Nurse titrated analgesia and sedation in intensive care increases the frequency of comfort assessment and reduces midazolam use in paediatric patients following cardiac surgery.

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Abstract:

Background: Pain and sedation protocols are suggested to improve the outcomes of patients within paediatric intensive care. However, it is not clear how protocols will influence practice within individual units.

Objectives: Evaluate a nurse led pain and sedation protocols impact on pain scoring and analgesic and sedative administration for post-operative cardiac patients within a paediatric intensive care unit

Methods: A retrospective chart review was performed on 100 patients admitted to a tertiary paediatric intensive care unit pre and post introduction of an analgesic and sedative protocol. Stat12 was used to perform Chi 2 or student t tests were used to compare data between the groups.

Results: Post protocol introduction documentation of pain assessments increased (pre protocol 0.2 assessments per ventilated hours vs post protocol 0.3, p=0.02). Along with a reduction in administration of midazolam (57.6 mcg/kg/min pre protocol vs 24.5 mcg/kg/min post protocol, p=0.0001). Children's pain scores remained unchanged despite this change, with a trend towards more scores in the optimal range in the post protocol group (5 pre protocol vs 12 post protocol, p=0.06).

Conclusions: Introducing a pain and sedation protocol changed bedside nurse practice in pain and sedation management. The protocol has enabled nurses to provide pain and sedation management in a consistent and timely manner and reduced the dose of midazolam required to maintain comfort according to the patients COMFORT B scores. Individual evaluation of practice change is recommended to units who implement nurse led analgesic and sedative protocols to monitor changes in practice.

Nurse titrated analgesia and sedation in intensive care increases the frequency of comfort assessment and reduces midazolam use in paediatric patients following cardiac surgery.

Introduction

Providing optimal analgesia and sedation for children in intensive care is a challenge for clinicians (Ramelet, Abu-Saad, Rees, & McDonald, 2004). Children who are not provided with sufficient analgesics are at risk of experiencing pain due to invasive treatments; if children are also not adequately sedated, they may be at risk of discomfort (Wolf & Jackman, 2011). Alternatively, children treated with excessive analgesics or sedatives are at risk of developing withdrawal or tolerance (Cho, O'Connell, Cooney, & Inchiosa, 2007; Neunhoeffer et al., 2015). Potential long-term consequences of administering sedatives include apoptosis of brain cells (Istaphanous & Loepke, 2009) and learning difficulties (Sun, 2010). However, obtaining an accurate assessment of the child's level of pain and discomfort, in order to provide an appropriate level of treatment, is challenging in pediatric intensive care (PICU) (Bennett, 2001; Boerlage et al., 2015). Developmental age, administration of sedatives and intubation all impair the child's ability to adequately communicate their needs (Baulch, 2010; Lamas & Lopez-Herce, 2010).

Self-report remains the gold standard of pain assessment (Giordano, Abramson, & Boswell, 2010), though children are not always able to self-report their pain or discomfort due to different developmental stages (Wong & Baker, 1988). Pain assessment tools utilise behavioural and physiological parameters in order to overcome developmental communication barriers with children (Wong & Baker, 1988). Specific pain tools for children within intensive care have been developed and validated in order to assess children who may be unable to communicate due to developmental age and intensive treatments such as intubation and sedation (Curley, Harris, Fraser, Johnson, & Arnold, 2006; Johansson & Kokinsky, 2009; van Dijk et al., 2000; Voepel-Lewis, Zanotti, Dammeyer, & Merkel, 2010). Utilising a pain and sedation protocol that incorporates a validated assessment tool may aid clinicians to provide evidence- based treatment to children, and avoid incidences of under or over treatment of pain and discomfort (Sessler & Pedram, 2009).

