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Infant with Transposition of Great Arteries with Shock, Renal Failure and Metabolic Disturbances following Prostaglandin E_1 Infusion

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Abstract. To report a Saudi newborn with transposition of great arteries that developed a rare side effects shock, renal failure, intraventricular hemorrhage and metabolic disturbances following prostaglandin E_1 infusion at the recommended therapeutic dose.

Keywords: Prostaglandin E_1, Adverse effects, and Congenital heart diseases.

Introduction

For the neonate who presents with cyanosis, congestive heart failure, or shock, and simultaneous attention is devoted to the basics of advanced life support and maintains of patent ductus arteriosus. Prostaglandin E_1 (PGE_1) has been used to maintain the patency of the ductus arteriosus, thereby improving the circulation and the oxygenation until palliative surgery can be performed. Although PGE_1 treatment was intended as a short-term measure, long-term therapy is occasionally needed and this may cause serious side effects.

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Despite the safe and successful administration of (PGE_1); apnea, hyperpyrexia and cutaneous vasodilatation are a few of the side effects that were commonly encountered due to PGE_1 infusion. Side effects such as shock, renal failure and serious metabolic disturbances such as hypoglycemia and hypocalcaemia are extremely uncommon.

Case History

A full term Saudi male was born by normal vaginal delivery; his birth weight was 3.5 kg. Cyanotic at birth required intubation. Echocardiogram revealed transposition of great artery (TGA), coarctation of the aorta (COA), ventricular septal defect (VSD), and patent ductus arteriosus (PDA). Balloon atrial septostomy was done and the baby was extubated two days later and transferred to our hospital for further management. He arrived in stable condition, and received PGE_1 (prostin) 0.01 ug/kg/min. through umbilical venous catheter (UVC).

His respiratory rate, blood pressure, and body temperature was monitored none invisibly every hour in our neonatal intensive care unit (NICU). The baby was on oxygen 0.25 l/min, amoxicillin and gentamicin. Feeding consisted of breast milk and formula. Medical examination was normal apart from waxy color and pansystolic murmur grade 2-3/6. A trial of weaning him from PGE_1 was unsuccessful as his oxygen saturation went down from 92% to 60%.

His liver was 2 cm below the right costal margin. On the 5^{th} day of life, suddenly the baby developed severe hypotension, which was managed by normal saline boluses, dopamine and dobutamine 10 ug/kg/min each. Severe metabolic acidosis, PH 6.68, Pco2 (7 kpa), Po2 (10 kpa), Hco3 (6 mmol/L) was corrected with sodium bicarbonate infusion.

His PT/PTT/INR increased (120, 86, 10, respectively) and his blood sugar was 15 mmol/L; the baby received Insulin infusion. A full septic workup including blood culture and lumber puncture for cerebrospinal fluid were negative for infections. The patient remained critically sick. He developed a seizure, which was treated with phenobarbitone.

Oliguria developed, serum creatinine increased to 150 umol/L, and his Serum potassium was 7 mmol/L. The baby commenced on peritoneal

dialysis, a liver function test showed elevated liver enzymes. CT brain showed diffuse lucency involving both cerebral hemispheres and hemorrhagic components in the left frontal region (Fig. 1). Abdominal ultra sound was normal.

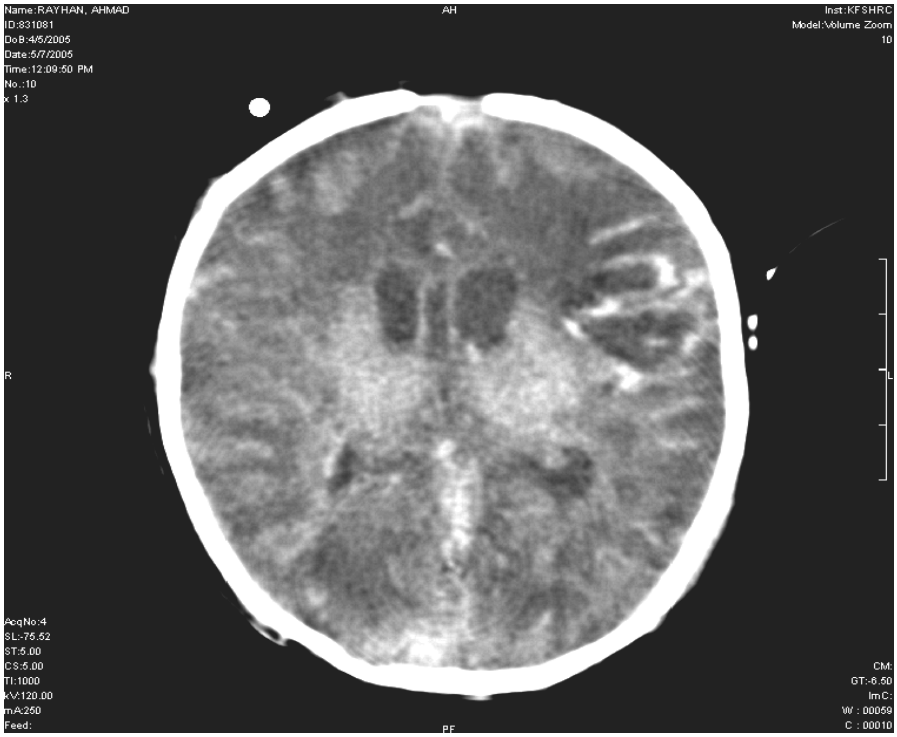

Fig. 1. CT scan of the brain showing the IVH and Hypoxic changes.

