Sources and magnitude of error in preparing morphine infusions for nurse/patient controlled analgesia in a UK paediatric hospital

Introduction

Preparing infusions for administration to children requires complex dosage calculations, infusion rate adjustments and several manipulations; putting children at risk [1]. Wrong diluent or volume of infusion prepared, or wrong infusion rate administered are commonly reported, with incidence rates between 1.6% to 91.7% [1-2]. A previous UK study identified errors occurred in almost half of intravenous (IV) medicine preparations observed (49%, n=212/430), of which 1% of errors were severe and 29% were moderately severe [3]. Causes of such error include poor knowledge of correct methods for IV medicine preparation or administration and high workload [4]. Ten-fold or greater dose calculation errors have been reported through misplacement of the decimal point [5]. There is no standard preparation methods for these infusions and children have a 200 times difference in weight range (i.e. 0.5 - 100 kg) compared to 3 times in adults (i.e. 40 - 120 kg).

In a system prone to the errors described above, there are high risk consequences if potent drugs such as opiates are not delivered accurately, i.e. respiratory depression in overdose. The calculations required to produce paediatric preparations increase the risk of error. Currently, nurse- and/or patient-controlled analgesia (N/PCA) for children are prepared as 'individually made products', i.e. prepared for each patient based on their weight, using variations of the "rule of six" formula [6] to calculate the infusion concentrations prescribed in micrograms per kilogram per minute. This formula is described as: 6 x patient's weight (kg) equals the amount of drug in milligrams that should be added to 100 mL of solution, when administered at 1 mL/h to give an infusion rate of 1 micrograms/kg/min [6].

Aim of the study

To investigate the current practice and accuracy of preparation of nurse/patient controlled analgesia N/PCA morphine infusions in theatres and wards at a large UK children's hospital.

Ethical Approval

This study was approved by the Research and Development (R&D) department at Guy's and St Thomas' NHS Foundation Trust (GSTT) and categorised by the local NHS Research Ethics Committee as a non-Ethics study.

Methods

Setting

This study was conducted at the Evelina London Children's Hospital (ELCH). Morphine infusions for N/PCA are prepared in theatres and on wards individually for children based on a prescribed content of 1 mg/kg of morphine in a 50 mL solution.

Design

Direct observation of preparing and administering morphine for N/PCA in children by healthcare professionals (HCP), i.e. paediatric nurses and anaesthetists, was undertaken over three months. Observation was conducted by a single researcher (an experienced clinical pharmacist - ANR). The researcher explained the study and obtained permission from HCPs in theatres and wards to observe the preparation and administration process of morphine infusions for N/PCA. Data collected from direct observation included patient demographics (age, gender, weight) and morphine N/PCA prescription details. Data for the preparation and administration process included location; nurse or anaesthetist; infusion preparation procedure and infusion pump programming with delivery parameters (continuous infusion rate, bolus dose, lockout period between bolus doses). Syringe sizes used to draw up the morphine and diluent solution for the infusion preparation were recorded. Appropriate syringe size was defined as 'the next largest syringe size to the volume to be measured', e.g. a 5 mL syringe should be used to measure 3.2 mL of solution.

Accuracy of morphine infusions

Over a 5 week period, nurses were asked to retain morphine syringes containing residual unused morphine solution from N/PCA morphine infusions administered to patients. All infusions were collected irrespective of whether preparation was observed by the researcher although these samples were identified. The infusions were analysed by the Pharmacy Quality Control laboratory. The morphine concentration in the infusions was measured based on the British Pharmacopoeia (BP) method for analysis of morphine sulphate injection [7] using a validated UV spectrophotometric assay covering the concentration range analysed in the current study. Samples were stored at room temperature and analysed within 4 weeks of collection. This storage was internally validated as morphine has been shown to be stable when stored in polypropylene syringes at room temperature for up to 6 months, with loses of less than 3% over that period (unpublished data).