Introducing a protocol to manage pain and sedation may influence other outcomes than performing pain assessments, such as analgesic and sedative administration (Ista, de Hoog, Tibboel, & van Dijk, 2009; Jin et al., 2007). Evaluation of PICU pain and sedation protocols in current literature reveals that there are differences in primary outcome measures. Some studies have reported an increase in administration of sedatives and analgesics following the introduction of a pain and sedation protocol into PICUs (Alexander, Carnevale, & Razack, 2002; Ista et al., 2009) whilst others report a decrease (Deeter et al., 2011; Jin et al., 2007). At the time that this study was conducted, a consensus on how pain and sedation protocols influence ICU length of stay and duration of ventilation was unclear(O'Connor, Bucknall, & Manias, 2010).

Background

In 2010 the COMFORT B tool was introduced into the PICU for the assessment of both pain and sedation. The COMFORT B tool has demonstrated internal consistency (Cronbach's alpha 0.78), concurrent validity (Kruskal-Wallis chi squared = 237, df = 2, p= <0.001) and interrater reliability (Kappa 0.71) within the paediatric intensive care for patients aged 0-18 years (Johansson & Kokinsky, 2009; van Dijk et al., 2000).Using one tool to assess for both pain and sedation is controversial, however the COMFORT B tool has been used for this purpose previously (Boerlage et al., 2015). The COMFORT B tool is used to assess intubated patients on six behavioural categories to provide a score between 6-25 (van Dijk et al., 2017). These categories include alertness, respiratory response, calmness and agitation, physical movement, muscle tone and facial tension. Nurses examined the category where the patient had the highest score to determine if they were likely in pain or in need of sedation. The comprehensive sedation scale developed by the American Association of Critical

Care Nurses acknowledges consciousness, agitation, anxiety and ventilator synchronisation as areas of sedation assessment in intensive care (De Jong et al., 2005). Therefore patients who score high in the COMFORT B areas of alertness, respiratory response and calmness and agitation are considered to need a sedative rather than an analgesic. In the PICU where this study was conducted scores less than 10 were indicative of heavy sedation, 10-20 the optimal range and greater than 20 indicated the patient was a high risk of pain or distress. An audit that was conducted following the introduction of the tool revealed that compliance with the tools use decreased over time (Larson & McKeever, 2011). In order to further improve assessment and management of pain and sedation a clinical practice guideline (CPG) was developed. Following introduction of the CPG an increase in the use of a validated pain and sedation assessment was observed in our setting, along with increased communication of plans for patient's pain and sedation and prescription of analgesic and sedative boluses (Larson, Arnup, Clifford, & Evans, 2013). However, as a guideline will only provide a summary of best practice recommendations. Further improvements to pain and sedation management were thought to be achievable through the introduction of a pain and sedation protocol consisting of a treatment algorithm (Morris, 2003). This paper will focus on how the introduction of this protocol might have impacted management of pain and sedation by the bedside nurse. The protocol was to provide a prescription for the escalation of pharmacological treatment. One major recommendation of the protocol was to optimise analgesia post operatively by providing boluses of morphine prior to increasing the rate of infusion. Another recommendation of the protocol that differed from usual practice was the use of clonidine rather than midazolam as a first line sedative agent.

The protocol was developed with contributions from nursing, medical and pharmacy teams. The protocol was introduced following in-service education for both nursing and medical staff. A medical and nursing lead ensured ongoing education for staff members in their respective teams. Printed copies of the protocol were available at each bedside and online copies were placed on the department intranet.

Aim

To assess the influence of using a pain and sedation protocol on management of children admitted to PICU following cardiac surgery. Key outcomes included frequency of pain and sedation assessments, dosage / administration of analgesics or sedatives and length of ventilation.

Methods

The setting was a 21 bed PICU that cares for children within the Victorian state of Australia. The unit provides cardiac surgery to approximately 900 children per year.

