Angiotensin converting enzyme inhibitor as an additive treatment after successful balloon dilation of a critical pulmonary valve stenosis

M.O. Galal\textsuperscript{a,b,e}, A.M. Alzahrani\textsuperscript{a}, M.E. Elhoury\textsuperscript{a}

\textsuperscript{a}Prince Salman Heart Center, King Fahad Medical City, Riyadh; \textsuperscript{b}University Children’s Hospital in Essen

\textsuperscript{a} Saudi Arabia; \textsuperscript{b} Germany

A 2 days old, 2.7 kg heavy baby boy with critical pulmonary stenosis, underwent successful balloon dilation. After the uneventful procedure, he remained oxygen dependent. The baby was given oral angiotensin converting enzyme inhibitor (ACE inhibitor), instead of an infusion of alpha blocker. Within few hours, in the afternoon of the same day after administration of ACE Inhibitor, the baby could be weaned off oxygen, maintaining on room air, oxygen saturation between 87% and 92%. At follow-up, two months later, his saturation was 99% on room air.

We believe that some neonates with critical pulmonary valve stenosis who remain oxygen dependent despite successful balloon dilation, could benefit from such management.

Keywords: Critical pulmonary valve stenosis, Alpha blocker, ACE inhibitor

Infants with critical pulmonary valve stenosis irrespective of successful balloon valvuloplasty, will still need more tailored medical attention. It has been shown that some of these patients at different times after the intervention can benefit from the administration of an alpha blocker [1].

In this report we present a 2 day old, 2.7 kg heavy baby boy with critical pulmonary valve stenosis, who was successfully and uneventfully ballooned. The oxygen and duct dependent baby did not need ventilation. It was elected to do the intervention on conscious sedation while the anesthesiologist was in the catheterization laboratory. The pulmonary valve annulus measures 7 mm, a 8 mm PTCA balloon catheter was used. After successful balloon dilation as judged by decrease in echo Doppler gradient, oxygen saturation remained below 80%. The procedure was uneventful. But after the procedure the baby remained oxygen dependent to maintain an oxygen saturation of above 85%. As the baby was not in significant distress we thought of giving him oral angiotensin converting enzyme inhibitor (ACE inhibitor), instead of infusion of the alphablocker [1,3].

Within few hours (Fig. 1) after administration of ACE Inhibitor, the baby could be weaned off
oxygen, maintaining on room air and oxygen saturation between 87% and 92%.

We believe that some infants with critical pulmonary stenosis post successful balloon valvuloplasty, can benefit from such management.

Case report

A 2 days old (48 cm height, 2.7 kg weight) full term baby of normal delivery was discovered to have cyanosis and a systolic murmur 3 h post delivery. Saturation on room air went down to 65%. He was put on 40% oxygen and on prostaglandin (PGE1) 0.02 ugs/kg/min infusion. He did not need ventilation. On auscultation, there was a 2/6 continuous murmur. ECG showed sinus rhythm with biventricular hypertrophy. X-ray of the chest revealed a small heart with reduced vascularity.

Echocardiography

Echocardiography diagnosed a critical pulmonary valve stenosis. The tricuspid valve measured 1.2 cm in diameter (z value +0.21) and was comparable with the mitral valve. The patent foramen ovale (PFO) showed bidirectional shunting. There was neither tricuspid regurgitation nor stenosis. Well sized right ventricle with good biventricular function and intact ventricular septum was observed. The pulmonary valve annulus measured 7 mm with no infundibular stenosis. The peak gradient across the doming pulmonary valve was elevated with 80 mmHg. There was mild to moderate pulmonary valve regurgitation. In the left aortic arch, no coarctation with a moderate size PDA with left to right shunt across it was observed. It was decided to take the patient to the cardiac catheterization laboratory in view of balloon valvuloplasty.

Cardiac catheterization

Cardiac catheterization was done under conscious sedation. The intervention was performed uneventfully using a 4 Fr sheath through the right femoral vein. Before balloon dilation the right ventricular pressure was 121 mmHg, while the systemic pressure of the baby was 50/45 mmHg, with a mean of 33 mmHg. The pulmonary artery pressure was 46/23 with a mean of 35 mmHg. The maximum gradient between right ventricle (RV) and pulmonary artery (PA) was 75 mmHg.

The pulmonary valve was gradually ballooned with a 8 mm, 2 cm long Tyshak balloon catheter (Numed, Canada). The gradient across the pulmonary valve after the intervention was 17 mmHg. The RV pressure dropped to 57 mmHg, while the PA pressure was 40 mmHg. The systemic pressure at that time remained as the one before balloon dilation. Fluoroscopy time was 18 min and the procedure time was 72 min.

The procedure was uneventful and the baby was sent back to NICU on Prostaglandin infusion and oxygen mask, in good condition. Prostaglandin was discontinued due to a misunderstanding between the pediatric cardiologist and the intensivist. The child remained for the next 2 days oxygen dependent to maintain acceptable oxygen saturation on room air of >85%.