Accuracy of infusions was defined as the percentage of the deviation from target concentration (label strength) within the pharmacopoeial limit for drug content of morphine sulphate injection, 92.5-107.5% [7].

Data Analysis

Data were analysed using Stata 11 (StataCrop, College Station, TX, USA). Descriptive statistics were performed on all data. Data are presented as number, percentage and mean ± s.d., unless otherwise specified. The Chi-squared test was used to test for statistical significant ($p<0.05$), for categorical variables, between nurses (wards) and anaesthetists (theatres).

Results

Anaesthetists (n=28) and nurses (n=36) prepared 153 infusions for 128 children, (7.5 ± 5.6 years and 27.4 ± 18.1 kg (mean ± s.d.), 65.3% male). The majority were prepared by anaesthetists in paediatric theatres (64%), while the reminders were prepared by nurses in wards.

Two strengths of morphine ampoule were available to prepare the infusions. Morphine 10 mg in 1 mL was used to prepare all 98 infusions prepared in theatres, compared to only 16 of the 55 infusions prepared on the wards, where 60 mg in 2 mL ampoules were used for 39 infusions. Various methods to mix drug with diluent were identified (online appendix 1 shows the preparation methods followed by HCPs). Mean time for preparation in theatres, 10.5 min, was four minutes less than in wards. A variety of omissions or errors were identified, categorised as relating to the preparation or administration of the infusion and their frequency was recorded (Table 1). A significantly higher rate of error or non-compliance with good clinical practice was observed in the theatre setting for most types of errors, e.g. aseptic technique for IV drug preparation was not followed (15.3% vs. 1.8%), e.g. avoiding touching syringe-tip/needle, put down syringe attached to an unsheathed needle, no independent dose calculation checks (82.6% vs. 12.7%) and use of inappropriate syringe size for the volume to be measured (67.3% vs. 16.4%, $p<0.001$).

'Insert Table 1 here'

Although no calculation errors were identified, incorrect volume was withdrawn in many instances. The entire content of the morphine ampoule (10 mg/mL) including overage i.e. volume in excess of the nominal content (e.g. ampoule labelled as 10 mg/mL 1 mL ampoule, but contents actually closer to 11 mg in 1.1 mL) was withdrawn without measuring using 60 mL syringes in 52 (53.1%) of the infusions made in theatres, compared to 2 infusions (3.6%) made on the wards. In some cases, the total volume was made up with the contents of whole ampoules plus an extra fraction measured in a syringe, e.g. 2.3 mL measured using the entire content of 2 ampoules plus 0.3 mL measured in a syringe. Errors were also observed in the final volume, i.e. volume was more or less than 50 mL (target volume), by at least one graduation line in syringe, of the infusion in around one third of the cases in both theatres and wards.

The “purge” function (running the pump mechanism before connecting to the patient’s cannula to ensure that the pump’s driver has engaged the syringe plunger and that the line is primed) was not used in a majority of administrations made in theatres and wards (Table 1). In preparations where the purge function of the infusion pump was not used, between 0.3 mL – 2.5 mL of infusion fluid was required to prime the system, despite the IV giving set being primed manually before the syringe was placed into pump syringe drive. However, in four instances in theatre (4.2%, 4/94), the anaesthetist administered a bolus dose via the pump once it was connected to the patient’s cannula as an alternative to purging.

Accuracy of morphine infusions

A total of 78 syringes (theatres 35, wards 43) containing unused morphine infusion were collected, of which 23 had been observed during preparation (theatres 14, wards 9). More than half (61.5%) of these infusions (48/78) had concentrations outside the BP limit for drug content (theatre 31; ward 17). A furthermore, ten infusions deviated by more than 20% (theatres 9, wards 1, $p<0.001$), (Figure 1), and one deviated by 100% (theatre).

