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DISSERTATION

Factors related to peripheral venous cannulation pain pre-operation in pediatric patients

zur Erlangung des akademischen Grades
Doctor medicinae (Dr. med.)

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Table of contents

Abbreviations

IV	intravenous
N_2O	nitrous oxide
NIR	near infrared
BPS	Behavioral Pain Scale
FPS-R	Faces Pain Scale-Revised
OR	Odds Ratio
CI	95% confidence interval
SD	standard deviation
IQR	interquartile range
nm	nanometer
kg	kilogram
mg	milligram
min	minute
G	gauge

1 Introduction

Pain associated with peripheral intravenous (IV) cannulation is common and frequently suffered by pediatric patients requiring needle related medical procedures.[1] The painful experience is full of fear and distress, but is transient for most cases. However, lasting negative consequences and long-term adverse influence on developments of nervous system, pain sensitivity and emotionality could result from poor or unmanaged acute pain control.[2-4] Children with previous negative experiences of medical procedures were more distressful and uncooperative and tended to show high level of anxiety before the subsequent needle-based procedures.[5-9] Those who had experienced medical procedure pain in childhood tend to feel fear and pain, and try to avoid clinical care which they have to face in adulthood.[10-12] In addition, severe pain leads to more missed future medical appointments and low follow-up of health care due to fear and distress, or even needle phobia affecting at least 10% of the population.[13-16]

1.1 Approaches to IV cannulation pain relief in pediatric patients

Strategies for improving pain management and reducing negative pain memory during IV insertion in pediatric patients can be divided into pharmacological and nonpharmacological techniques. The former is mainly referred to topical (e.g. EMLA could reduce IV access pain in 85% of the population[17])and general anesthetics(such as nitrous oxide, N_2O, could alleviate distress effectively during painful procedures[18]). The latter includes distraction, cognitive behavior therapy, relaxation, music, massage, breathing and counting.[19-22]

1.2 Strategies to facilitate IV cannulation in pediatric patients

Fewer attempts and skillful operations with the sterile venous catheters should be helpful for pain relief of IV cannulation in principle. Many different methods were tried to dilate the target vein because bigger veins seem to be easier to be located and accessed.[23-25] Recently, a variety of nonpharmacological techniques have been

employed to facilitate peripheral IV access in pediatric patients, such as transillumination by light-emitting diode, vein-entry indicator devices, ultrasound-guided peripheral IV insertion, and near-infrared(NIR) light-based devices to locate superficial veins at a peripheral site.[26-29]

1.3 Pain assessment tools used in pediatric patients

1.3.1 Behavioral Pain Scale (BPS)

BPS, adapted from Children's Hospital of Eastern Ontario Pain Scale, was applied in assessment of needle insertion related pain for the first time by Robieux and her colleagues in infants and toddlers.[30] This new tool consists of three parameters, including 'facial expression', 'cry', and 'movements', with the minimum score of 0 and the maximum score of 8 (the higher the score is, the more severe the pain is). In addition, this modified BPS was also used in evaluation of acute pain in children during their postoperative stay in ICU.[31]

1.3.2 Faces Pain Scale-Revised (FPS-R) (English)

It was reported that the use of scales with a smiling facial expression often led to higher pain scores compared to those with a neutral 'no pain' face.[32] FPS-R has been recommended for application in clinical research because of its utility and psychometric features.[33] It was also observed that scoring with the FPS-R was consistent with Visual Analogue Scale or Coloured Analogue Scale, and appropriate for assessment of acute pain in children aged older than 4 years.[34-36] But response biases are found to be common in children younger than 5 years old.[37, 38] Stanford and other colleagues argued in another publication that pediatric patients' ability to report pain with FPS-R improved with increasing age.[37]

1.4 Aim of the study

The primary aim of the study was to investigate the factors related to IV cannulation pain in pediatric patients in a pre-operative setting where the acute pain could be controlled or avoided by anesthesiologists and nurses. It could be studied through (1)

the evaluation of pain intensity changes during venous insertion, (2) the relationship between pain scores recorded at the beginning and the end of the whole process of IV catheterization, (3) factors related to pain and pain increment in venous access (to judge whether measures for facilitating IV access would reduce pain indirectly, and whether endeavours for pain relief would really work), (4) meanwhile, observing if FPS-R employed in observational pain rating would correlate with BPS in pediatric patients aged 4 to 16 years.

2 Methods

2.1 Ethics

This study was performed as a project for clinical quality control management. The institutional review board (Ethikkommission der Charité) gave its consent to the publication of the results.

2.2 Duration of the observation

From January 10th, 2011 to March 4th, 2011, the trial was carried out pre-operation in all pediatric patients coming for surgical procedures who needed effective vein access, the primary requirement for anesthesia induction or medication before and during the subsequent surgery procedures in pediatric operating-rooms, Campus Virchow-Klinikum, Charité-Universitätsmedizin Berlin.

2.3 Patients

All pediatric inpatients to receive elective surgical procedures in operating-rooms could be enrolled in our cohort study.

2.3.1 Inclusion criteria

We included the patients in whom one or more IV line placement(s) would be required for subsequent anesthesia induction or medication in the coming elective operation but was planned to be done in operating-rooms.

2.3.2 Exclusion criteria

Those who had been cannulated in the wards or emergency department before coming to operating-rooms and didn't require more IV accesses, such as some emergency cases, those who were to undergo re-operations, and those patients who had been hospitalized for a long time, were excluded from our study.

2.4 Intravenous cannulation

2.4.1 General process

All IV insertions were performed by skilled and experienced residents and nurses. A rubber tourniquet was always applied when an appropriate vein was located in one of the limbs of a patient. It would be positioned proximal to the puncture site. Then a suitable size of IV catheter (Becton Dickinson Therapy AB, SE-251 06 Helsingborg, Sweden) was selected for the IV cannulation. Timing was started as the operator pointed a needle towards the site fit for IV line placement and ended as a successful vein access was available and easily flushed by sterile 0.9% sodium chloride solution. Pain intensity was evaluated at the beginning and the end of a successful IV cannulation.

2.4.2 IV access with the aid of AV 300 vein viewing system

For some cases, AV300 vein viewing system (AccuVein, LLC, 40 Goose hill Rd, Cold Spring Hrbr, NY), a device based on NIR, was employed to facilitate IV access following the User Manual.[39] The whole process of IV cannulation for each site was carried out directly in NIR beam. During IV insertion, AV300 was held by an assistant about 7 inches (180mm) over the vein to be located at a 90° right angle (perpendicular) to the direction the vein extends or is expected to do. Sometimes, in order to get a good quality of the target vein shown, the height or the angle at which the device was held would be slightly altered. The AV300 was not allowed to shine vein display light into the eyes because the device emits two Class 2 lasers, a red one with a wavelength of 642nm and a near-infrared one at 785nm. Due to the absorption of the NIR by hemoglobin, the vein can be presented.[39]

2.5 Data collection

A data collection form was used to record demographic and clinical information including gender, age, weight, premedication (oral midazolam) or not, using local anesthetic (EMLA®, a mixture of lidocaine and prilocaine, AstraZeneca Pty Ltd, Alma Road, North Ryde NSW 2113, Australia) or not, whether general anesthetic (N_2O from

Linde AG, Corporate Responsibility, Klosterhofstr. 1, Munich, Germany or sevoflurane from Abbott GmbH & Co. KG, Knollstr. 50, Ludwigshafen, Germany) was necessary for IV cannulation, size of needles, duration and number of attempts until successful IV cannulation, and pain sores evaluated with BPS and FPS-R (observation by the investigator, no self-report by the patients).

2.6 Statistics

Data were analyzed by SPSS for Windows version 18 (SPSS Inc, Chicago, IL). After being checked for normal distribution of pain scores (Q-Q-plots), results were expressed as mean $\pm$ standard deviation (SD), from the two scales for evaluating needle pain. Paired t-test was used to detect the differences between the scores at the beginning and those at the end of IV access. After visualization by scatter plots, bivariate Pearson's correlation was utilized to assess the correlation of pain scores measured by BPS or FPS-R at the two time points, and the correlation of BPS scores and FPS-R scores at either point. Then, multiple linear regression was used to examine factors recorded in this study associated with pain intensity at either time point. Risk factors for IV insertion pain were detected by binary logistic regression. Odds Ratios (ORs) and 95% confidence intervals (CIs) from the regressions above would indicate effects of different factors on peripheral IV cannulation pain.

Clinical characteristics and demographic data were recorded and expressed as median (interquartile range, IQR), except for categorical data as count (proportion). Frequencies were tested by χ^2-test. Mann-Whitney U-test was applied to evaluate the differences of basic characteristics between pain increment and no changes of pain intensity in the process of IV cannulation. *P*-values < 0.05 with two-tailed test of significance were considered statistically significant.

3 Results

3.1 Pain intensity measured by BPS in all patients

3.1.1 Basic characteristics and demographic data

There were 238 pediatric patients involved in the study, with a median age of 24 (IQR: 8 - 76) months, a median weight of 9.5 (IQR: 7.6 - 14.2) kg, 45% were female, 55.5% received EMLA before coming to operating-rooms, 60.9% were considered to require inhaled general anesthetic before IV insertion, 47.9% were cannulated with the help of the vein viewing system, AV300, 66.8% took oral midazolam as premedication with a median duration of 43 (IQR: 35 - 57) min and a median dose of 0.8 (IQR: 0.4 - 1.3) mg/kg before cannulations. The first-attempt success rate was 59.2% and the median time taken until a successful cannulation was 1 (IQR: 0.6 - 3.0) min (**Table 1**).