A retrospective audit of medical records before and after the pain and sedation protocol was performed. Hospital ethics approval was obtained prior to commencing the study. The medical records of 100 patients were audited, as this was deemed achievable within the timeframe required to perform the study. The patients included 50 patients admitted six months prior to the introduction of the protocol and 50 patients admitted 12 months following (Figure 1). Patients meeting the inclusion criteria were selected in chronological order until a total of 100 patients had been reached. Medical records for the first 48 hours of the patient's admission were reviewed, or until the patient was breathing spontaneously using their own airway, which ever occurred first. Medical records were accessed through the scanned medical record database Cerner PowerChart®(Cerner Corporation, North Kansas City, Missouri)

Inclusion criteria

Intubated and ventilated patients less than 18 years of age admitted into the PICU after cardiac surgery.

Exclusion criteria

Patients were excluded if they received more than two doses of neuromuscular blocking agents once they arrived in PICU.

Collected data included basic demographic information such as age, weight and diagnosis according to the Risk Adjusted Congenital Heart Surgery (RACHS-1) fields (Larsen et al., 2005). Duration of mechanical ventilation and PICU length of stay was also collected. The type of pain and sedation assessment performed was collected, along with the overall score.

 Data collection also included amount of analgesics and sedatives patients received via both infusion and bolus during the data collection time frame. Patients who weighing more than 50kg received a standard strength of analgesia and sedation via infusion, rather than a weight based dose. These groups of children were analysed separately.

Collected data were entered into Epidata 3.1 (Lauritsen, 2008), and double data entry was performed to identify data entry errors. Analysis was performed using Stata 12 (StataCorp. 2011. Stata: Release 12. Statistical Software. College Station, TX: StataCorp LP.), descriptive analysis was performed to examine trends and differences (Myles & Gin, 2000). Chi squared was used to test for differences in percentages between the two groups (Polito et al., 2011) and two group t-tests were used to compare means in groups that were normally distributed (Gruenberg et al., 2006). Data that were normally distributed was reported as medians and interquartile range (Myles & Gin, 2000). The Wilcoxon rank sum test was performed on non-parametric data to test for equality in the pre and post groups (Gruenberg et al., 2006). Inferential statistics were used to examine the different outcomes before and after protocol introduction(Myles & Gin, 2000).

Probability for an outcome being statistically significant was considered at a value of less than 0.05.

Results

A total of 100 patients admitted to PICU following cardiac surgery were included in the study (figure 1). Double data entry revealed 80 out of 7500 data points (1.07%) required review to address errors or to correct missing fields. As detailed in Table 1, there were significantly younger patients in the post protocol group, mostly in the 5 weeks to 12 month group (22% pre protocol vs 50% post protocol, p=0.004) and the 13 months to 4 years (32% pre protocol vs 2% post protocol, p=0.001). There was also a statistically significant difference in the median weight between the groups (Table 1). Diagnosis according to the RACHS-1 categories was evenly distributed between the two groups. There was also a longer duration of ventilation in the post protocol group (11.53 hours pre protocol vs 18.95 hours post protocol, p=0.008).

Pain and sedation assessments

The majority of patients received a pain and sedation assessment using the Comfort B score whilst receiving mechanical ventilation (41 pre protocol and 47 post protocol). COMFORT B assessments were performed more frequently in the post protocol group (pre protocol 3/24 hours, post protocol 5/24 hours, p=0.006), see table 2.

Type and amount of analgesics and sedatives administered

There was no statistical difference to the number of morphine infusions prescribed between the pre and post group, pre protocol n=47 (94%), post protocol n=46 (92%). However the dose of infusion in mcg/kg/hr was higher in the pre protocol group, see table 2. Morphine boluses were given to more patients in the post protocol group n=35 (70%) versus pre protocol group n= 4 (8%) (p=0.0001). The dose of morphine bolus was also seen to increase to a median of 0.41mg/kg (IQR 0.21-0.89) in the post protocol group compared to 0.20mg/kg (IQR 0.07-0.31) in the pre protocol group (p= 0.04).