‘Insert Fig. 1 here’

Sixteen of the infusions found to be outside the BP limit were observed during preparation), (Table 2). The infusions prepared in theatre showed drug content deviations up to 26.7% while maximum deviation of infusions prepared in ward was 14.4%, (Table 2). The whole content of the drug ampoule, including the overage was drawn up in 8 of the 10 infusions prepared in theatre. This practice was not observed in the wards. The syringe size used to withdraw the required amount of drug from ampoule was inappropriate in 10 of the 16 infusions (theatre 7, ward 3). In theatre, a 60 mL syringe was used to withdraw both drug and diluent in 6 preparations. In all of these 6 preparations the entire content of ampoules was withdrawn directly into the infusion without measuring the volume. In two cases, part ampoules were

required to complete the total volume and the additional volume from a part ampoule was measured and added separately.

'Insert Table 2 here'

Discussion

This study is unique in combining observational assessment of paediatric infusion preparation in practice with drug content analysis of the prepared product. The results showed that preparation procedures for individualised infusions are not standardised and identified significant differences in practice between different clinical settings; theatres (anaesthetists) and wards (nurses). This resulted in children receiving morphine doses significantly higher or lower than those prescribed. Inaccuracy of intravenous infusions prepared in clinical settings has been previously reported in paediatric studies of continuous infusions [8-9]. The study was undertaken in a single hospital, and infusions prepared for emergency cases were not included. However, the findings from this study are likely to be generalisable as similar errors during preparation have been reported in other countries for infusions prepared on wards [8,10].

The deviations from the prescribed dose identified in this study could potentially put children at risk of side effects, e.g. respiratory depression [11]; or change the prescriber's views of the child's clinical management because the child may be perceived as requiring more or less analgesia because the morphine concentration was inaccurate. Inaccuracy of volume measurement, or no measurement was one factor associated with infusions which deviated from the label strength. Another factor was failure to select the appropriate syringe size to withdraw the drug accurately from an ampoule. Sometimes the same syringe was used to draw up the drug and then the diluent; meaning that the drug retained in the dead space of the syringe will also be transferred to the product, resulting in an overdose. Understanding the impact of drug retained in the dead space is important in children as significant overdose of drugs has been reported [12]. Disregard of the ampoule excess volume (overage) could be

one of the contributing factors of greater infusion concentration deviation in theatres. This is consistent with outcome of the focus group we conducted with the HCPs where participants, mainly anaesthetists, explained their confusion about the exact volume of morphine solution in an ampoule and reported their practice of withdrawing the entire ampoule contents including the overage [13].

Another potential cause of the deviations in morphine concentration was the difficulty of drawing up small drug volumes accurately and diluting up to 500 times for preparation of the infusions. The use of morphine 30 mg/mL led to measurements of very small volumes, thus the use of 10 mg/mL (a less concentrated product) would be recommended to improve accuracy. There is a lack of standardisation for preparation of infusions that needs to be addressed through staff familiarisation with good practice through training and protocols.

This study provides a clear imperative to improve current practice for N/PCA, ideally through removal of the complex preparation which is prone to error. Potential solutions include standardisation of morphine concentrations for N/PCA use and/or performing bulk manufacture of 'ready-to-use' infusions in a quality-controlled environment. Using standardised concentrations in conjunction with advanced infusion apparatus has been reported to reduce errors. A study in children identified that the number of reported errors associated with continuous medication infusions was reduced by 73% following implementation of standard drug concentrations solutions administered using advanced safety pumps with inbuilt 'drug libraries' and default settings to facilitate pump programming [14].
Less technical solutions include interventions to increase knowledge on the use of correct syringe size and raise awareness of overage in ampoules.

Conclusions

This study identified that HCPs use a variety of techniques and manipulations when preparing IV infusions of morphine N/PCA for children, which includes practices leading to medication

errors. A lack of understanding about the overage in ampoules, together with the challenge of selecting one or more syringe of the correct size, raises concern about the accuracy of the morphine infusions. The difficulty of drawing up very small drug volumes and combining these in large diluent volumes makes this practice error prone and inaccurate. Training and standardisation to improve the accuracy and promote safer provision of these infusions should be developed.