Table 1. Demographic data and basic characteristics of patients

Characteristics	**Total** Count (% within groups), median(IQR), n=238	**Those aged 4 to 16 years** Count (% within groups), median(IQR), n=89
Gender		
Male	131 (55.0)	49 (55.1)
Female	107 (45.0)	40 (44.9)
Age (months)	24 (8-76)	96 (72-134)
0-3	31 (13.0)	0 (0.0)
4-12	52 (21.8)	0 (0.0)
13-24	37 (15.5)	0 (0.0)
25-71	48 (20.2)	20 (22.5)
≥ 72	70 (29.4)	69 (77.5)
Weight (Kg)	9.5 (7.6-14.2)	27.7 (20-40)
< 5	20 (8.4)	0 (0.0)
5-9.99	78 (32.8)	1 (1.1)
10-19.99	67 (28.2)	24 (22.5)
20-39.99	48 (20.2)	44 (49.4)
≥ 40	25 (10.5)	24 (27.0)
General anesthetic		

Characteristics	Total Count (% within groups), median(IQR), n=238	Those aged 4 to 16 years Count (% within groups), median(IQR), n=89
No	93 (39.1)	54 (60.7)
Yes	145 (60.9)	35 (39.3)
Local anesthetic		
No	106 (44.5)	42 (47.2)
Yes	132 (55.5)	47 (52.8)
Needles (G)		
26	3 (1.3)	0 (0.0)
24	122 (51.3)	13 (14.6)
22	95 (39.9)	60 (67.4)
20	18 (7.6)	16 (18.0)
AV300		
Not used	124 (52.1)	46 (51.7)
Used	114 (47.9)	43 (48.3)
Midazolam (mg/kg)	0.8 (0.4-1.3)	0.3 (0.2-0.5)
Not administered	79 (33.2)	27 (30.3)
Administered	159 (66.8)	62 (69.7)
Duration (min)	43.0 (35.0-57.0)	43.0 (34.0-55.0)
Number of attempts		
1	141 (59.2)	66 (74.2)
2	41 (17.2)	14 (15.7)
3	24 (10.1)	6 (6.7)
4	19 (8.0)	1 (1.1)
5	6 (2.5)	1 (1.1)
6	7 (2.9)	1 (1.1)
Time taken (min)	1.0 (0.6-3.0)	1.0 (0.2-2.0)
≤ 0.5	59 (24.8)	36 (40.4)
0.5-1	70 (29.4)	27 (30.3)
1-3	54 (22.7)	18 (20.2)
≥ 3	55 (23.1)	8 (9.0)

Data are expressed as median (IQR), except for categorical data as count (percentage). G, gauge. IQR, interquartile range

3.1.2 Comparison of pain intensity at different time points of IV cannulation

Through paired t-test of the BPS scores, more pain was demonstrated at the end of IV insertion than at the beginning (mean ± SD, 3.97 ± 1.639 versus 2.80 ± 0.951, t = 14.398, *P* < 0.001) (**Figure 1**).

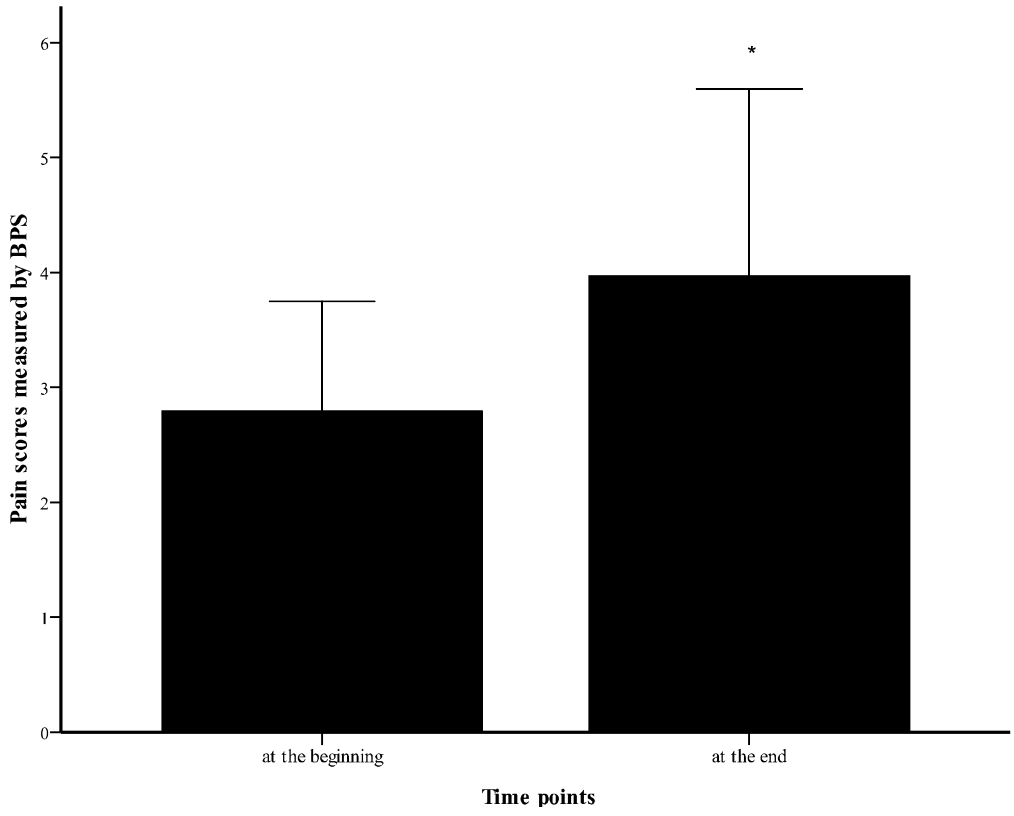

Figure 1. Bars and comparison of pain scores measured by Behavioral Pain Scale (BPS) during peripheral vein cannulation. * indicates a significant difference of pain level between the two points. Error bars: +/- 1 SD

3.1.3 Linear correlation of pain scores in peripheral IV cannulation

There is a linear correlation, with an *r*-value of 0.646 (*P* < 0.001), between the mean pain levels measured by BPS at different time points during peripheral vein cannulations (**Figure 2**).

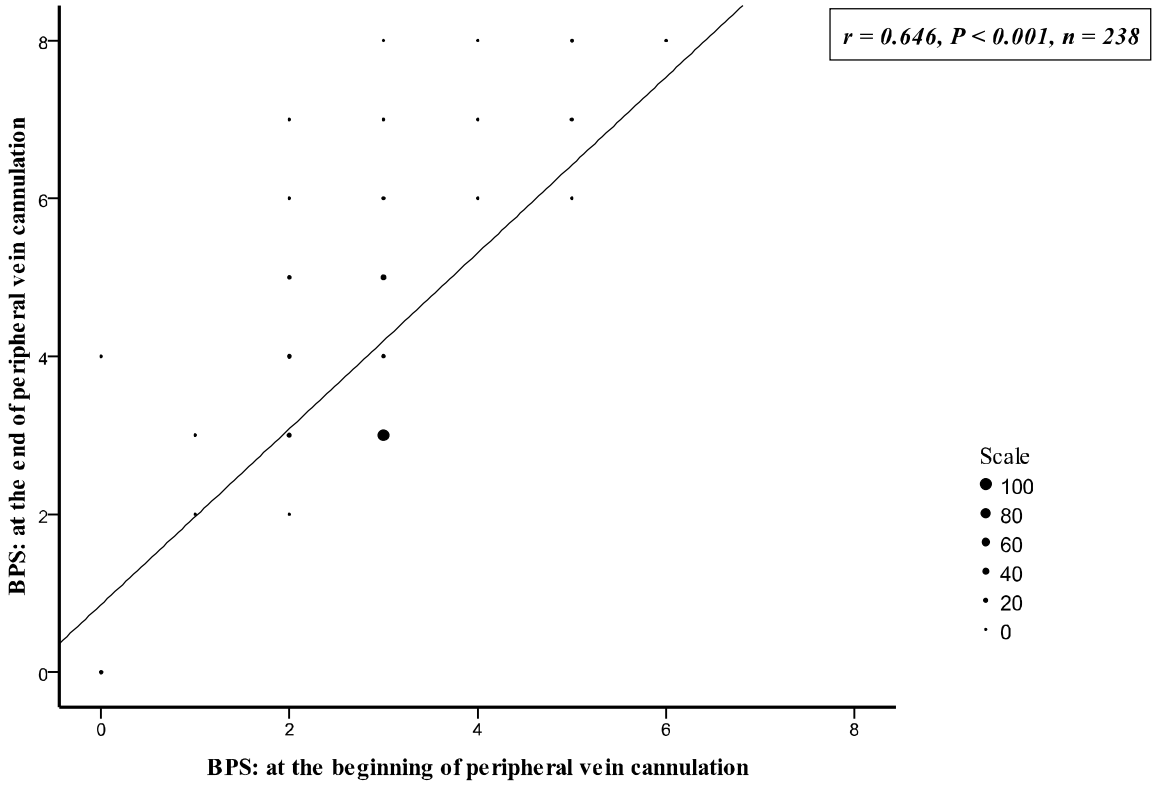

Figure 2. Scatter plots and correlations of Behavioral Pain Scale (BPS) scores at the beginning and at the end of peripheral vein cannulation in all patients. The bigger a marker is, the more patients are in a certain rank of the scale

3.1.4 Risk factors for pain levels at different points of IV cannulation

The following models were gained via multiple linear regressions.