Discussion

Since Coceani and Olley showed that PGE (E_1 and E_2) were potent dilators of the PDA, and after the Food and Drug Administration (FDA) approved the use of PGE_1 in 1981in United States, there have been numerous reports about its side effects[1]. Prostaglandin E is one of the important autacoids which exert diverse physiological and pathophysiological effects in various systems and organs, thus, that would explain the variable side effects encountered[2]. The effect of PGE depends on the type of tissues, which takes into account the receptor and the receptor coupling[2].

Several investigators have observed occasional episodes of peripheral vasodilatation; seizure- like activity, apnea, and temperature elevation associated with PGE_1 infusion[1].

The serious side effects which this case patient had, had been reported in cyanotic heart defects on PGE_1 infusion in one series rather than ductus dependent non-cyanotic heart defects. The incidence was estimated to be 2% for renal insufficiency, hypotension and shock 3% , and metabolic disturbances (hypoglycemia, hypocalcaemia) 1-3%, respectively[1]. Electrolytes disturbances associated with PGE_1 infusion were reported[3]. Patient's electrolytes disturbances, however were most likely related to the renal insufficiency, which has been corrected with the peritoneal dialysis.

Disseminated intravascular coagulopathy (DIC), and necrotizing enterocolitis (NEC) were described as side effect of PDE_1 in patient with congenital cyanotic heart disease[1,4]. Our patient did not have any clinical or radiological evidence of NEC. Abdominal X-ray and abdominal ultrasound were normal. IVH has been reported in a patient with COA who received PGE_1[3]. The patient also has COA and did develop IVH (Fig. 1).

Admission to our NICU was about 100 cases of cyanotic heart disease per year for the last 5 years, most of them were referred for cardiac surgery and they require PGE_1. However, this was the first case to develop such severe complications.

It was proposed that the most likely cause for these adverse effects in our patient is accumulative dose effects of PGE_1, since we were using the standard recommended dose[3]. Also it was reviewed the possibility of PGE_1 over dose, thus this hypothesis could not be proven.

Our patient had TGA which usually did not require PGE_1 infusion following septostomy procedure; however our failure to wean from prostaglandin most likely was related to the coexistence of COA along with TGA.

PGE_1 is excreted by the kidneys, and typically cause peripheral vasodilatation and manifests as hypotension or cutaneous flushing. Because of this phenomenon, it was emphasized of the previous recommendation; a separate intravenous line should be secured for a volume administration in any infant receiving PGE_1[5].

In conclusion, in centers where PGE_1 infusion therapy is to be used for over 48 hours; awareness about these serious side effects, a separate and adequate intravenous access has to be used for PGE_1; the patient should be monitored carefully for metabolic disturbances and hypotension preferably in an ICU setting. Should any of these complications appear an immediate aggressive intervention has to take place along with discontinuation of the PGE_1 infusion.

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References

[1] **Lewis AB, Freed MD, Heymann MA, Roehl SL, Kensey RC**, Side effects of therapy with prostaglandin E1 in infants with critical congenital heart disease, *Circulation*, 1981; **64**(5): 893-898.

[2] **Wright DH, Abran D, Bhattacharya M, Hou X, Bernier SG, Bouayad A, Fouron JC, Vazquez-Tello A, Beauchamp MH, Clyman RI, Peri K, Varma DR, Chemtob S,** Prostanoid receptors: ontogeny and implications in vascular physiology, *Am J Physiol Regul Integr Comp Physiol*, 2001; **281**(5): R1343-1360.

[3] **Tálosi G**, **Katona M**, **Rácz K**, **Kertész E**, **Onozó B**, **Túri S**, Prostaglandin E1 treatment in patent ductus arteriosus dependent congenital heart defect, *J Perinat Med*, 2004; **32**(4): 368-374

[4] **McElhinney DB**, **Hedrick HL**, **Bush DM**, **Pereira GR**, **Stafford PW**, **Gaynor JW**, **Spray TL**, **Wernovsky G**,Necrotizing enterocolitis in neonates with congenital heart disease: risk factors and outcomes, *Pediatrics*, 2000; **106**(5): 1080-1087.

[5] **Rikard DH,** Nursing care of the neonate receiving prostaglandin E1 therapy, *Neonatal Netw ,* 1993; **12**(4): 17-22.

استخدم دواء (بروستاجلاندين إي ١) كتسريب وريدي للأطفال المصابين بانعكاس وضع الشرايين الكبيرة، والتأثيرات الجانبية لهذا الدواء والمتمثلة في الصدمة، والقصور الكلوي، والاضطرابات الاستقلابية

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المستخلص. تبين أن مستحضر (بروستاجلاندين إي ١) يعمل كموسع فعال للقناة الشريانية عند الأطفال الرضع، ويمكن أن ينقذ حياة المرضى الذين يعانون من عيب القلب الذي يعتمد على القناة، ورغم الاستخدام الآمن والناجح لهذا المستحضر الدوائي، إلا أن انقطاع النفس، وزيادة الحرارة، وتوسع الأوعية الجلدية، تعتبر بعضًا قليلاً من التأثيرات الجانبية التي صاحبت استخدام هذا الدواء. لكن بقيت الأعراض الجانبية كالصدمة، والقصور الكلوي، والاضطرابات الاستقلابية الخطيرة (نقص سكر الدم، ونقص الكلس في الدم) غير منتشرة إلى حد كبير. فيما يلى تقرير عن مريض ظهرت لديه مثل هذه التأثيرات الجانبية النادرة بعد أن استخدم مستحضر (بروستاجلاندين إي ١) حسب الجرعة المقررة.