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Conflict of interest

ANR was funded by the Health Foundation. Other authors declared no financial interests.

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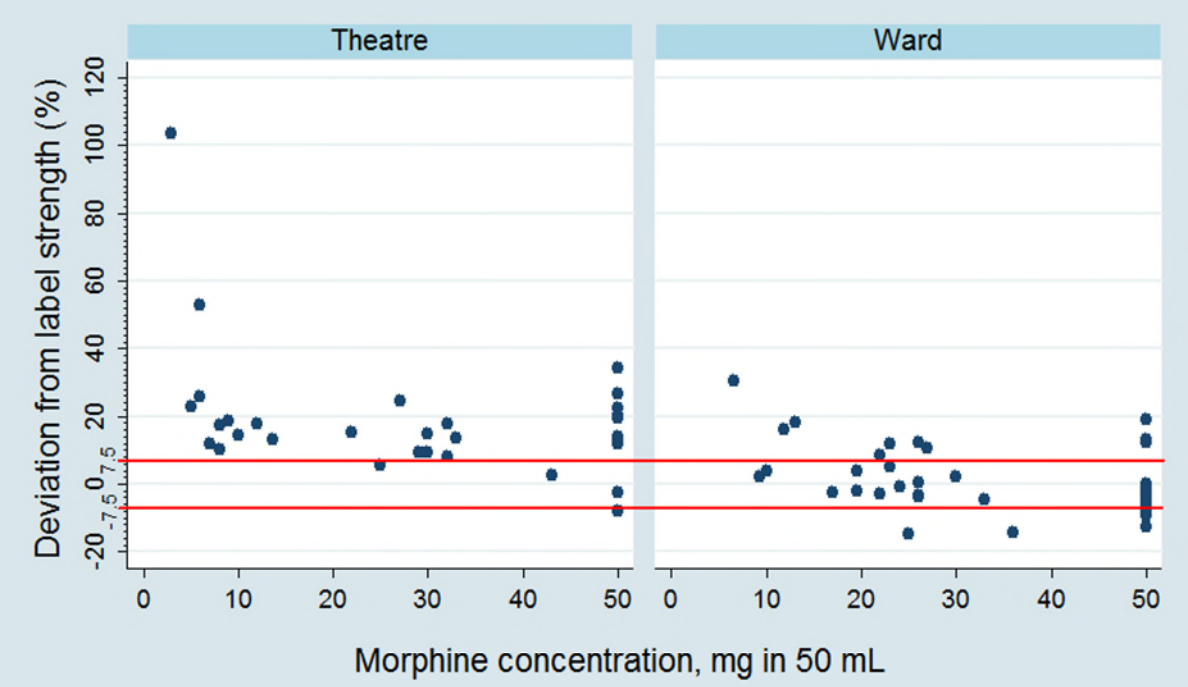
Figure 1. Deviation from the label strength of morphine concentrations in the individual 50 mL syringes prepared by healthcare professionals in theatres and wards



The red lines show the target concentration within the British Pharmacopoeia acceptable limits of ±7.5% and which data fall outside these limits.

Table 1. Number and percentage of various types of errors identified during observations

