Clinical Reports

The anaesthetic management of the child with Eisenmenger's syndrome

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There is little clinical data in the literature on the anaesthetic management of paediatric patients with Eisenmenger's syndrome undergoing non-cardiac surgery. This paper reviews our experiences with eight such patients who underwent a total of 11 surgical procedures. Of the eight children, six had Down's syndrome and an atrio-ventricular septal defect, one had a ventricular septal defect and one an atrial septal defect. Nine of the eleven operations consisted of minor dental, plastic or ENT procedures, while one patient underwent two laparotomies. Premedication (trimeprazine/meperidine combination or midazolam) was administered on three occasions. Induction of anaesthesia was achieved by either inhalation of halothane (2), or intravenously with thiopentone (6), ketamine (2) or propofol (1). Muscle relaxation and mechanical ventilation were employed only for both intra-abdominal procedures, otherwise patients were allowed to breathe spontaneously with, or without, manual assistance. Halothane (8), isoflurane (2) and enflurane (1) were all used for maintenance of anaesthesia. Non-invasive monitoring was applied intraoperatively for minor procedures, and arterial and central venous catheters inserted for the laparotomies. Postoperative analgesia for both these cases was provided by an epidural infusion of bupivacaine 0.125% and fentanyl 5 $\mu g \cdot ml^{-1}$. A single im bolus of morphine was required following a dental clearance, otherwise pain relief for the rest of the cases was achieved by local anaesthetic infiltration and NSAIDS. With the exception of a single episode of bradycardia, induction, maintenance and recovery from anaesthesia were well tolerated in all cases. In conclusion, our experience suggests that despite theoretical risks, children with Eisenmenger's syndrome appear to tolerate a variety of anaesthetic techniques.

Nous possédons peu de renseignements cliniques sur la gestion anesthésique d'enfants souffrant du syndrome d'Eisenmenger soumis à une chirurgie non cardiaque. Cet article décrit l'expérience des auteurs qui ont anesthésié huit de ces patients pour onze interventions. De ces huit enfants, six avaient un syndrome de Down et une communication auriculoventriculaire, un avait une communication interventriculaire et le dernier, une communication interauriculaire. Neuf des onze interventions étaient des interventions mineures dentaires, plastiques ou ORL, alors qu'un patient a subi deux laparatomies. On a administré à trois occasions une prémédication (triméprazine/mépéridine ou midazolam). L'induction a été réalisée avec soit de l'halothane (2) en inhalation, soit par la voie intraveineuse avec du thiopentone (6), de la kétamine (2) ou du propofol (1). La relaxation musculaire et la ventilation mécanique n'ont été utilisées que pour la chirurgie intra-abdominale. Les autres patients ont respiré spontanément avec ou sans assistance manuelle. L'anesthésie a toujours été entretenue avec de l'halothane (8), de l'isoflurane (2) ou de l'enflurane (1). Pendant les interventions mineures, le monitorage a été non effractif alors que, pour les laparotomies, une canule artérielle et une tension veineuse centrale ont été insérées. Après ces deux interventions l'analgésie postopératoire a été obtenue avec une perfusion épidurale de bupivacaïne 0,125% et de fentanyl 5 $\mu g \cdot ml^{-1}$. Un seule injection de morphine a été requise après une extraction dentaire complète; pour les autres, l'analgésie a été procurée par infiltration d'un anesthésique local et des AINS. A part un épisode isolé de bradycardie, l'induction, le maintien et la récupération ont été bien tolérés. Les auteurs concluent que leur expérience démontre que malgré certains risques théoretiques, les enfants porteurs du syndrome d'Eisenmenger semblent bien tolérer des techniques anesthésiques variées.

Key words
ANAESTHESIA: paediatric;
HEART SYNDROMES: Eisenmenger.