Clinical follow-up

As the neonate for two days after the procedure remained unchanged, was oxygen dependent and the baby was on oral feed and not on any infusion, we elected to start him because of his young age on

Figure 1. The dramatic improvement of the oxygen saturation and concomitantly the rapid weaning of oxygen from 30% to room air, few hours after starting ACE inhibitor.
low dose oral ACE inhibitor (Captopril 0.15 mg/kg/day). He received 0.3 mg TID. The afternoon of the same day (<15 h), oxygen supply could be stopped as the baby was saturating on room air between 87% and 92%, as measured by pulse oximetry (Fig. 1).

After two more days of observation, the baby was sent home on the same dose of oral ACE inhibitor. He was seen in the clinic two months later and his weight was now 3.5 kg, his saturation on room air was 99% on room air. The peak systolic gradient across the pulmonary valve as measured by echo Doppler was 37 mmHg with only mild pulmonary regurgitation. ACE inhibitor was stopped.

Discussion

Based on previous studies it has been shown that patients with valvar pulmonary stenosis have increased density and responsiveness of alpha2 adrenoceptors on the circulating cells [2]. After balloon dilation there is an immediate drop in these values to normal levels. It was speculated that alpha2 adrenoceptors on the circulating cells represent distribution of these receptors on cardiac, systemic and pulmonary vascular myocytes. It was further hypothesized that occasionally (for some unknown reasons) alpha2 adrenoceptors do not decrease after balloon valvuloplasty and elevated alpha2 receptor activity could explain oxygen desaturation in a subset of these patients despite apparently having a successful balloon valvuloplasty [1].

Based on this speculation, phentolamine infusion has been used successfully in two neonates who remained critically ill after a successful intervention. Phentolamine application improved their clinical status dramatically [1].

In another case, phentolamine was used to check whether an alpha2 blocker might also have a role in the subacute management of such patients. The patient remained prostaglandin and oxygen dependent for 2 weeks post successful pulmonary valvuloplasty. It only started to be weaned off PGE and oxygen, when phentolamine was introduced in the regimen. [3]. Before discontinuing phentolamine, oral angiotensin converting enzyme inhibitor was initiated with the idea that this medication might have similar effect on pulmonary vasculature and right ventricular compliance to that of phentolamine, but through a different mechanism of action. At least in the rat model ACE inhibitor has been found to have a role in pulmonary vascular remodeling and decreasing the pulmonary arterial pressure through preservation of endothelial nitric oxide synthase. [5] The action of angiotensin converting enzyme inhibitor is known to block the conversion of angiotensin I to angiotensin II. As angiotensin II is known to lead to vasoconstriction of the peripheral as well as the pulmonary vascular- ity, blocking its action, not only lowers arteriolar resistance and increases venous capacity, but also can lower the resistance in the pulmonary vasculature. In a study from John Hopkins it has been shown that angiotensin converting enzyme inhibition increases bradykinin, an agonist of Nitric oxide synthase (NOS). Nitric oxide is a well known vasodilator of the pulmonary vascularity [6]. Theoretically, by facilitating forward flow into the lung as well reducing the afterload, by reducing vasoconstriction in the systemic vessels, all this could help to increase cardiac output and hence improve perfusion and overall oxygenation. Interestingly it has been shown that nitric oxide (NO) modulates cardiac function by abbreviating the systolic contraction and leads to an enhancement of diastolic relaxation and this was also seen in patients with severe pressure-overload hypertrophy. Additionally, NO exerts a marked decrease in left ventricular end-diastolic pressure without affecting left ventricular systolic pump function [4]. This mechanism would facilitate the inflow into the right ventricle and also would add to the noticed improvement of oxygenation in our patient.

The action of alpha adrenergic receptors on the peripheral vessels is to increase vasoconstriction. Therefore, alpha2 blocker blocks the effect of sympathetic nerves on blood vessels by binding alpha adrenoceptors located on the vascular smooth muscle. This will lead to diminishing of this action and hence will help dilate the vessels. Hence our statement, that angiotensin converting enzyme inhibitor has similar effects as alpha blockade but works on the vessels through different pathways.

Encouraged by the previous experience [3], in the underlying case with oxygen dependency in the absence of major clinical distress and the need for any infusion, it was decided from the start to give the patient oral angiotensin converting enzyme inhibitor. We were rewarded with the unexpected prompt clinical response. The patient within <15 h of initiation of the medication could be weaned off oxygen supply completely.

Even though it is an anecdotal observation, all the different reports suggesting the beneficial
actions of angiotensin converting enzyme inhibitor support our hypothesis that this medication is useful in such a disease.

On the other hand, hoping for a controlled study is most probably very difficult to achieve, as the disease we are dealing with is extremely rare, and a control study might take few years to accomplish.

This report shows that angiotensin converting enzyme inhibitor might have an important role in the management of patients with critical pulmonary stenosis, who remain oxygen dependent despite successful balloon dilation. It is believed that using this therapeutic approach as early as possible in such patients may either shorten their need for oxygen or even prostaglandin dependency. This might reduce the need for intensive care and hospital stay, and possibly save them from any further surgical or catheter intervention. Of course this will allow the neonates to go home early and no doubt might even help to reduce health care costs.

References