	Theatres N=98	Wards N=55	*p*- value	Total N=153
Preparation time; mean (±sd)	10.5 (±3.3)	14.5 (±4.0)	<0.001	11.9 (±4.1)
Incorrect preparation technique; n(%):				
Drug dose calculation was not checked by second person before preparation*	81 (82.6)	7 (12.7)	<0.001	88 (57.5)
No double checking of volume withdrawn from ampoule by second person	58 (59.2)	12 (21.8)	<0.001	70 (45.8)
Aseptic technique (i.e. non-touch technique) not followed in preparing IV infusion, e.g. avoiding touching syringe-tip/needle.	15 (15.3)	1 (1.8)	<0.01	16 (10.5)
No decontamination of ampoules	98 (100)	55 (100)	-	153 (100)
Wrong diluent†	0	1 (1.8)	0.180	1 (0.7)
Wrong syringe size used to withdraw drug amount (in mL) from its ampoule;	66 (67.3)	9 (16.4)	<0.001	75 (49.0)
Prescribed dose (in mL); *n(%)*††:				
0.3 - 0.9	4 (6.1)	0		4 (5.5)
1 - 1.9	11 (16.7)	1 (14.3)		12 (16.4)
2 - 2.9	12 (18.2)	2 (28.6)		14 (19.2)
3 - 3.9	10 (15.2)	0		10 (13.7)
4 - 5	29 (43.9)	4 (57.1)		33 (45.2)
Mixture was not mixed properly	58 (59.2)	19 (34.5)	<0.01	77 (50.3)
Air bubbles not expelled from syringe	1 (1%)	1 (1.8)	0.677	2 (1.3)
Final volume not correct (> or <50mls)	38 (38.8)	17 (30.9)	0.331	55 (35.9)
Final volume >50 mL	36 (36.7)	15 (27.3)	0.234	51 (33.3)
Final volume not *checked by second person	88 (98.9)	51 (27.3)	<0.001	139 (90.8)
No gloves used during preparation	82 (83.7)	0	<0.001	82 (53.6)
Incorrect administration techniques; n(%):				
IV giving set not primed	0	1 (1.8)	0.180	1 (0.7)
No purging of the pump	94 (95.9)	51 (92.7)	0.584	145 (94.8)
No flushing of IV access (cannula) before connecting the new IV set	98 (100)**	45 (81.9)	<0.001	143 (93.5)
No alcohol swab for IV access (cannula) before connecting IV giving set	98 (100)	18 (32.7)	<0.001	116 (75.8)
Patient identification not checked	na**	9 (16.4)	-	9 (5.9)
No double checking of prescription against pump programme	4 (4.1)	30 (54.5)	<0.001	34 (22.2)

*according to hospital IV preparation protocol and nurse training programme, **na=not applicable, N/PCA IV infusion was prepared at the same time the patient in theatre, †near miss error (selecting wrong diluent glucose 5% instead of NaCL 0.9%) which was on prescription), ††percentage was calculated based on total number of preparations with wrong syringe size used in theatre (66), ward (7) and total cohort (73).

Table 2. Observed errors on preparation of morphine infusions deviating from the label strength by ±7.5% (i.e. outside British Pharmacopoeia limit)

Location	Target infusion concentration (mg in 50 mL)	Ampoule strength used for preparation (mg/mL)	Volume required (mL)	Actual volume withdrawn (mL)	Entire content of ampoule used	Syringe size used to withdraw volume (mL)	Correct syringe size	Deviation (%)
Theatres	8	10	0.8	0.8	no	1	yes	+17.5
	8	10	0.8	0.8	no	1	yes	+10.1
	9	10	0.9	not measured	yes	10†	no	+18.5
	27	10	2.7	not measured	yes	60 + 1*	no	+24.5
	29	10	2.9	not measured	yes	60 + 1*	no	+9.5
	30	10	3	not measured	yes	5	yes	+14.9
	50	10	5	not measured	yes	60	no	+26.7
	50	10	5	not measured	yes	60	no	+12.7
	50	10	5	not measured	yes	60	no	+20.3
	50	10	5	not measured	yes	60	no	+14.0
Wards	10	10	1	1	no	3	no	+14.4
	7	30	0.233	0.24	no	1	yes	+11.7
	22	30	0.733	0.74	no	1	yes	+8.5
	23	30	0.766	0.77	no	1	yes	+12.0
	26	30	0.866	~0.87	no	3	no	+12.3
	27	30	0.9	1	no	3	no	+10.7

†The whole content of the ampoule was withdrawn using 10 mL syringe then diluted up to 10 mL, and then 9 mL of the solution was added into the 60 mL syringe then volume completed to 50 mL with diluent. *not measured, i.e. whole ampoule's content was withdrawn.