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Eisenmenger's syndrome is defined as the presence of high pulmonary vascular resistance (PVR) in association with pulmonary hypertension at systemic levels, and a reversed or bi-directional shunt through an aorto-pulmonary, intra-cardiac or inter-arterial communication.[1,2] The complex was first described in 1897 by Dr. Victor Eisenmenger when he reported the post-mortem findings of a 32-yr old man who died of a large haemoptysis after a life-long history of dyspnoea and cyanosis.[3] Necropsy revealed a 2–2.5 cm ventricular septal defect (VSD), a large right ventricle, an overriding aorta and evidence of increased PVR. However, Eisenmenger failed to recognise that the elevated PVR was responsible for the right-to-left shunt and cyanosis. In 1958 Wood clarified the pathophysiology, and suggested that the Eisenmenger syndrome should include any communication between pulmonary and systemic circulations which results in the development of pulmonary hypertension severe enough to cause a right-to-left shunt.[4]

The progression from a left-to-right shunt to development of this syndrome may be gradual over a decade, but can be as little one to two years.[2,5] Rapid progression is particularly common in children with associated transposition of the great vessels (TGA). Children with Down's syndrome and a VSD, or atrio-ventricular canal defect, are also prone to the early development of pulmonary hypertension and reversal of shunt, probably related to the presence of an abnormal upper airway predisposing to chronic upper airway obstruction, hypoxaemia and elevated pulmonary artery pressures.[5]

The natural history of the disease is such that the majority of patients are symptomatic in infancy due to congestive cardiac failure. Later, as PVR rises, and the magnitude of the left-to-right shunt diminishes, symptoms improve. The subsequent development of a right-to-left shunt may precipitate dyspnoea and chest pain secondary to right ventricular hypoxia. Sudden death can occur from right ventricular failure, pulmonary artery rupture and cardiac arrythmias, usually in the third and fourth decades.[4,6]

As these patients commonly survive childhood and early adulthood the anaesthetist may therefore encounter them on elective or emergency surgical lists. Operative procedures in these patients have been associated with a high mortality rate,[2] but the anaesthetic literature on non-parturients undergoing surgery unrelated to their cardiac defect is sparse. The series reported by Lumley *et al.* implied tht the risk of mortality for these patients was less than previously indicated.[7] Apart from the two children included in that series, we could find little published clinical data on the anaesthetic management of paediatric patients with Eisenmenger's syndrome undergoing non-cardiac surgery. This paper reviews our experience with eight such patients who underwent a total of 11 general anaesthetics.

Pathophysiology

A variety of histological changes occur in the pulmonary arteries as a consequence of the high pulmonary blood flow that exists in the presence of a large left-to-right shunt. The gradual thickening of intimal and medial layers, and eventual fibrotic occlusion of pulmonary arteries results in a reduction in surface area of the pulmonary vascular bed, an elevated PVR, and ultimately irreversible pulmonary hypertension.[8] The consequent right-to-left shunt produces hypoxaemia and a compensatory elevation in haemoglobin production resulting in polycythaemia, thereby increasing oxygen carrying capacity. Cardiac output does not increase at rest and effects on the oxyhaemoglobin dissociation curve are minimal, but oxygen extraction is greatly enhanced, and the capacity for anaerobic metabolism increased.[9,10]

In Eisenmenger's syndrome pulmonary (PVR) and systemic vascular resistances (SVR) are approximately equal and thus the shunt is balanced. However, either an increase in PVR or a decrease in SVR will augment the right-to-left shunt. A number of factors may precipitate this: hypoxia, hypercarbia, acidosis and some anaesthetic agents. All of these have implications for the anaesthetist.

Case reports

The records of eight children with Eisenmenger's syndrome, who underwent a total of 11 general anaesthetics for a variety of surgical procedures, were reviewed. Data were recorded prospectively for four procedures, and retrospectively for the other seven. Demographic and diagnostic characteristics are listed in Table I, and operative and anaesthetic data in Table II. All diagnoses were made by clinical and echocardiographic evaluation. Of the eight cases reviewed, five were cyanosed at rest and three on mild exertion. Six of the children had Down's syndrome. One child underwent cardiac catheterisation which revealed a complete atrio-ventricular canal defect. Pulmonary and systemic arterial pressures were equal at 100/64 mmHg, and PVR was elevated at 14 Wood units (normal value <2 units). This decreased to 10 units when the FiO_2 was increased to 1.0, but the administration of nitric oxide 20 ppm during catheterisation failed to have a significant effect on PVR.