For the pain intensity at the beginning of the cannulation BPS0 (Y), age (months, X_1) and AV300 (used or not, X_2) were included in the equation (**Tables 2**).

$$Y = 3.177 - 0.005X_1 - 0.330X_2, \quad R^2 = 0.082, \quad P < 0.001$$

Table 2. Risk factors related to BPS0

Model	Unstandardized Coefficients		Standardized Coefficients	t	P	95.0% Confidence Interval for B	
	B	Std. Error	Beta			Lower Bound	Upper Bound
(Constant)	3.177	0.103		30.865	0.000	2.974	3.379
Age	-0.005	0.001	-0.244	-3.890	0.000	-0.007	-0.002
AV300	-0.330	0.119	-0.174	-2.768	0.006	-0.565	-0.095

Age (0 to 3 months, 4 to 12 months, 13 to 24 months, 25 to 71 months, ≥ 72 months) and AV300(used or not) are included in the multiple linear regression model

For the pain intensity at the end of the cannulation BPS1 (Y), general anesthetic (used or not, X_1), size of sterile catheters (X_2) and number of attempts (X_3) were included in the equation (**Tables 3**).

$$Y = -1.409 - 1.534\,X_1 + 0.262\,X_2 + 0.162\,X_3, \qquad R^2 = 0.238, \qquad P < 0.001$$

Table 3. Risk factors related to BPS1

Model	Unstandardized Coefficients		Standardized Coefficients	t	P	95.0% Confidence Interval for B	
	B	Std. Error	Beta			Lower Bound	Upper Bound
(Constant)	-1.409	1.695		-0.831	0.407	-4.748	1.930
General anesthetic	-1.534	0.197	-0.458	-7.770	0.000	-1.923	-1.145
Size of catheters	0.262	0.076	0.209	3.471	0.001	0.113	0.411
Number of attempts	0.162	0.078	0.129	2.086	0.038	0.009	0.315

General anesthetic (administered or not), size of angiocatheters and number of attempts are included in the multiple linear regression model

3.1.5 Changes of pain intensity at different points

3.1.5.1 Proportion of pain changes

A comparison of pain scores at the beginning and at the end of IV cannulation showed no changes or increase of pain. Even though no differences were manifested by one-sample χ^2-test between the ratios (106 out of 238 for the no changes versus 132 out of 238 for the more pain, P = 0.092), there was a trend towards an increase of pain (**Figure 3**).

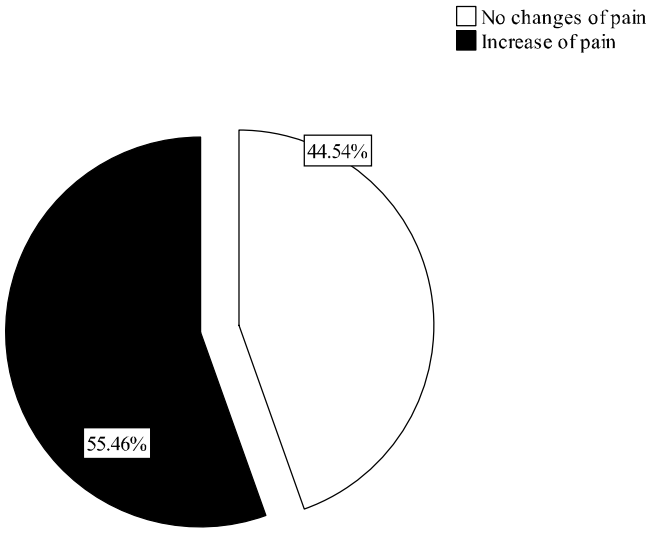

Figure 3. Pie plots and the proportion of pain intensity changes measured by Behavioral Pain Scales (BPS). The black part indicates the ratio of patients feeling more pain at the end of intravenous insertions compared with the beginning, and the white part shows no changes of pain intensity during the whole process

3.1.5.2 Basic characteristics and demographic data

Compared with those who felt no changes of pain intensity during the whole process of IV cannulation, a total of 132 pediatric patients still showed increase of pain at the end of IV access, who were older with a median age of 48 (IQR: 11 - 95) months *versus* 15 (IQR: 7.8 - 44.5) months (P = 0.001), heavier with a median weight of 15.3 (IQR: 8.8 - 28.0)kg *versus* 9.6 (IQR: 8.0 - 16.0)kg (P = 0.001), and treated by topical anesthetic (EMLA) in a larger proportion, 64.4% *versus* 44.3% (P = 0.002), but fewer of them were controlled by general anesthetics before IV access with 31.8% versus 97.2% (P < 0.001). More details and information are presented in **Table 4**.

Table 4. Demographic data and basic characteristics of all patients with different pain intensity changes (measured by Behavioral Pain Scale) during peripheral IV cannulation

Characteristics	No changes of pain Count (% within groups), median(IQR), n=106	Increase of pain Count (% within groups), median(IQR), n=132	P
Gender			0.096
Male	52 (49.1)	79 (59.8)	
Female	54 (50.9)	53 (40.2)	
Age (months) [a]	15 (7.8-44.5)	48 (11-95)	0.001
0-3	13 (12.3)	18 (13.6)	
4-12	33 (31.1)	19 (14.4)	
13-24	23 (21.7)	14 (10.6)	
25-71	20 (18.9)	28 (21.2)	
≥ 72	17 (16.0)	53 (40.2)	
Weight (Kg) [b]	9.6 (8.0-16.0)	15.3 (8.8-28.0)	0.001
< 5	6 (5.7)	14 (10.6)	
5-9.99	52 (49.1)	26 (19.7)	
10-19.99	29 (27.4)	38 (28.8)	
20-39.99	13 (12.3)	35 (26.5)	
≥ 40	6 (5.7)	19 (14.4)	
General anesthetic			< 0.001
No	3 (2.8)	90 (68.2)	
Yes	103 (97.2)	42 (31.8)	
Local anesthetic			0.002
No	59 (55.7)	47 (35.6)	
Yes	47 (44.3)	85 (64.4)	
Needles (G)			0.329
26	1 (1.3)	2 (1.5)	
24	61 (51.3)	61 (46.2)	
22	36 (39.9)	59 (44.7)	
20	8 (7.6)	10 (7.6)	
AV300			0.469
Not used	58 (54.7)	66 (50.0)	

Characteristics	No changes of pain Count (% within groups), median(IQR), n=106	Increase of pain Count (% within groups), median(IQR), n=132	P
Used	48 (45.3)	66 (50.0)	
Midazolam (mg/kg)	0.9 (0.6-1.5)	0.6 (0.3-1.2)	0.484
Not administered	34 (32.1)	45 (34.1)	
Administered [c]	72 (67.9)	87 (65.9)	
Duration (min)	41.0 (30.3-60.3)	45.0 (35.0-55.0)	0.144
Number of attempts			0.633
1	61 (57.5)	80 (60.6)	
2	20 (18.9)	21 (15.9)	
3	8 (7.5)	16 (12.1)	
4	11 (10.4)	8 (6.1)	
5	3 (2.8)	3 (2.3)	
6	3 (2.8)	4 (3.0)	
Time taken (min) [d]	1.0 (0.9-4.0)	1.0 (0.5-3.0)	0.753
≤ 0.5	26 (24.5)	33 (25.0)	
0.5-1	32 (30.2)	38 (28.8)	
1-3	20 (18.9)	34 (25.8)	
≥ 3	28 (26.4)	27 (20.5)	

Data are expressed as median (IQR), except for categorical data as count (percentage). [a] P<0.001 in subgroups by age, [b] P<0.001 in subgroups by weight, [c] P=0.743 in subgroups by midazolam, [d] P=0.536 in subgroups by duration of vein cannulation. G, Gauge. IQR, interquartile range

3.1.5.3 Factors for pain changes

Through binary logistic regression, general anesthetic (OR = 0.007, 95%CI: 0.002 - 0.026), gender (OR = 0.360, 95%CI: 0.167 - 0.777) and first-attempt success (OR = 0.336, 95%CI: 0.156 - 0.724) were included in the final model and acted as protective factors against the pain increment measured by BPS (**Table 5**).

Table 5. Variables in the final model

model	B	Std. Error.	Wald	df	P	Exp(B)	95% CI for EXP(B)	
							Lower	Upper
Gender	-1.021	0.392	6.769	1	0.009	0.360	0.167	0.777
General anesthetic	-4.964	0.673	54.368	1	0.000	0.007	0.002	0.026
First-attempt success	-1.090	0.391	7.767	1	0.005	0.336	0.156	0.724
Constant	4.924	0.747	43.435	1	0.000	137.598		

Gender (male versus female), general anesthetic (administered or not) and first-attempt success (yes or no) are included in the final binary logistic regression model

3.1.5.4 Factors related to first-attempt success rate

3.1.5.4.1 Binary regression

General anesthetic (OR = 0.417, 95%CI: 0.216 - 0.803), AV300 (OR = 0.36, 95%CI: 0.167 - 0.777), weight (OR = 1.819, 95%CI: 1.352 - 2.446) and midazolam as premedication (OR = 2.113, 95%CI: 1.118 - 3.994) were included. Weight and midazolam contributed to improve the first-attempt success rate (**Table 6**).

Table 6. Variables in the final model

Model	B	Std. Error	Wald	df	P	Exp(B)	95% CI for EXP(B)	
							Lower	Upper
AV300	-1.343	0.311	18.617	1	0.000	0.261	0.142	0.480
General anesthetic	-0.875	0.334	6.853	1	0.009	0.417	0.216	0.803
Weight	0.598	0.151	15.659	1	0.000	1.819	1.352	2.446
Midazolam	0.748	0.325	5.305	1	0.021	2.113	1.118	3.994
Constant	-0.558	0.566	0.970	1	0.325	0.573		

AV300 (used or not), general anesthetic (administered or not), weight (< 5kg, 5 to < 10kg, 10 to < 20kg, 20 to < 40kg, ≥ 40kg) and midazolam (pre-medicated or not) are included in the final binary logistic regression model

3.1.5.4.2 Linear correlation between weight and age

An evident linear correlation ($r = 0.898$, $P < 0.001$) was found between weight and age in all patients involved in the study.