The number of midazolam infusions prescribed significantly decreased, pre protocol n=45 (90%), post protocol n=8 (12%), p=0.0001. Although there was no statistical difference in amount or dose of midazolam boluses given between the groups, pre protocol median dose 0.25mg/kg (IQR 0.10-0.95)

n=3 (6%) versus 0.20 mg/kg (IQR 0.12-0.5) in post group, n= 7 (14%) (p =0.73). There was an increase in the number of clonidine infusions prescribed, pre protocol n=0, post protocol n=12 (p=0.001) along with an increase in the number of boluses prescribed, pre group n= 0 versus post group n= 18 (36%) (p<0.0001).

Nine children in the post group and three in pre group weighing less than 50 kg received propofol via infusion. More children under 12 years of age received propofol infusions in the post protocol group 10% (n=5) than in the pre protocol group 6% (n=3), although this was not statistically significant (p 0.46, using chi-squared). Propofol was administered for less than 24 hours in all cases, with a median duration of 11.6 (IQR 9.9-14.9) hours.

There was a significantly younger cohort in the post protocol group, therefore the dose of morphine via infusion was analysed by subgroup of age to examine if this may have had an influence on the dose of morphine. This found there was no significant difference in doses administered due to age.

Discussion

This study demonstrated that following the introduction of a pain and sedation protocol, the frequency of documented validated pain scores increased. Secondly, there was no change to the score level despite a reduction in the amount of midazolam administered to patients post protocol introduction. However, there was a trend towards an increase in the duration of ventilation.

Frequency of pain and sedation assessments and the level of sedation

Following introduction of the pain and sedation protocol, COMFORT B assessments were performed more frequently in the first 24 hours post cardiac surgery. This is not a unique outcome to this study and has been demonstrated in two other studies that introduced a protocol into PICU or NICU (Deindl et al., 2013; Ista et al., 2009). Increased surveillance of patient's comfort level could provide nursing staff with more opportunity to recognise and treat patient's distress. Improved recognition of pain or discomfort and subsequent treatment may reduce likelihood that children will experience adverse physiological or psychological effects linked to untreated pain (Wolf & Jackman, 2011).

Following the pain and sedation protocol's introduction there was no significant difference in COMFORT B scores, and more importantly in amount of COMFORT B scores above 20. According to the literature, a patient with a score of greater than 22 is considered to be at high risk of being in pain or being under-sedated (Ista et al., 2009). There was also a trend towards more scores in the 10-20 range in children treated with the protocol, what is considered optimal range at RCH. Although this was not statistically significant, this trend may have clinical relevance, as children that have optimal sedation and analgesic relief have been shown to have better clinical outcomes, such as earlier discharge from PICU, decreased incidence of withdrawal and fewer long term psychological consequences (Cho et al., 2007; Suominen et al., 2004; Wolf & Jackman, 2011). This outcome coupled with increased frequency of assessment indicates that implementation of a pain and sedation protocol has potential to improve recognition and treatment of pain or distress.

Amount and type of analgesic and sedation administered

Patients who weighed less than 50kg were found to receive lower mean doses of morphine via infusion in the post protocol group compared to pre protocol group. This was in conjunction with an increased median dose of morphine via bolus in post protocol group. Increased dose of morphine via bolus may have contributed to a lower background requirement for morphine via infusion. The pain and sedation protocol directed administration of a 0.1mg/kg bolus of morphine to children if their COMFORT B score was greater than 20. If three boluses were required in one hour the infusion could be increased by 5mcg/kg/hr. This recommendation was made as a bolus dose of morphine will reach peak plasma levels in the blood faster than increasing the rate of an infusion alone (Morton, 1999). Prior to introduction of the protocol there was considerable variation in pain or sedation management. This suggests that introduction of the protocol may have acted as a facilitator to

enable nurses to deliver analgesia in a consistent and timely manner in response to the patients pain score.