For nine of the 11 procedures non-invasive monitoring (pulse oximeter, capnograph, electrocardiogram (ECG) and blood pressure (Dinemapp)) was employed, while invasive monitors (intra-arterial (twice) and central venous catheter (once)) were utilised in one child who underwent two laparotomies several weeks apart.

TABLE I Demographic data. Values are expressed as mean (range)

Age (yr)	7.2 (4.5–12.7)
Sex (m:f)	3:5
Weight (kg)	21.5 (11.5–47.5)
Cardiac lesion	ASD (ostium secundum) × 1
	VSD × 1
	A-V canal defect × 6
Haemoglobin ($g \cdot dl^{-1}$)	17 (14.3–19.5)
Haematocrit (%)	51.2 (44–60.7)

TABLE II Operative and anaesthetic data. Duration of anaesthesia expressed as mean value; (range)

Operative procedure	
- Dental extraction	5
- Tonsillectomy	1
- Adenoidectomy	1
- Myringotomies + tubes	1
- Suturing of a laceration	1
- Laparotomy	2
Premedication	
- Trimeprazine 3 $mg \cdot kg^{-1}$ + meperidine 1 $mg \cdot kg^{-1}$	2
- *iv* midazolam	1
- antibiotic prophylaxis	11
Pre-induction	
- Atropine	2
Induction	
- Inhalational induction (halothane)	2
- Thiopentone	6
- Ketamine	2
- Propofol	1
Muscle relaxation	
- Succinylcholine	7
- Vecuronium	2
Maintenance	
- Halothane	8
- Isoflurane	2
- Enflurane	1
Ventilation	
- Spontaneous ventilation	7
- Spontaneous ventilation + manual assistance	2
- IPPV	2
Analgesia	
- Local anaesthetic infiltration	6
- NSAID	7
- *im* Morphine bolus	1
- Epidural infusion (bupivacaine + fentanyl)	2
Duration of op. (min)	
- 88.7 (15–240)	

Premedication (opioid/sedative combination or midazolam) was prescribed on two occasions (for a total of three procedures) for children who were judged to be sufficiently anxious to warrant preoperative sedation. Although no measurements were taken in these children before premedication, the recorded oxygen saturations on arrival in theatre (81%, 81% and 85% respectively) were similar to the rest of the group (Figure).

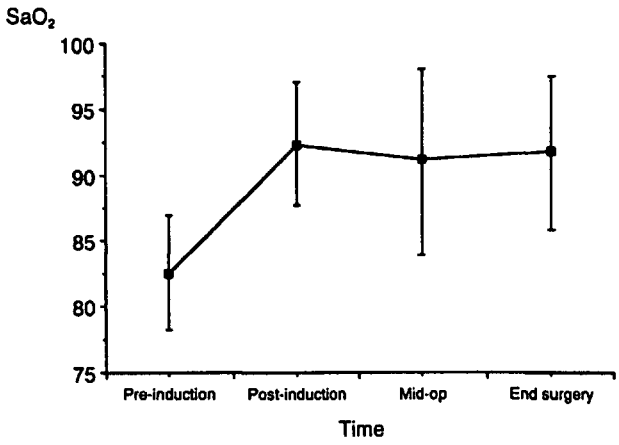

FIGURE Oxygen saturation during anaesthesia in children with Eisenmenger's syndrome.

A variety of inhalational and intravenous agents were used to induce anaesthesia (Table II). No episodes of either acute hypotension or arrythmia were noted during this period. Oxygen saturation increased from baseline levels in all cases following induction of anaesthesia, thereby indicating an increase in pulmonary blood flow (Figure). One five-year-old child had a single episode of bradycardia (heart rate = 42 bpm) during a dental procedure which responded promptly to atropine 20 $\mu g \cdot kg^{-1}$. Otherwise no patient died or suffered a life-threatening complication either intra- or postoperatively. Induction, maintenance and emergence from anaesthesia were uneventful in all other cases.