3.2 FPS-R and BPS applied in the corresponding pediatric patients

3.2.1 Basic characteristics and demographic data

A total of 89 patients aged 4 to 16 years were considered for the further analyses, with a median age of 96 (IQR = 72 - 134) months and a median weight of 22.7 (IQR = 20 - 40) kg, 44.9% were female, 52.8% received topical anesthetic management before coming to operating-rooms, 39.3% were considered to require inhaled general anesthetic before IV insertion, 48.3% were cannulated with the help of AV300, 69.7% took oral midazolam as premedication with a median dose of 0.3 (IQR = 0.2 - 0.5) mg/kg and a median duration of 43 (IQR = 34 - 55) min before IV access. The first-attempt success rate was 74.2% and the median time taken until a successful cannulation was 1 (IQR = 0.2 - 2.0) min (**Table 1**).

3.2.2 Comparison of pain intensity at different time points of IV cannulation

Through paired t-test, pain scores by BPS were higher at the end (mean ± SD, 3.97 ± 1.496) of IV insertion compared with those at the beginning (mean ± SD, 2.53 ± 0.854) (t = 11.925, $P < 0.001$) (**Figure 4**). And a similar situation also occurred as the acute needle pain evaluated by FPS-R (observation) (mean ± SD, 2.75 ± 2.030 versus 1.19 ± 1.176) (t =10.481, $P < 0.001$) (**Figure 5**).

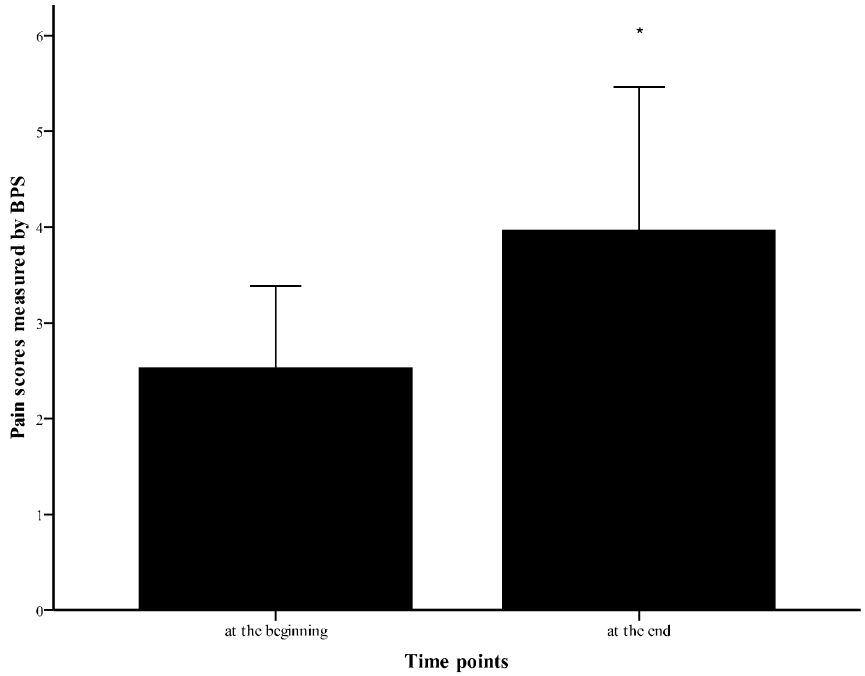

Figure 4. Bars and comparison of pain scores measured by Behavioral Pain Scale (BPS) during the peripheral vein cannulation in patients 4 to16 years of age. * indicates a significant difference of pain level between the points. Error bars: +/- 1 SD

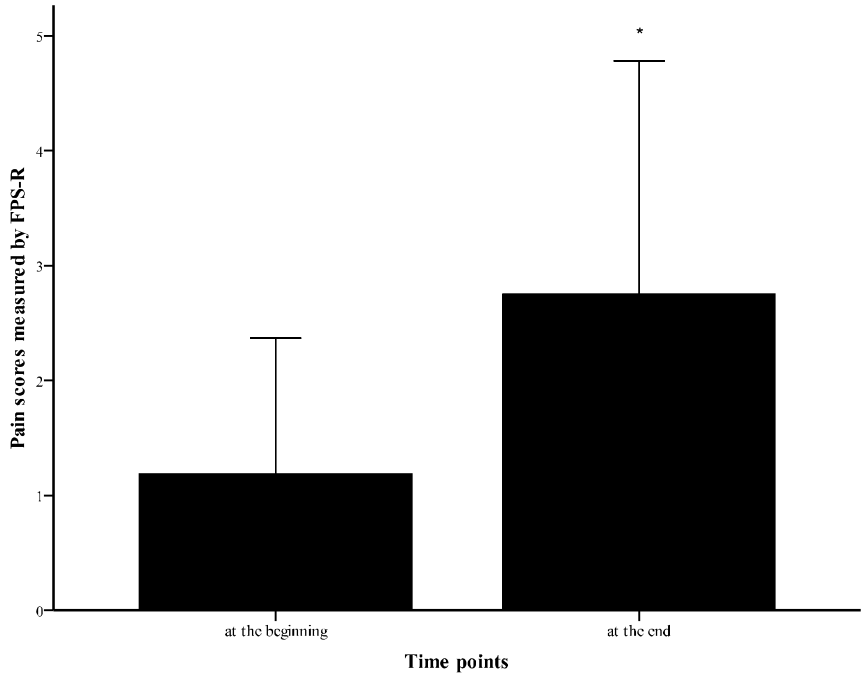

Figure 5. Bars and comparison of pain scores measured by Faces Pain Scale-Revised (FPS-R) during the peripheral vein cannulation in patients 4 to 16 years of age. * indicates a significant difference of pain level between the points. Error bars: +/- 1 SD

3.2.3 Linear correlation of pain scores in peripheral IV cannulation

As to the children aged 4 to16 years, for either of the pain scales, there is a linear correlation between the mean levels of pain at the two time points during the peripheral vein cannulation (BPS, r = 0.655, P < 0.001, and FPS-R, r = 0.739, P < 0.001), respectively (**Figures 6 and 7**). Also, BPS scores correlated with pain intensity measured by FPS-R at the beginning (r = 0.351, P = 0.001) (**Figure 8**) and at the end (r = 0.750, P < 0.001) of peripheral vein cannulations (**Figure 9**).

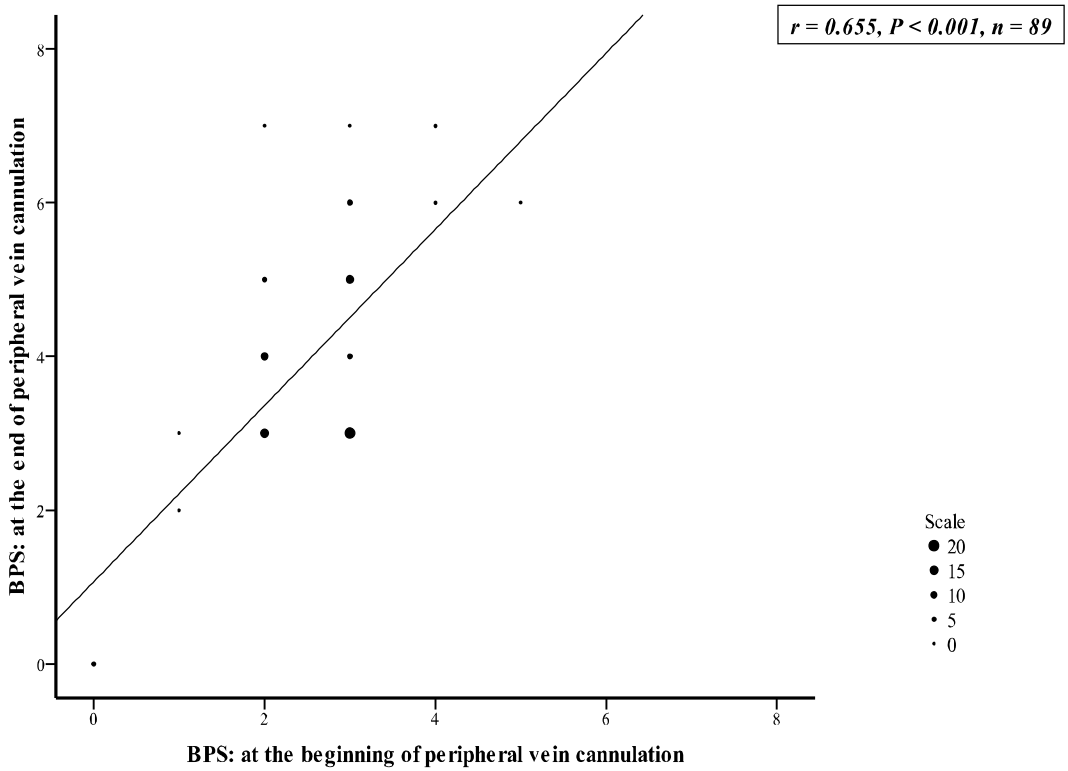

Figure 6. Scatter plots and correlations of Behavioral Pain Scale (BPS) scores at the beginning and at the end of peripheral vein cannulation in patients aged 4 to 16 years. The bigger a marker is, the more patients are in a certain rank of the scale