For institutions that are considering implementation of a pain and sedation protocol, they may need to consider that individual factors specific to their institutions will influence the outcome of analgesic and sedative administration. For example, Curley et al. (2015) suggests that different approaches to protocol implementation appear to work differently in individual institutions. One example of this is that Ista et al. (2009) and Jin et al. (2007) report using different implementation strategies to introduce their protocols and both report different outcomes in relation to administration of analgesic and sedatives post introduction of a protocol.

Midazolam infusions were used on fewer children, and patients began receiving more clonidine infusions for sedation in the post protocol group. The protocol recommended clonidine instead of midazolam as the first line sedative treatment if the patient required sedation. Considering potential long term benzodiazepine side effects, including its contribution to the development of withdrawal syndromes and delirium this outcome may be of benefit. Recent consensus guidelines from the European Society of Paediatric and Neonatal Intensive Care (ESPNIC) recognises withdrawal syndrome as an area of concern in PICU (Harris et al., 2016). A recent study examining the introduction of an analgesia and sedation protocol in PICU found a reduction in withdrawal symptoms post implementation (Neunhoeffer et al., 2015).

Administration of benzodiazepines should be based on evidence that medication is required (Istaphanous & Loepke, 2009; Sun, 2010). The pain and sedation protocol introduced in this study used COMFORT B assessments to inform nurses of the patient's level of pain or need for sedation and recommended treatment of pain as first priority in order to moderate administration of midazolam.

A reduction in the use of midazolam may cause concern that patients were not adequately sedated. However, despite results indicating a statistically significant reduction in the use of midazolam, this appeared not to be at expense of under sedation. Under sedation is a concern for children in PICU as it can contribute to psychological distress and may compromise some of the treatments provided (Wolf & Jackman, 2011). The level of sedation as determined by COMFORT B scores was not significantly different between the groups in this study. Reduction in use of midazolam without compromising patient's comfort levels indicates that the traditional combination of analgesics and sedatives in our PICU may not be necessary to ensure patients are comfortable. These results also indicate that a pain and sedation protocol may influence a nurse's decision of what first line medication to use. There was also an increase in the use of clonidine infusions used in the post group, this may have also had an influence on patient's level of sedation that received these infusions. For institutions that wish to streamline the nurse's approach to pharmacological treatment of pain and sedation, a treatment protocol may be of benefit.

Increased duration of ventilation

The post protocol group remained mechanically ventilated for a median duration of 7.42 hours more than the pre protocol group. It is suggested that sedation protocols in adults may reduce duration of mechanical ventilation and ICU length of stay (Bucknall, Manias, & Presneill, 2008). However, this has not been demonstrated in the majority of paediatric studies evaluating the impact of pain and sedation protocols. There is only one paediatric study that reports a decrease in duration of mechanical ventilation following the introduction of a pain and sedation protocol (Jin et al., 2007). Alexander et al. (2002), Ista et al. (2009) and Deeter et al. (2011) reported no change to the duration of mechanical ventilation in their studies of patients. No change to the duration of ventilation has also been recently reported in a multicentre study examining the impact of a sedation protocol versus usual care in paediatric intensive care units in America (Curley et al., 2015). The decreased duration of ventilation and ICU length of stay reported by Jin et al. (2007) may be due to differences

in the clinicians responsible for executing the protocol or differences in the patient cohort that was studied.

One variable that may explain the longer ventilated time in this study is that the post group were a younger demographic compared to the pre group. Children less than 12 months are less likely to be extubated within 24 hours (Aitken, Marshall, Elliott, & McKinley, 2009; Polito et al., 2011; van Dijk et al., 2000). The younger cohort in the post audit group may have influenced the trend towards an increased time spent mechanically ventilated.

Limitations

In interpreting the study results several limitations are considered; this includes the small number of patients in each group and that the study was performed as a single centre retrospective chart audit. This increases the risk to internal validity through uncontrolled confounding variables (Ho, Peterson, & Masoudi, 2008). However, due to the resources available, this design was the most feasible and thus a sample size calculation would have been inappropriate. The authors considered it important to evaluate the impact of the protocol following its introduction.