All children who underwent relatively minor procedures were monitored postoperatively on the ward by continuous ECG plus pulse oximetry, and were discharged home the following day. The nine-year-old girl on whom two laparotomies were performed, was admitted to the Intensive Care Unit (ICU) on both occasions for more intensive monitoring, and the provision of epidural analgesia.

Pain relief was provided by a combination of local anaesthetic techniques and non-steroidal anti-inflammatory drugs in the majority of cases. One child received a single bolus of morphine *im* following a dental clearance. An epidural infusion was used to achieve analgesia following both laparotomies. For the first procedure the infusion (bupivacaine 0.125% and fentanyl 5 $\mu g \cdot ml^{-1}$) was started following surgery in the ICU, and run for three days. For the second operation the epidural was started prior to incision and run throughout the operation at 2 $ml \cdot hr^{-1}$. It permitted maintenance of anaesthesia, with haemodynamic stability, using 0.5% halothane in 100% O_2. Postoperatively the infusion was run at 1–4 $ml \cdot hr^{-1}$ for five days, providing excellent anal-

gesia. Cardiorespiratory parameters remained close to preoperative cardiac catherisation levels, without wide swings in blood pressure or PaO_2.

Discussion

A number of theoretical dangers are associated with anaesthesia in these children. The ideal anaesthetic would ensure a reasonable balance between SVR and PVR while maintaining cardiac output and thus oxygen delivery.

Heavy premedication has previously been advocated in these children as it seemed to be well tolerated, and had the beneficial effect of reducing the dose of induction agent required.[7] The purpose of providing premedication for these children is to decrease patient anxiety, thereby decreasing total body oxygen consumption. However, oversedation may precipitate hypoventilation thereby increasing right-to-left shunt and desaturation. The requirement for premedication must therefore be balanced against the potential risks. Two children in this series were deemed to be sufficiently upset to need preoperative sedation, which did not appear to affect their clinical condition adversely. All patients were administered appropriate antibiotics before and after the surgical procedure to prevent the development of infective endocarditis.

Arm-brain circulation time is short due to the right-to-left shunt and thus intravenous induction agents will act rapidly. Ketamine (1–2 $mg \cdot kg^{-1}$) has been successfully used for induction of anaesthesia in patients with Eisenmenger's syndrome,[11] and has subsequently been recommended as the drug of choice for induction[12] as it has little effect on either PVR or SVR.[13] Both thiopentone and propofol cause hypotension due to a decrease in systemic vascular resistance.[14] While this effect appears to be dose-dependent with thiopentone,[15] haemodynamic changes consequent on induction with propofol appear to be unrelated to the dose used.[16] Pretreatment with a vasoconstrictor, such as phenylephrine, may prevent this change in SVR. However, it has been suggested that phenylephrine will produce similar degrees of vasoconstriction in both pulmonary and systemic circulations, and may therefore have little effect on the shunt direction or magnitude.[18] Thiopentone (6), ketamine (2) and propofol (1) were used to induce anaesthesia for nine of the described procedures. All were administered slowly, and none adversely affected shunt size or direction as indicated by haemodynamic status and pulse oximetry.

Inhalational induction will be slow because of the reduction in pulmonary blood flow.[19] This effect is inversely related to blood solubility and of little importance with more modern potent volatile agents. All three agents used in this series cause systemic hypotension because of a varying combination of myocardial depression and vasodilation. Foster and Jones advocate the avoidance of isoflurane because of its potent vasodilating activity.[20] We used isoflurane in two cases. In both, the initial choice of vapour was halothane but the development of ventricular ectopy precipitated a change to isoflurane. This change in volatile agent was made without inimical effects on the patients' cardio-respiratory status, and in both cases prolonged isoflurane anaesthesia (85 and 130 min respectively) was well tolerated.