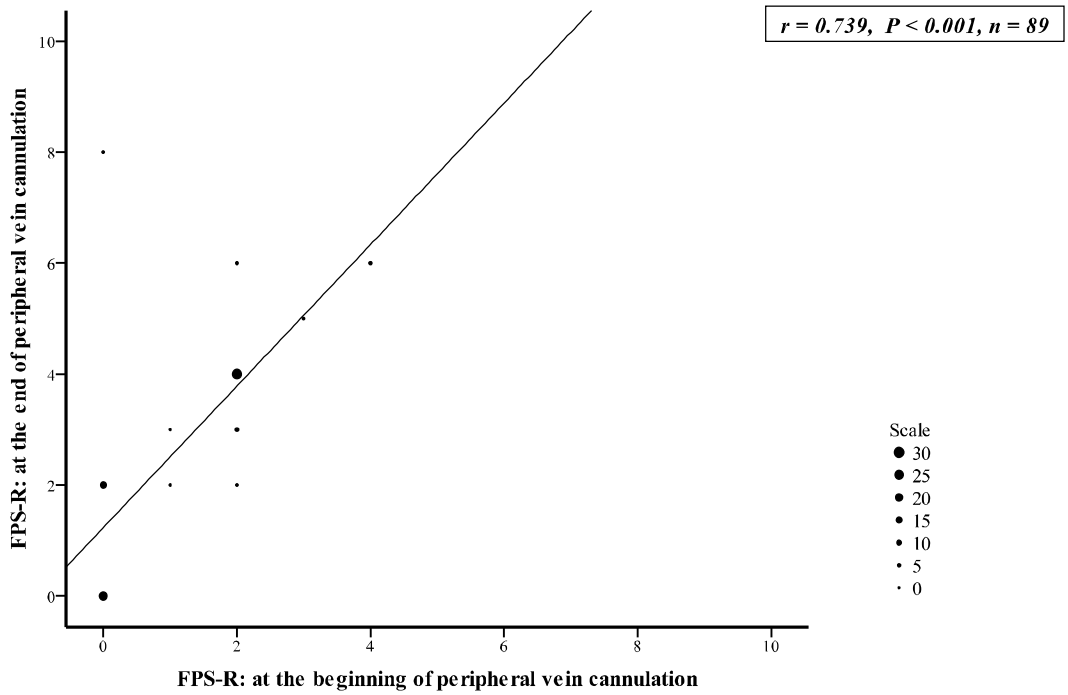

Figure 7. Scatter plots and correlations of Faces Pain Scale-Revised (FPS-R) scores at the beginning and at the end of vein cannulation in patients 4 to 16 years of age. The bigger a marker is, the more patients are in a certain rank of the scale

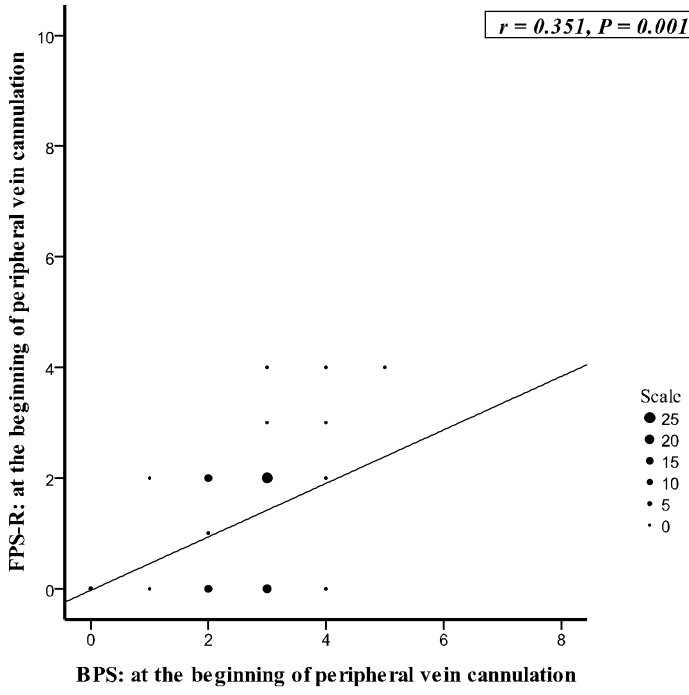

Figure 8. Scatter plots and correlations of Faces Pain Scale-Revised (FPS-R) scores and Behavioral Pain Scale (BPS) scores at the beginning of peripheral vein cannulation in patients aged 4 to 16 years. The bigger a marker is, the more patients are in a certain rank of the scale

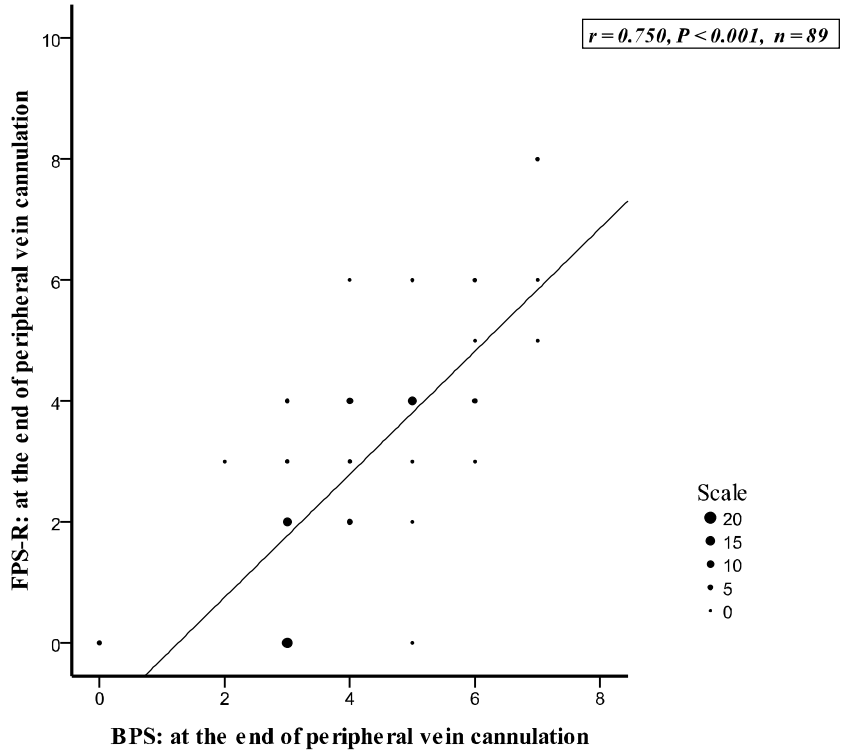

Figure 9. Scatter plots and correlations of Faces Pain Scale-Revised (FPS-R) scores and Behavioral Pain Scale (BPS) scores at the end of peripheral vein cannulation in patients aged 4 to 16 years. The blacker a marker is, the more patients are in a certain rank of the scale

3.2.4 Risk factors for pain levels at different points of IV cannulation

For the pain intensity at the beginning of IV cannulation BPS0 (Y), size of sterile catheter (X_1), general anesthetic (received or not, X_2) and AV300 (used or not, X_3) were included in the equation through multiple linear regressions (**Tables 7**).

$$Y = -3.801 + 0.287X_1 + 0.518X_2 - 0.343X_3, \quad R^2 = 0.213, \quad P < 0.001$$

Table 7. Risk factors for BPS0

Model	Unstandardized Coefficients		Standardized Coefficients	t	P	95.0% Confidence Interval for B	
	B	Std. Error	Beta			Lower Bound	Upper Bound
(Constant)	-3.801	1.621		-2.345	0.021	-7.024	-0.578
Size of sterile catheter	0.287	0.073	0.385	3.911	0.000	0.141	0.433
General anesthetic	0.518	0.172	0.298	3.018	0.003	0.177	0.859
AV300	-0.343	0.165	-0.202	-2.081	0.040	-0.671	-0.015

Size of catheter, general anesthetic (administered or not) and AV300 (used or not) are included in the multiple linear regression model.

For the pain rating at the end of vein cannulation BPS1(Y), size of catheter (X_1) and gender (X_2) were included in the model (**Tables 8**).

$Y = -8.555 + 0.583X_1 - 0.600X_2$, *$R^2 = 0.230$,* *$P < 0.001$*

Table 8. Risk factors related to BPS1

Model	Unstandardized Coefficients		Standardized Coefficients	t	P	95.0% Confidence Interval for B	
	B	Std. Error	Beta			Lower Bound	Upper Bound
(Constant)	-8.555	2.712		-3.155	0.002	-13.946	-3.165
Size of sterile catheter	0.583	0.124	0.447	4.717	0.000	0.337	0.829
Gender	-0.600	0.283	-0.201	-2.120	0.037	-1.164	-0.037

Size of sterile catheter and gender (male versus female) are included in the multiple linear regression model

For the pain score at the beginning of cannulations FPS-R0 (Y), general anesthetic (X_1) and number of attempts (X_2) were included in the equation (**Tables 9**).