Another limitation was that this study only examined patients that were admitted following cardiac surgery, this limits the ability to generalise the findings (Hickson, 2008). It would be difficult to apply the findings to children admitted for general surgery or general medical treatments as they have a different progression of their illness or surgery.

Another limitation was the younger cohort in the post protocol group. In this study children in the post group were younger than the children in the pre group. This difference may have had an influence on the outcome of duration of mechanical ventilation (Davis, Worley, Mee, & Harrison, 2004).

Implications for practice

Implementing a nurse titrated pain and sedation protocol has contributed to increased frequency of pain and sedation assessment scores and administration of morphine boluses performed by nurses. This is an important outcome of the treatment protocol as it enables nurses to provide timely pain relief in response to the patient's needs and has the potential to improve patient outcomes in PICU through increased recognition of children's pain or distress.

Less midazolam was delivered to patients, with an increase in the use of clonidine when nursing staff managed sedation as per the protocol. Considering midazolam administration in PICU may contribute to neuro apoptosis, this outcome may be of benefit (Istaphanous & Loepke, 2009).

 Increased duration of ventilation may be of concern following the introduction of a sedation protocol. Other studies have reported varied outcomes regarding duration of ventilation when evaluating sedation protocols into PICUs (Curley et al., 2015; Jin et al., 2007). Departments / units who are planning to introduce a pain and sedation protocol should consider monitoring for changes in duration of ventilation.

Conclusion

Introducing a pain and sedation protocol into the PICU at RCH was associated with important changes in pain and sedation management. Notably an increase in COMFORT B documentation and moderation of sedative administration. Protocolisation enabled nursing staff to provide pain and sedation management in a consistent and timely manner. However, a trend towards increased duration of ventilation is of concern, although may be due to propensity matching not being performed between the patient groups in this study. For the future, ongoing evaluation of the long-term impact of the protocol is important.

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Figure 1: Flow chart of data collection process

Pre Group
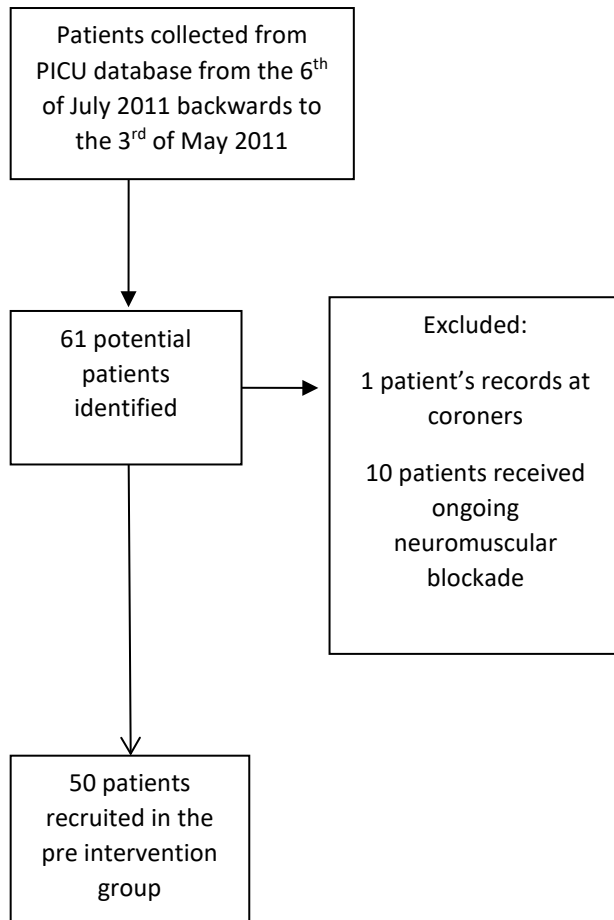
Post Group
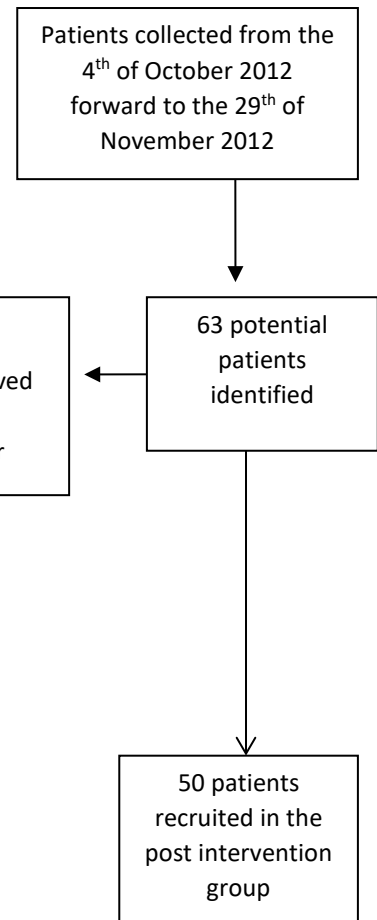
Table 1: Patient demographics between the pre (n = 50) and post (n = 50) protocol groups