Online appendix 1. Preparation methods followed by healthcare professionals

Mixing method description	Frequency n (%)
1. Draw diluent amount first into 60-mL syringe, 2. Draw drug amount from ampoule into another syringe using different needle, 3. Add amount of drug into diluent syringe.	81 (52.9)
1. Draw up diluent amount first into 60-mL syringe, 2. Draw up the whole content of drug ampoule directly into diluent syringe using diluent needle. Example: Morphine 50mg in 50 mL of Sodium Chloride 0.9% w/v Draw up 45mL of diluent (normal saline) into 60-mL syringe, then draw up the whole content of 5 ampoules of the drug (concentration 10mg/ml) directly into the 60ml-syringe using same needle of the diluent.	21 (13.7)
1. Draw diluent amount first into 60-mL syringe, 2. Add the whole content of drug ampoule into diluent syringe using same diluent needle 3. Using 10-mL syringe draw up whole content of another drug ampoule, then diluent into 10ml with normal saline, then add the required amount of the drug into diluent syringe (60-mL syringe) using diluent needle. Example: Morphine 25 mg in 50 mL of Sodium Chloride 0.9% w/v Draw up 43 mL of diluent (normal saline), then draw up the whole contents of 2 ampoules (10 mg/mL) of the drug directly into diluent syringe (60mL-size), then dilute the whole content of a 3rd ampoule of the drug (10mg/ml) into 10 mL normal saline. Resultant concentration 10 mg/10 mL, then, using diluent needle take 5 mL (5 mg) of this solution and add it into diluent syringe.	9 (5.9)
1. First draw up the whole content of drug from ampoule into 60-mL syringe, 2. Then add diluent to complete volume up to 50 mL.	19 (12.4)
1. Draw up amount of diluent first into 60-mL syringe, 2. Draw up the whole contents of ampoule of drug directly into diluent syringe (60 mL-size) 3. Using 1 mL-syringe draw up the remaining amount of from another ampoule and added it into diluent syringe. Example: Morphine 36 mg in 50 mL of Sodium Chloride 0.9% w/v Draw up ~47mL of diluent (normal saline) then draw up the whole content of 3 ampoules of the drug directly into 60 mL-syringe, then using 3 mL-syringe to draw up 0.6 mL of the drug from the 4th ampoule and add it into 60 mL syringe.	10 (6.5)
1. Draw up content of whole ampoule into 60-mL syringe, 2. Using 10-mL syringe dilute the whole content of another ampoule (10 mg/mL) of the drug into 10 mL normal saline, then add the required amount into the 60-mL syringe 3. Complete the volume up to 50 mL with normal saline. Example: Morphine 34 mg in 50 mL of Sodium Chloride 0.9% w/v First draw up the contents of 3 ampoules (10 mg/mL)of drug directly into diluent 60 mL-syringe, then dilute the whole content of the 4th ampoule of the drug into 10 mL normal saline then add 4 mL (4mg) of this solution into 60-mL syringe, then complete the volume up to 50ml with normal saline.	8 (5.2)
1. Draw up amount of diluent first into 60-mL syringe, 2. Dilute the content of one drug ampoule (concentration 10mg/1mL) in 10 mL of normal saline, then added required amount to the into diluent syringe (new needle used) Example: Morphine 7 mg in 50 mL of Sodium Chloride 0.9% w/v First draw up 43 mL of normal saline (diluent) into 60-mL syringe, then using 10-mL syringe dilute the whole content of drug ampoule (10 mg/mL) into 10 mL normal saline, then add 7 mL (7 mg) of this solution into the diluent syringe.	5 (3.3)