$Y = -0.924 - 0.718X_1 + 0.385X_2$, *$R^2 = 0.159$,* *$P = 0.001$*

Table 9. Factors related to FPS-R0

Model	Unstandardized Coefficients		Standardized Coefficients	t	P	95.0% Confidence Interval for B	
	B	Std. Error	Beta			Lower Bound	Upper Bound
(Constant)	0.924	0.230		4.023	0.000	0.467	1.380
General anesthetic	-0.718	0.238	-0.300	-3.016	0.003	-1.191	-0.245
Number of attempts	0.385	0.129	0.296	2.975	0.004	0.128	0.643

General anesthetic (administered or not) and number of attempts are included in the multiple linear regression model

For the pain score at the end of cannulations FPS-R1 (Y), general anesthetic (X_1) and number of attempts (X_2) were included in the equation (**Tables 10**).

$$\boldsymbol{Y = 2.832 - 1.994X_1 + 0.494X_2,} \qquad R^2 = 0.259, \qquad P < 0.001$$

Table 10. Risk factors related to FPS-R1

Model	**Unstandardized Coefficients**		**Standardized Coefficients**	**t**	**P**	**95.0% Confidence Interval for B**	
	B	**Std. Error**	**Beta**			**Lower Bound**	**Upper Bound**
(Constant)	2.832	0.372		7.617	0.000	2.093	3.571
General anesthetic	-1.994	0.386	-0.483	-5.173	0.000	-2.761	-1.228
Number of attempts	0.494	0.210	0.220	2.357	0.021	0.077	0.911

General anesthetic (administered or not) and number of attempts are included in the multiple linear regression model

3.2.5 Changes of pain level at different points in 4 to 16-year-old children

3.2.5.1 Proportion of pain changes

A comparison of pain scores at the two time points of IV insertion for each patient manifested no changes or increase of pain. Results from one-sample χ^2-test indicated that more patients in this subgroup experienced more pain (by BPS, 66 out of 89 for the more pain *versus* 23 out of 89 for the no changes, $P < 0.001$, and by FPS-R, 64 out of 89 for the more pain *versus* 25 out of 89 for the no changes, $P < 0.001$, respectively) (**Figures 10 and 11**).

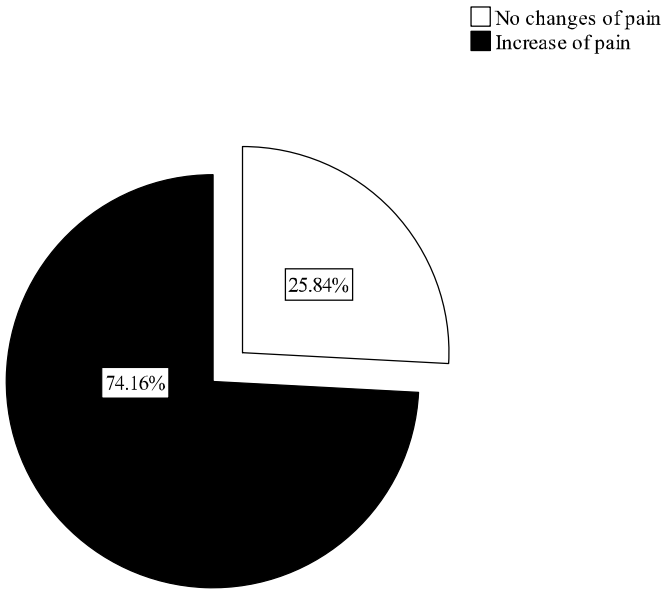

Figure 10. Pie plots and the proportion of pain level changes measured by Behavioral Pain Scales (BPS) in patients aged 4 to 16 years. The black part indicates the ratio of patients feeling more pain at the end of intravenous insertions compared with the beginning. And the white part shows no changes of pain intensity

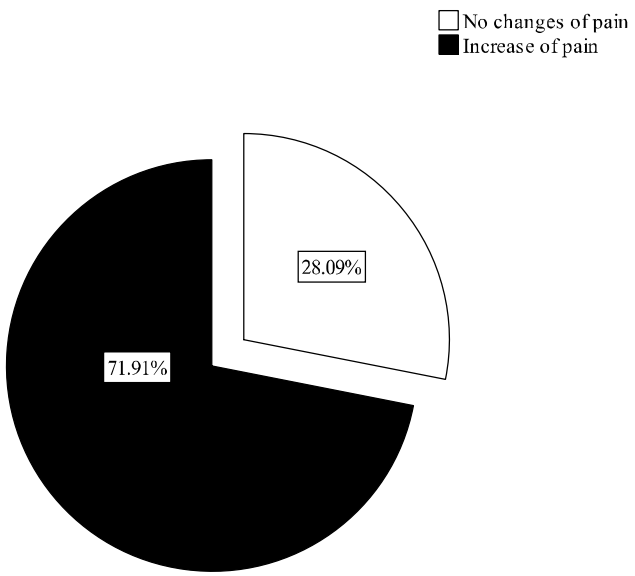

Figure 11. Pie plots and the proportion of pain intensity changes measured by Faces Pain Scales-Revised (FPS-R) in patients aged 4 to 16 years. The black part indicates the ratio of patients feeling more pain at the end of intravenous insertions compared with the beginning. And the white part shows no changes of pain intensity

3.2.5.2 Basic characteristics and demographic data

Compared with those who felt no changes of pain intensity at the end of cannulations, a total of 66 patients still showed more pain measured by BPS and fewer of them received general anesthetics, 21.2% *versus* 91.3% ($P < 0.001$), during IV cannulations. Similar situations emerged using FPS-R. More details and other information are presented in the following tables (**Tables 11 and 12)**.

Table 11. Demographic data and basic characteristics of patients aged from 4 to 16 years with different pain level (BPS) changes during peripheral vein cannulation

Characteristics	No changes of pain Count (% within groups), median(IQR), n=23	Increase of pain Count (% within groups), median(IQR), n=66	P
Gender			0.195
Male	10 (43.5)	39 (59.1)	
Female	13 (56.5)	27 (40.9)	
Age (months) [a]	96 (67-126)	91 (72.8-135)	0.936
0-3	0 (0.0)	0 (0.0)	
4-12	0 (0.0)	0 (0.0)	
13-24	0 (0.0)	0 (0.0)	
25-71	6 (26.1)	14 (21.2)	
≥72	17 (73.9)	52 (78.8)	
Weight (Kg) [b]	27 (19.6-42.0)	28(20.0-40.0)	0.757
< 5	0 (0.0)	0 (0.0)	
5-9.99	1 (4.3)	0 (0.0)	
10-19.99	5 (21.7)	15 (22.7)	
20-39.99	11 (47.8)	33 (50.0)	
≥ 40	6 (26.1)	18 (27.3)	
General anesthetic			< 0.001
No	2 (8.7)	52 (78.8)	
Yes	21 (91.3)	14 (21.2)	
Local anesthetic			0.127
No	14 (60.9)	28 (42.4)	
Yes	9 (39.1)	38 (57.6)	
Needles (G)			0.179
26	0 (0.0)	0 (0.0)	
24	2 (8.7)	11 (16.7)	
22	14 (60.9)	46 (69.7)	
20	7 (30.4)	9 (13.6)	
AV300			0.667
Not used	11 (47.8)	35 (53.0)	

Characteristics	No changes of pain Count (% within groups), median(IQR), n=23	Increase of pain Count (% within groups), median(IQR), n=66	P
Used	12 (52.2)	31 (47.0)	
Midazolam (mg/kg)	0.36 (0.19-0.59)	0.31 (0.21-0.51)	0.309
Not administered	7 (30.4)	20 (30.3)	
Administered [c]	16 (69.6)	46 (69.7)	
Duration (min)	42.0 (32.5-55.0)	43.0 (34.0-55.0)	0.832
Number of attempts			0.102
1	19 (82.6)	47 (71.2)	
2	2 (8.7)	12 (18.2)	
3	0 (0.0)	6 (9.1)	
4	1 (4.3)	0 (0.0)	
5	0 (0.0)	1 (1.5)	
6	1 (4.3)	0 (0.0)	
Time taken (min) [d]	1.0 (0.2-1.0)	1.0 (0.2-2.0)	0.450
≤0.5	11 (47.8)	25 (37.9)	
0.5-1	7 (30.4)	20 (30.3)	
1-3	3 (13.0)	15 (22.7)	
≥3	2 (8.7)	6 (9.1)	

Data are expressed as Median (IQR), except for categorical data as number (percentage). [a] P=0.630 in subgroups by age, [b] P=0.506 in subgroups by weight, [c] P=0.991 in subgroups by midazolam, [d] P=0.769 in subgroups by duration of vein cannulation. G, gauge. IQR, interquartile range

Table 12. Demographic data and basic characteristics of patients aged from 4 to 16 years with different pain level (FPS-R) changes during peripheral vein cannulation

Characteristics	No changes of pain Count (% within groups), median(IQR), n=25	Increase of pain Count (% within groups), median(IQR), n=64	P
Gender			0.190
Male	11 (44.0)	38 (59.4)	
Female	14 (56.0)	26 (40.6)	
Age (months) [a]	96 (68.5-124.5)	91 (72.3-137)	0.982
0-3	0 (0.0)	0 (0.0)	
4-12	0 (0.0)	0 (0.0)	
13-24	0 (0.0)	0 (0.0)	
25-71	6 (24.0)	14 (21.9)	
≥ 72	19 (76.0)	50 (78.1)	
Weight (Kg) [b]	27 (19.8-41.0)	28 (20.0-40.0)	0.931
< 5	0 (0.0)	0 (0.0)	
5-9.99	1 (4.0)	0 (0.0)	
10-19.99	5 (20.0)	15 (23.4)	
20-39.99	13 (52.0)	31 (48.4)	
≥ 40	6 (24.0)	18 (28.1)	
General anesthetic			< 0.001
No	2 (8.0)	52 (81.3)	
Yes	23 (92.0)	12 (18.8)	
Local anesthetic			0.130
No	15 (60.0)	27 (42.2)	
Yes	10 (40.0)	37 (57.8)	
Needles (G)			0.224
26	0 (0.0)	0 (0.0)	
24	2 (8.0)	11 (17.2)	
22	16 (64.0)	44 (68.8)	
20	7 (28.0)	9 (14.1)	
AV300			0.664
Not used	12 (48.0)	34 (53.1)	