	Pre audit median [IRQ]	Post audit median [IRQ]	P value
Median age days	792 [125-1951]	163 [52-1830]	0.03
Median weight kg	11.75 [6.4-21]	5.75 [4.3-14]	0.039
Median PICU LOS in hours	27.5 [23.25-49.25]	47.33 [25.33-70.5]	0.069
Median duration of ventilation hours	11.53 [8.16-23.33]	18.95 [11.58-35.33]	0.008
	n (%)	n (%)	
Patients ventilated 24hrs or more	12 (24%)	18 (32%)	0.19
Patients that received procedural muscle relaxants	10 (20%)	23 (46%)	0.006

Table 2: Pain assessment type and frequency

	Pre protocol n (%)	Post protocol n (%)	P value
Patients assessed by COMFORT B	41 (82%)	47 (94%)	0.06
Frequency in 24 hours (median/IQR)	3 (1-5)	5 (3-7)	0.006*
COMFORT B score range	Pre protocol	Post protocol	P value
Range <10 *	7 (14)	11 (22)	0.29
Range 10-20 *	5 (10)	12 (24)	0.062
Range >20 *	1 (2)	4 (8)	0.16

*Interpretation of scores at RCH <10 Over sedated, 10-20 optimal range, >20 under-sedated, high risk of pain

Table 2: Analgesic and sedative infusion doses used before and after the introduction of the pain and sedation protocol in children who weigh less than 50kg and greater than 50kg.

Analgesic or sedative agent administered via infusion	Pre protocol *Dose in mcg/kg/hr* mean {SD} Median[IQR]	Post protocol *Dose in mcg/kg/hr* mean {SD} Median[IQR]	P value (95% CI)
Morphine			
Less than 50kg	23.86 {10}	18.37 {8.9}	0.006 (0.003-0.997)
Greater than 50kg	20 [16-21]	15 [10-18]	0.12
Fentanyl			
Less than 50kg	-	1.28	
Greater than 50kg	1.71	-	
Midazolam			
Less than 50kg	57.6 [30.8-94.6]	24.5 [10-48.9]	0.024
Greater than 50kg	20.97 [8.8-33]	8.29	0.22
Clonidine			
Less than 50kg	-	0.69 [0.55]	
Greater than 50kg	0	0	
Propofol			
Less than 50kg	0.39 [0.12-0.68]	0.40 [0.2-1.3]	0.60
Greater than 50kg	-	0.24 [0.08-1.17]	
Dexmedetomidine			
Less than 50kg	-	0.48	
Greater than 50kg	0	0	