Spontaneous ventilation may increase right-to-left shunting because of hypercarbia. Intermittent positive-pressure ventilation may similarly affect the shunt by a reduction in pulmonary blood flow which is dependent on the transpulmonary pressures applied. Thus a rate and tidal volume which is consistent with a normal $PaCO_2$ and low inflation pressures should be chosen to avoid deleterious effects.[7] The technique of spontaneous ventilation with manual assistance was chosen to prevent hypoventilation, hypoxaemia, hypercarbia and thus an increase in right-to-left shunt in two cases.

Despite the potentially hazardous effects of autonomic blockade and peripheral vasodilatation, epidural anaesthesia has been successfully used in patients with Eisenmenger's syndrome.[21,22] We found that an epidural infusion of bupivacaine 0.125% and fentanyl 5 $\mu g \cdot ml^{-1}$ provided excellent postoperative analgesia following laparotomy. This analgesic technique was used following both laparotomies, for periods of three and five days, without haemodynamic or respiratory upset.

Non-invasive monitoring would appear to be adequate for minor procedures. Pulse oximetry is particularly useful in these patients as changes in SaO_2 can reflect changes in the pulmonary/systemic flow ratio and the magnitude of blood flow through the cardiac defect. The place of invasive monitoring in Eisenmenger's syndrome is controversial.[7,21] While there is a risk inherent in the insertion of invasive catheters in any patient, a number of factors increase the probability of adverse events in those with Eisenmenger's syndrome. Post-cannulation thrombosis, due to polychythaemia, and paradoxical air embolus are both likely to have a higher incidence in this population. Gliecher *et al.* have suggested that all parturients with Eisenmenger's syndrome should have pulmonary artery catheters inserted,[23] a concept which has not been universally embraced.[12] Measurement of the cardiac output by thermodilution is of limited benefit in the presence of a right-to-left shunt, and thus the potential risks (pulmonary artery rupture, life-threatening arrythmias and embolisation) would appear to outweigh the value of the information gleaned. Indeed, Devitt *et al.* have reported a fatal outcome in a patient who suffered systemic embolisation across a congenital cardiac defect following insertion of a Swan-Ganz catheter.[24] We would

recommend the insertion of a central venous catheter in cases where major fluid shifts are anticipated.

Meticulous attention to fluid balance is required as fluid loss is poorly tolerated,[2] while volume overload may easily precipitate right ventricular failure.[25] All our patients were administered intravenous fluids during the fasting period. Because of the high haematocrit it would seem sensible to replace blood loss initially with crystalloid or colloid solution; however, clinical judgment should balance the risks of hyperviscosity during anaesthesia against the loss of oxygen carrying capacity. Preoperative phlebotomy has been recommended for patients with significant symptomatic hyperviscosity and haematocrits greater than 65% once dehydration has been corrected.[26]

The children in this series responded well to induction and maintenance of anaesthesia despite the use of agents that have theoretical disadvantages. This suggests that, in this subgroup, our knowledge of the effect of individual anaesthetic agents on the pulmonary circulation is incomplete. In addition the routine use of preoxygenation and a high FiO_2 (1.0) intraoperatively improved oxygen saturation. There are several possible reasons for this. Firstly, a high FiO_2 will correct hypoxia due to intercurrent ventilation/perfusion abnormalities.[27] Secondly, although PVR is supposedly fixed in Eisenmenger's syndrome, some plasticity of the pulmonary vessels may persist in childhood, and thus supplemental oxygen may allow an improvement in pulmonary blood flow. This was seen during the cardiac catheterisation of one child where increasing the FiO_2 from 0.21 to 1.0 reduced PVR by 29%. Finally, in those cases where ventilation or manual assistance was employed, the consequent reduction in $PaCO_2$ may have beneficial effects on PVR.

All patients in this series were managed by a consultant anaesthetist and it would seem likely that the experience of the anaesthetist is more important than the anaesthetic techniqe chosen. In conclusion, our experience suggests that children with Eisenmenger's syndrome tolerate a variety of anaesthetic techniques, and the risks appear to be less than theoretical considerations indicate.

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