Characteristics	No changes of pain Count (% within groups), median(IQR), n=25	Increase of pain Count (% within groups), median(IQR), n=64	P
Used	13 (52.0)	30 (46.9)	
Midazolam (mg/kg)	0.4 (0.2-0.6)	0.3 (0.2-0.5)	0.272
Not administered	7 (28.0)	20 (31.3)	
Administered [c]	18 (72.0)	44 (68.8)	
Duration (min)	42.0 (32.3-57.0)	43.0 (34.0-55.0)	0.897
Number of attempts			0.065
1	21 (84.0)	45 (70.3)	
2	2 (8.0)	12 (18.8)	
3	0 (0.0)	6 (9.4)	
4	1 (4.0)	0 (0.0)	
5	0 (0.0)	1 (1.6)	
6	1 (4.0)	0 (0.0)	
Time taken (min) [d]	1.0 (0.2-1.0)	1.0 (0.2-2.0)	0.374
≤ 0.5	12 (48.0)	24 (37.5)	
0.5-1	8 (32.0)	19 (29.7)	
1-3	3 (12.0)	15 (23.4)	
≥ 3	2 (8.0)	6 (9.4)	

Data are expressed as Median (IQR), except for categorical data as number (percentage). [a] P=0.829 in subgroups by age, [b] P=0.521 in subgroups by weight, [c] P=0.764 in subgroups by midazolam, [d] P=0.653 in subgroups by duration of vein cannulation. G, gauge. IQR, interquartile range

3.2.5.3 Binary logistic regression

Through binary logistic regression, gender (OR = 0.126, 95%CI, 0.023 - 0.704 for BPS, and OR = 0.058, 95%CI, 0.006 - 0.584 for FPS-R), general anesthetic (OR = 0.009, 95%CI, 0.001- 0.070 for BPS, and OR = 0.003, 95%CI, 0.000 - 0.044 for FPS-R) and first-attempt success (OR = 0.159, 95%CI, 0.026-0.966 for BPS, and OR = 0.068, 95%CI, 0.007- 0.666 for FPS-R) were involved in the model and acted as protective factors from the pain increment (**Tables 13 and 14**).

Table 13. Variables in the final model (BPS)

Model	B	Std. Error	Wald	df	P	Exp(B)	95% CI for EXP(B)	
							Lower	Upper
Gender	-2.072	0.878	5.570	1	0.018	0.126	0.023	0.704
General anesthetic	-4.701	1.040	20.436	1	0.000	0.009	0.001	0.070
First-attempt success	-1.839	0.921	3.990	1	0.046	0.159	0.026	0.966
Constant	6.311	1.562	16.327	1	0.000	550.433		

Gender (male versus female), general anesthetic (administered or not) and first-attempt success (yes or no) are included in the binary logistic regression model

Table 14. Variables in the final model (FPS-R)

Model	B	Std. Error	Wald	df	P	Exp(B)	95% CI for EXP(B)	
							Lower	Upper
Gender	-2.845	1.177	5.839	1	0.016	0.058	0.006	0.584
General anesthetic	-5.736	1.331	18.582	1	0.000	0.003	0.000	0.044
First-attempt success	-2.685	1.162	5.336	1	0.021	0.068	0.007	0.666
Constant	7.823	2.132	13.467	1	0.000	2496.715		

Gender (male *versus* female), general anesthetic (administered or not) and first-attempt success (yes or no) are included in the binary logistic regression model

3.2.6 Factors for first-attempt success in 4 to 16-year-old children

3.2.6.1 Binary logistic regression

Through binary logistic regression, AV300 (OR = 0.228, 95%CI, 0.077- 0.680) and weight (OR = 2.399, 95%CI, 1.125 - 5.117) were included in the model and the latter acted as a positive factor to promote the first-attempt success rate (**Table 15**).

Table 15. Variables in the final model

Model	B	Std. Error	Wald	df	P	Exp(B)	95% CI for EXP(B)	
							Lower	Upper
AV300	-1.477	0.557	7.034	1	0.008	0.228	0.077	0.680
Weight	0.875	0.386	5.128	1	0.024	2.399	1.125	5.117
Constant	-1.524	1.514	1.014	1	0.314	0.218		

AV300 (used or not) and weight (< 5kg, 5 to < 10 kg, 10 to < 20 kg, 20 to < 40 kg, ≥ 40 kg) are included in the final binary logistic regression model

3.2.6.2 Linear correlation between weight and age

An evident linear correlation ($r = 0.767$, $P < 0.001$) was revealed between weight and age in pediatric patients aged 4 to 16 years.

4 Discussion

The findings of the study mainly consist of two parts, that is, for the whole population and for the 4 to16-year children. For the former, we found that (1) pain scores measured by BPS usually increased significantly at the end of the cannulations compared with those at the beginning, but evidently correlated with each other; (2) for the initial pain during the punctures, the older children and those assisted by the vein viewing system AV300 demonstrated less pain. But for pain at the end of the IV cannulation, general anesthetic was the sole protective factor from pain increment during the observation. Bigger IV catheters and more attempts were the major risk factors causing more pain; (3) however, more than half of all patients showed pain increase from the beginning to the end of IV cannulations; (4) female patients, administration of general anesthetic and high first-attempt success rate might contribute to pain relief; (5) moreover, high first-attempt success rate would be achieved in those who received oral midazolam as premedication and those who were heavier in weight with normal development corresponding to age. For those aged 4 to 16 years, similar findings are that (1) more pain at the end of IV catheterization was found with both BPS and FPS-R. There was a correlation between pain scores from either of the tools (BPS and FPS-R) at the both time points, and also BPS scores correlated with FPS-R scores at corresponding time points; (2) for BPS, AV300 seemed to be helpful to reduce pain indirectly at the beginning of IV cannulation, and the female patients often demonstrated less pain at end of the cannulations. For FPS-R, general anesthetic was the only protective factor from pain increasing, but low first-attempt success rate was always the major risk factor causing more pain; (3) both BPS and FRS-R scores showed more than two thirds of the patients felt pain increase over the entire process of IV access; (4) similar to the whole population, female patients, administration of general anesthetic and high first-attempt success rate in the 4 to 16-year-old patients protected from more pain during peripheral IV insertions; (5) AV300 did not seem to be helpful in improving the first-attempt success rate in the subgroup.

4.1 Midazolam and pain

Anxiety, fear and pain will always spread all over the mind of pediatric patients during any venous access.[1, 40, 41] What's more serious is needle phobia, a troublesome physiological dysfunction, would happen to some children and affect their health even for the rest of their lives.[15, 16] Oral premedication with a median dose of 0.8mg/kg midazolam in this study promoted a high first-attempt success rate. Preoperative 0.5mg/kg or even low-dose (0.25 mg/kg) midazolam orally administered was identified to be effective to reduce the prevalence of distress and fear in children undergoing peripheral venous access procedures.[22, 42-44] Although some publications reported it would delay the early recovery in children from sevoflurane anesthesia,[45, 46] oral midazolam is thought to be the best and easiest accepted way of premedication in pediatric patients.[47] Thus it might be the reduction of distress and fear by oral midazolam as premedication that contributed to a high rate of successful first-attempt cannulation which played a key role in inhibiting the level and the increase of peripheral venous cannulation pain in newborns, infants, children and adolescents in our study.

4.2 Anesthetics and IV cannulation pain

Sevoflurane or N_2O administered in this trial was effective for pain relief during IV insertions in pediatric patients. As for those who did not cooperate well with the IV insertion operators, we had to turn to inhaled anesthetics, such as sevoflurane or N_2O, both of which are widely employed in pediatric clinical anesthesia practices. With the advantages in less influences on circulation and respiratory systems, sevoflurane, an inhaled methyl ethyl ether halogenated solely with fluorine, serves as a good alternative for anesthesia induction in pediatric patients.[48-50] N_2O has been applied and proved to be effective in reduction of anxiety and pain, and facilitation of peripheral venous cannulations.[18, 51-55]

EMLA, an eutectic mixture of lidocaine and prilocaine, together with other products of topical anesthetics,[41, 56-60] is widely used to minimize the acute pain from medical procedures, such as IV insertion. It was reported that this eutectic mixture was effective to reduce discomfort and pain in venipuncture and IV insertion.[17, 56, 61-65] However, it could not be demonstrated in our study that EMLA could prevent from IV cannulation pain effectively. Lander[66] argued in her publication that EMLA was more effective for pain relief in venipuncture than vein cannulation. Though this anesthetic could offer

good superficial analgesia, moderate effectiveness on the deeper tissues took responsible for worse pain as the catheter moving subcutaneously.[30] However, investigators that reported the combination of N_2O and EMLA in IV cannulation was efficient for pain relief and facilitated sterile peripheral IV access.[54] Perhaps providing pain relief in this manner may bring much comfort for pediatric patients.

4.3 Vein viewing system and needle pain

We found in this trial, the efficacy of AV300 in peripheral IV access consisted of an evident conflict. The use of this device could lead to less pain indirectly at the beginning of the cannulation. But it played a negative part in terms of first-attempt success rate, resulting in more attempts and greater pain increase during the process of peripheral venous cannulation. So it may be helpful in pain relief during venipunctures, but no benefit of the imaging system was demonstrated in peripheral vein cannulations in our study. According to the findings, in order to relieve pain, maybe we could locate and puncture the target subcutaneous vein with the aid of this device, then finish the rest of the cannulation using traditional techniques.

