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ORIGINAL ARTICLE

Management of the changeover of inotrope infusions in children

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KEYWORDS

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Summary Inotropes are drugs that can assist the critically ill patient's heart to function more effectively by increasing contractility. Inotrope infusions are run continuously and fresh infusions are required on a regular basis. The two methods of changeover commonly used are the quick-change and the double-pump methods. Haemodynamic compromise can occur to some degree with both methods. Evidence regarding the most effective method is limited to individual experience and anecdote. Therefore, the aim of this project was to determine the best method of changing inotropic infusions in children.

Methods: Thirty children receiving inotropes post-cardiac surgery admitted to PICU were included in the study. There were two methods of changing over inotropes in this study: *Method 1*, quick-change and *Method 2*, double infusion. A rescue bolus of 0.1 ml of the changeover inotrope was given for drops in mean arterial pressure (MAP) $\geq 20\%$ during the changeover period.

Results: Repeated measures analysis for MAP demonstrated no significant difference in the mean percentage change from baseline during the 30-min changeover period. Quick-change: -0.297 (95% CI: -6.43 to 0.5) and double-pump: 3.73 (95% CI: -2.81 to 10.27) ($P = 0.078$).

Conclusions: There was no statistically or clinically significant difference detected in changes to MAP. A rescue bolus was required on only one occasion during quick-change over for a reduction in MAP of $\geq 20\%$ in the quick-change group. Therefore, a quick-change method can be considered more effective as it reduces the time required for changeover and the risk of tolerance to higher levels of inotrope, while maintaining haemodynamic stability in children after cardiac surgery.

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Introduction

Inotropes are drugs used to improve cardiac output by increasing contractility and chronotropy.

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Inotropes are normally secreted by the body during times of stress, but need augmentation when the stressors have exhausted the body's supplies. Improving cardiac output in the critically ill has many effects including improving oxygenation, cell metabolism and acid–base balance (Craig et al., 2001). Inotrope infusion, like all drug infusions, require changeover to a fresh infusion on a regular basis, usually 24–48 h, depending on individual institutional policy. In addition, with a half-life of only 2–3 min, a continuous supply of the drugs must be ensured.

Two methods of inotrope changeover have evolved in this PICU and in other centres. These are the quick-change and the double infusion methods. Haemodynamic compromise, which may affect the recovery time of the patient, can occur to some degree with both methods. With the quick-change method it is thought that there may be a greater drop in the mean arterial pressure (MAP) following changeover. The double-pump method, however, may result in unwanted increases in the MAP and heart rate, and there may be a risk of developing a rebound drop in MAP following the double-pump method of changeover.

Drug tolerance or dependence on the transiently higher dose of inotrope is a potential problem with double infusion of inotropes, particularly if the double infusion period is extended past the recommended 10 min (Karch, 2003). This occurs as a result of adrenergic receptor down-regulation. Excess catecholamines, both endogenous and exogenous, can deplete adrenergic receptor sites faster than the cell can replace them (Harvey, 1998). Thus, an individual's response to inotrope infusions may be diminished when a double infusion method is employed for syringe changeover, particularly if the changeover time is prolonged.

Rivers et al. (1994) suggest that higher doses of epinephrine given during resuscitation increases acidosis and systemic vascular resistance, adversely affecting oxygen delivery and consumption. This phenomenon may potentially occur during the double infusion method of inotrope changeover as there is, temporarily, a higher dose being delivered. This hypothesis is supported by the pharmacology of inotropes such as epinephrine and norepinephrine, where higher doses may result in higher oxygen demand arrhythmias (Elliott, 1999).

Despite these concerns there is little research literature that exists as to whether either of these two methods of changeover is more likely to result in haemodynamic instability. Crisp (2002) investigated the practice of double pumping in an adult intensive care and found wide variability in indicators used to initiate double pumping, in ad-

dition to methods used to prime the line and the double pumping process. The survey was then distributed to other intensive care units with similar results. Powell and Carnevale (2001) used an in vitro methodology to investigate the volumes infused during double pumping and single infusion. Their experiment found that the volumes delivered were more reliable using the double-pump method, however, their methodology did not allow evaluation of haemodynamic stability. Thus, there is a need to establish the most effective method of changing inotropes that produces the least haemodynamic instability.

