kg^{-1} \cdot min^{-1}$) in combination, and without epinephrine. However, this was unsuccessful (HR decreased from 165 to 104, sBP < 40 mmHg, and the right ventricle was strained) and therefore epinephrine was added to the combination of drugs. Although high doses of epinephrine ($2.5\,\mu g \cdot kg^{-1} \cdot min^{-1}$) and amrinone ($15\,\mu g \cdot kg^{-1} \cdot min^{-1}$) were needed to wean the patient from CPB, she improved over time after CPB and epinephrine was gradually stopped following ICU admission. Interestingly, in spite of such a high dose of epinephrine, her skin temperature in the dorsal region of her foot was maintained above 33°C and more than $10\,ml \cdot h^{-1}$ urine was produced throughout.

Discussion

We studied two pediatric patients with severe LOS following open heart surgery, in whom LOS was unresponsive to conventional combinations of inotropes. However, by using epinephrine and amrinone in combination, these patients showed remarkable improvement in cardiac performance, i.e., successful weaning from CPB, decreased requirement of other inotropes, and improved metabolic status.

Epinephrine is one of the most powerful drugs available to treat myocardial dysfunction [5], and is particularly useful in the management of pediatric patients with severe LOS. However, the use of this drug usually is accompanied by unfavorable side effects related to its strong α action, especially in high doses. These include increased afterload, peripheral vascular constriction, decreased urine production, and metabolic acidosis. Furthermore, pulmonary vasoconstriction, which can disturb right-ventricular performance and lead to postoperative cardiac failure in small pediatric patients with congenital heart disease, often follows high doses of epinephrine. Hence, a maximum dose of $0.5\,\mu g \cdot kg^{-1} \cdot min^{-1}$ epinephrine is recommended to prevent these complications [6]. Therefore there is a serious problem when a high dose of epinephrine (more than $1\,\mu g \cdot kg^{-1} \cdot min^{-1}$) is required to treat severe cardiac failure.

Amrinone, on the other hand, is a positive inotrope whose vasodilating action has a different mechanism from other catecholamines. It is suggested that amrinone inhibits phosphodiesterase III, and therefore synergistic effects can be expected when it is used with other catecholamines. Royster et al. [2] also found that in adult patients the increase in stroke volume and right-ventricular ejection fraction after a combination of amrinone and epinephrine was greater than after epinephrine alone, and that systemic vascular resistance and pulmonary vascular resistance also decreased remarkably using this combination.

Potent vasodilators such as nitroprusside and PGE_1 have been shown to counteract the strong vasoconstrictive effect of epinephrine, and many authors have reported that inotropes in combination with vasodilators provide beneficial circulatory support [5,7]. However, the advantages of using amrinone rather than other vasodilators are its effects on the pulmonary vessels and cardiac contractility. In the cases described above, neither high-dose epinephrine nor amrinone alone was effective enough to achieve satisfactory hemodynamic effects upon weaning from CPB. However, the combined use of these two drugs resulted in significant improvement in hemodynamics.

In summary, the combination of amrinone and high-dose epinephrine is useful in treating pediatric LOS, not only to enhance the inotropic effects of epinephrine, but also to ameliorate its vasoconstrictive action.

Acknowledgments. The authors wish to thank Dr. Tanigawa, Department of Anesthesia, University of Occupational and Environmental Health, for correcting the manuscript.

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