Nursing specialists in other paediatric intensive care units in Australia, the USA and UK contacted by the investigators similarly acknowledge the lack of evidence as to which is the most effective manner of managing this procedure. Both within and between these centres the practices pertaining to the changeover of inotrope infusions varied widely within common themes of double-pump and quick-change. In addition, staff had a considerable level of autonomy for the management of changeover procedures in all but one of the institutions contacted, indicating that guidelines for this practice were either not available or not used. This issue has also been a topic of discussion on the PICU-Nursing-International e-mail list several times over the past 2 years. Maintaining haemodynamic stability during and after the changeover of inotrope infusions was a commonly identified problem.

Therefore, in light of the paucity and contradictory nature of the available research and the potential for adverse effects for patients, there is a need for a study that investigates the method of inotrope changeover that ensures continuous supply of the drug without compromising the patient's cardiac output.

Objectives

To determine which method of inotrope changeover, quick-change or double infusion, causes the least amount of haemodynamic instability in children.

Methods

This randomised-controlled trial was conducted in a 23-bed paediatric intensive care unit at a stand-alone, tertiary, university-affiliated children's hospital in Sydney, Australia. The study was approved by the hospital Research Ethics Committee and written informed consent for participation was obtained from the parents of all the subjects.

Subjects

All children receiving inotropes after having undergone cardiac surgery and receiving a dose range of epinephrine and norepinephrine of 0.1–5 µg/kg/min and dopamine and dobutamine of 5.0–20 µg/kg/min were eligible for inclusion. All children had continuous electrocardiography and invasive blood pressure monitoring. Twenty children had monitoring of central venous pressure (CVP) and left atrial pressure (LAP). All children had a central line with a three-way stopcock on each lumen for infusion of inotropes.

A power analysis established that a total sample size of 30 subjects allowed demonstration of a mean within-subject change from baseline of 0.5 standard deviations, significant at the 0.05 level with a power of 80%.

Each child was eligible for inclusion for one inotrope changeover only. Random allocation was achieved by utilising an opaque sealed envelope method. Half of the envelopes contained Method 1 (quick-change) and half the envelopes contained Method 2 (double infusion). The envelopes were shuffled and sequentially numbered. Envelopes were then selected in numerical order and the order of selection recorded against patient names.

Interventions

There were two methods of changing inotropes infusions in the study. Quick-change: Load the new infusion into a new syringe pump and prime the line. Turn the pump on. Programme the pump to same rate and settings as the old infusion and start the pump. Turn the three-way stopcock off to the old infusion, quickly disconnecting old infusion and connecting new infusion. Turn the three-way stopcock on to the new infusion. Double infusion: Load new infusion into a new syringe pump and prime line. Turn the pump on. Programme the pump to same rate and settings as old infusion. Connect new infusion to patient at spare port of the three-way stopcock. Turn the three-way stopcock on to the new infusion and start infusion. Run both old and new infusions at the same rate and dose. Begin to wean old infusion by 0.1 ml decrements when mean arterial pressure (MAP) starts to rise. Continue to decrease old infusion until ceased, maintaining MAP at baseline levels, approximately 10 min.

A rescue bolus of 0.1 ml of the new inotrope infusion was given for drops in MAP of $\geq 20\%$ below baseline.

Measuring instruments

The MAP, CVP and LAP were recorded at 1-min intervals for 5 min prior to the changeover of inotropes to determine the baseline and continued at 1-min intervals for 30 min following the start of changeover. All of the data recorded after the start of changeover was expressed as a percentage change in the MAP from the mean baseline reading.

Data was also recorded as to how many boluses of inotrope each patient required in the 30 min during and following changeover. Graseby™ 3100 Syringe pumps with 60 ml BD syringes were used for all infusions.

Statistical analysis

The statistical package SPSS Version 11.5.1 (SPSS, Inc., Chicago) was used for all statistical calculations. Any demographic differences between patient groups were analysed by *t*-test for continuous data and by Chi-Square for categorical data. Repeated measures Analysis of Variance (ANOVA) was used to test for differences between the quick-change and the double-pump groups in the percentage change from baseline for MAP, LAP and CVP over the 30-min changeover period.

Results

Thirty children were included in the study. Seventeen patients were allocated the quick-change method and 13 patients had their inotrope double infused during changeover. All children were post-operative cardiac surgery and required inotropic support for more than 48 h. Table 1 shows the characteristics of the participants in each group, including the types of cardiac surgery.

The study inotropes were epinephrine ($n = 7$), norepinephrine ($n = 13$) and dopamine ($n = 10$). Table 1 indicates the changeover inotrope for each group. There was no significant difference between the two groups for type of inotrope ($P = 0.86$), infusion rate ($P = 0.99$) or dose level ($P = 0.54$). Table 2 indicates the mean change in MAP for each dose level for the two groups. Dose level was defined as low (dopamine ≤ 5 µg/kg/min; nor/epinephrine 0.1–0.4 µg/kg/min), medium (dopamine 7.5–12.5 µg/kg/min; nor/epinephrine 0.5–0.9 µg/kg/min) and high (dopamine >15 µg/kg/min; nor/epinephrine ≥ 1 µg/kg/min). There were insufficient numbers in each group to provide meaningful analysis on the effects of dose.

Table 1 Patient characteristics.

	Quick-change (17)	Double-pump (13)
Age—median (S.D.)	0.18 (3.6)	0.24 (0.76)
Male	11 (65%)	7 (54%)
Time (h) on inotrope prior to change—median (S.D.)	22 (19.6)	27.75 (38.6)
Dose level (low, medium, high)— <i>M</i> (S.D.)	1.24 (.56)	1.38 (.77)
Infusion rate— <i>M</i> (S.D.)	1.5 (1.2)	1.5 (1.7)
Inotrope type		
Epinephrine (<i>n</i>)	4	3
Norepinephrine (<i>n</i>)	8	5
Dopamine (<i>n</i>)	5	5
Other inotropes in same CVL lumen	11 (65%)	11 (85%)
Vasodilators (other lumen)	12 (55%)	10 (46%)
Type of surgery		
AVSD	4	2
ASD		1
VSD	2	1
TAPVR	2	
Shunt	1	1
Truncus arteriosus		2
Tetralogy of Fallot	1	4
Arterial switch	4	2
HLHS	1	
Fontan	2	

Twenty-two (73%) children had another inotrope infusing through the same lumen of the central line, however, there was no significant difference between the two groups ($P = 0.22$). Twenty-two (73%) children had vasodilators infusing through another lumen of the central line and there were no significant differences between the two groups ($P = 0.15$).

Repeated measures analysis of the percentage change from baseline for MAP indicates no significant difference between the quick-change and the double infusion groups over the 30-min changeover period ($P = 0.078$). The mean percentage change in MAP for the quick-change group was 2.97 (95% CI: -6.4 – 0.5) and for the double infusion group was 3.73 (95% CI: -2.8 – 10.3). The variation from baseline was always less than 10% over the 30-min measurement period in both groups (see Fig. 1). This difference was not considered to be clinically significant as it was considerably less than the a priori definition of a clinically significant difference of

$\geq 20\%$. Therefore, it is unlikely that there was a lack of power in this study to detect a clinically significant effect. One child in the quick-change group required a rescue bolus. Therefore, there was not a significant difference between groups in the number of children receiving a rescue bolus. Repeated measures analysis of the percentage change from baseline for both LAP and CVP were not significant ($P = 0.06$ and 0.06 , respectively).

Discussion

The results from this study found that there was no statistical significant difference in MAP between the quick-change group and the double infusion group. The mean percentage change from baseline was small in both groups and this was not considered to be clinically significant, as it was considerably less than the 20% deviation from baseline that was considered clinically important at the commencement of the study.

This study provides an objective measure of the haemodynamic effects of two methods of inotrope changeover. Because, there was no statistical or clinical difference between the quick-change and double infusion groups, this study provides some evidence to assist in developing clinical guidelines for this practice. However, a limitation of the study

Table 2 Mean percent change in MAP for dose level.

Dose level	Quick-change	Double infusion
Low	−1.8026	4.8318
Medium	−10.9751	−9.8550
High	−3.2258	5.0275

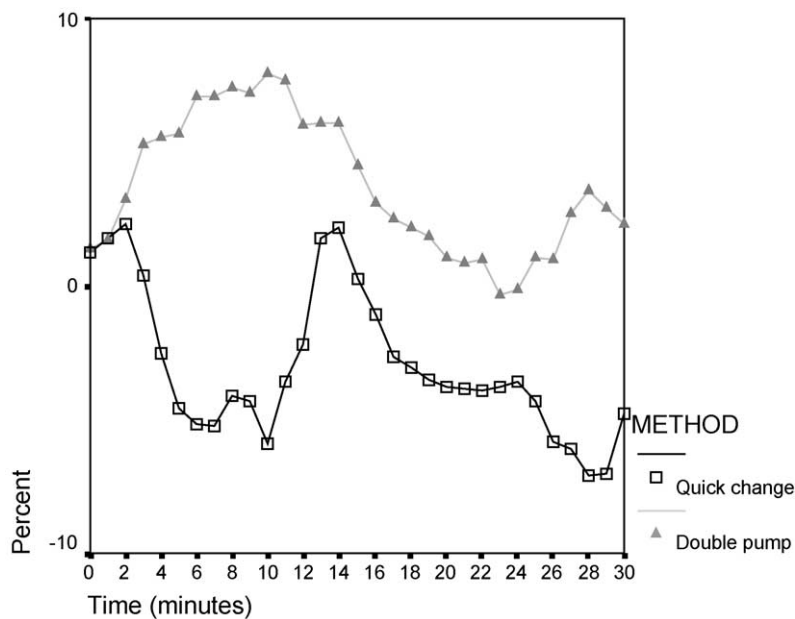


Figure 1. Mean change in MAP over time.

was that there were insufficient numbers to analyse between group differences for dose level. Another potential limitation of this study is the use of the Graseby™ 3100 Syringe pump. Other syringe pump brands may have different modes of action and plunger uptake speed or mechanical lag. However, most recent model syringe pumps have similar specifications in regards to plunger uptake and volume delivery. The effect of this limitation can be overcome by priming the line by running the pump or using a purge facility if available. This will reduce the effects of mechanical lag.

There is little literature relating to inotrope changeover, highlighting the issue of a lack of evidence in many intensive care practices (Randolph and Lacroix, 2002). Only one other study has reviewed methods of syringe changeover for inotrope infusions in children (Powell and Carnevale, 2001). However, this study used an *in vitro* methodology to compare the infusate volumes delivered by either a single-pump or double-pump methods. The authors' conclusions were that the double-pump method was more reliable in delivering the required volume. Our study has examined the haemodynamic effects of the two methods rather than measuring the volumes infused. However, our protocol for the quick-change method also differed from the single-pump method described by Powell and Carnevale (2001), in that our protocol uses a second pump to set up the fresh infusion rather than briefly stopping the infusion pump to allow syringe swapping.

The literature pertaining to inotrope changeover in critically ill adults is similarly lacking. One study by Crisp (2002) surveyed inotrope changeover practices in intensive care units in the UK. Crisp found considerable variation in this practice, however, there was unable to provide objective evidence as to which method was the most suitable.

Conclusion

Both the single and double infusion methods of inotrope changeover have advantages and disadvantages. However, as no clinically significant difference between the two methods was found, we would recommend the quick-change method as it is quick, simple and does not risk tolerance to a higher inotrope dose. But, further research is recommended to clarify the limitations associated with pump type and the effects of dose level.

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