A study with a randomized-controlled design on another non-contact vein viewing system reported a good visibility of peripheral veins, higher success rates at the initial attempt and less time taken until successful peripheral venous cannulation with the help of the device equipped with a light-emitting diode.[27] Vein Viewer (Luminetx Corporation, Memphis, Tenn), a product designed on the basis of NIR, presented prominent value in facilitating venipuncture and IV catheterization.[29, 67, 68] Using Vein Viewer, a clinical of a small sample without a control group reported 38 venipunctures and 12 cannulations in children whose mean age was 6.67 years, and found that on average it took 1.7 attempts per child, and the visibility of the peripheral veins was improved in 76% of children.[67] But consistent with our data, another investigator reported in a recent publication that no improvement was shown in the first-attempt success rate during the pediatric IV cannulation with the aid of Vein Viewer in a randomized controlled trial.[69] AV300 in our study did not improve the first-attempt success rate and indirectly resulted in increase of pain in peripheral vein cannulation. Errors in size and position between the vein shadow and the vein itself may contribute to the negative outcomes. In some cases, it was really difficult to get a perfect IV insertion due to the enlarged vein images

from AV300, meanwhile, the system's failure to detect the target vein depth was thought to be an obvious disadvantage of the system. So only a perfect two dimension visibility seems to be not enough for successful vein cannulation, the experience in tactile location and judgment of the reasonable puncture site is also essential. In addition, the target site chosen for IV insertion was just exposed in the NIR beam and punctured directly. This often led to deformation of the vessel image due to the needle pressing. To avoid the deformation of the vein image would offer one of the solutions to improve the first-attempt success rate as using the NIR devices.[67] It was reported that a new product based on NIR transillumination, NIR vascular imaging, was equipped with a liquid crystal display monitor allowing a normal vision of the target vein for the operator.[70] And in this way, the device can minimize the influence on the blood vessel image tortuosity.[67, 70] Maybe it is a wise choice to utilize AV300 to locate subcutaneous veins in dark-skinned children, and inexperienced residents or nurses would benefit from training in peripheral venipuncture with its assistance.

4.4 Gender difference and needle pain

Our data showed that male pediatric patients tend to show more pain compared with female ones. A lot of studies demonstrated high ratings of self-reported pain were often associated with females.[20, 32, 34] But assessment of gender differences by Fowler-Kerry and Lander in pediatric patients undergoing needle procedures showed that males tended to underestimate pain and females were inclined to overestimate pain.[71] So the female children often behaved more stilly as they felt actually less pain than they had anticipated. That's why observational pain ratings were high in males and low in females during the actual practice of IV catheterization.

4.5 Age, weight and needle pain

We found age and weight served as important protective roles in IV cannulation pain. IV insertion in the case of older and heavier pediatric patients was easier and less painful. In our study, weight correlated well with age, and as indicated previously most patients involved in our study were in a normal state of development. Many studies indicated younger children would report more pain than older ones.[34, 72] But Cummings and her

colleagues[1] argued that there was no correlation between pain intensity and age. Further randomised studies need to be done in order to clarify the issue.

4.6 Other factors and IV cannulation pain

As predicted, the size of sterile angiocatheter and number of attempts until successful IV line placement were both risk factors in venous cannulation pain. Patients would feel more intensive pain if the catheterization was done with a bigger needle and/ or if more attempts had to be made than if a smaller need was used and/ or the IV access was finished at the first attempt. However, time consumption showed no evident influence on changes of pain rating by either scale applied in our study.

4.7 BPS and FPS-R

Our findings indicate the reliability and validity of BPS and FPS-R as measures of pain during peripheral IV cannulation in pediatric patients pre-operation. However, our study identified in 4 to 16-year-old children, FPS-R for observational rating correlated well with BPS scores. The two scales could complement each other well in the practice of acute pain assessments in pediatric patients.

4.8 Limitations

Several limitations should be noted in our study. Firstly, with such a sample size, it is not powerful to detect the prevalence of acute pain during peripheral venous access in the subgroups divided by age, weight, and other possible parameters. Secondly, FPS-R was employed in observational pain rating as a complement to the 'facial expression' of BPS, instead of self-report rating by the pediatric patients. To our knowledge, the method was validated previously.[73] Rather than in all patients, only in the 4 to 16-year-old children and adolescents was the pain scale applied because of lack of reports from previous studies in even younger subgroups. Thirdly, patients' extent of anxiety which always accompanies with needle pain in children was not recorded in our study. Further studies with a random-controlled design and more elements related to acute IV cannulation pain should be conducted.

5 Conclusions and perspectives

Our data support (1) age, weight, gender, general anesthetic, size of sterile IV catheter, number of attempts, vein viewing system(AV300) are associated with the acute peripheral IV cannulation pain, (2) oral midazolam as premedication and inhaled general anesthetics administered before peripheral IV access contribute to pain relief during the IV insertion, (3) acute venous cannulation pain in the younger and/ or male pediatric patients should be paid more attention to, (4) FPS-R for observational rating can serve as a good tool in the evaluation of pain intensity during peripheral IV cannulation as a complementary part for BPS in 4 to16-year patients.

In addition, the efficacy of AV300 in peripheral IV insertions remains unclear at least in this study. Further studies on peripheral IV insertion with a randomized-controlled design, many more other methods of testing, and a larger population of patients in subgroups need to be conducted to clarify the benefit and utility of these devices based on NIR. What's more, much more endeavours should be made to improve the first-attempt success rate to reduce pain during peripheral vein cannulation.

Premedication with oral midazolam should be advocated in pediatric patients, and IV insertion should be skillfully carried out with a suitable size of sterile catheter after administering general anesthetic by inhalation, especially in younger and/ or male pediatric patients.

6 Summary

Background

IV cannulation pain is common and frequently occurs in pediatric patients during the hospitalization. However, it is one of the main causes for high level of anxiety and fear in children facing needle based procedures, which persists even as the patients reach adulthood. Also, such a repeated, long-term and lasting nociception or adverse stimulus poorly controlled or without management would have a negative influence on the development of the patient's psyche, nervous system, pain sensitivity and emotionality. Though many endeavours have been made to manage needle pain, there are many children who have suffered or are suffering from the painful and distressful experience, especially in a pre-operation setting. So there is still a lot for us to do for pain relief and it is imperative to find out what actually leads to changes of pain in needle-based procedures in pediatric patients.

Objectives

To investigate the factors for peripheral IV cannulation pain controlled or avoided by anesthesiologists and nurses in pediatric patients in operating-rooms.

Methods

This study was carried out pre-operation in pediatric patients all of whom were from 0 to17 years old and in whom IV cannulation would be required for subsequent anesthesia induction or medication before elective surgery but the IV insertion was planned to be done in operating-rooms, Campus Virchow-Klinikum, Charité-Universitätsmedizin Berlin.

Demographic and clinical data were collected, including gender, age, weight, premedication (oral midazolam) or not, received local anesthetic (EMLA) or not, whether general anesthetic (N_2O or sevoflurane) are necessary for IV cannulation, size of needles, the duration and number of attempts until successful IV cannulation, and pain sores evaluated by BPS and FPS-R (observation by the investigator, no self-report by the patients).

Data were analyzed by SPSS for Windows version 18(SPSS Inc, Chicago, IL). Mean ± standard deviation (SD) was used in the description of pain scores from the two scales mentioned above. Paired t-test, bivariate Pearson's correlation, multiple linear

regression, and binary logistic regression were employed for the specific analyses. Demographic data and clinical characteristics were calculated and expressed as median (interquartile range, IQR), except for categorical data as count (proportion). Frequencies were tested by χ^2-test. Mann-Whitney U-test was applied to evaluate the differences of basic characteristics between the related changes of pain intensity (increased or not) in the process of peripheral IV cannulation. *P*-values < 0.05 with two-tailed test of significance were considered statistically significant.

Results

A total of 238 pediatric patients were finally evaluated, with a median age of 24 (IQR = 8 - 76) months, a median weight of 9.5 (IQR = 7.6 - 14.2) kg, 45% were female, 55.5% received local anesthetic, EMLA, before their coming to the operating-rooms, 60.9% were thought to require inhaled general anesthetic (N_2O or sevoflurane) before IV insertion, 47.9% were cannulated with the aid of the AV300 vein viewing system, 66.8% took oral midazolam as premedication with a median duration of 43 (IQR = 35 - 57)min and a median dose of 0.8 (IQR = 0.4 -1.3) mg/kg before IV cannulation. The first-attempt success rate was 59.2% and the median time taken until a successful cannulation was 1 (IQR = 0.6 - 3.0) min.

Pain scores measured by BPS usually increased significantly at the end of the cannulations compared with those at the beginning (mean ± SD, 3.97 ± 1.639 versus 2.80 ± 0.951, t = 14.398, *P* < 0.001), but correlated with the latter (*r* = 0.646, *P* < 0.001). 55.46% of all patients still felt the increase of pain at the end of the IV access. General anesthetic (OR = 0.007, 95%CI, 0.002 - 0.026), gender (OR = 0.36, 95%CI, 0.167 - 0.777) and first-attempt success (OR= 0.336, 95%CI, 0.156 - 0.724) could protect from pain increment. Oral midazolam as premedication (OR= 2.113, 95%CI, 1.118 - 3.994) would help improve the first-attempt success rate. Similar results were gained in the subgroup of 4 to 16-year-old patients, pain scores from BPS correlated with those from FPS-R.

Conclusions

Our data support that (1) age, weight, gender, general anesthetic, size of sterile catheter, number of attempts, vein viewing system(AV300) were associated with the acute peripheral vein cannulation related pain, (2) premedication with oral midazolam and/ or management with inhaled general anesthetics contributed to pain relief during IV

insertion, (3) possible IV cannulation pain increment in the younger and/ or male pediatric patients should be paid more attention to, (4) FPS-R correlated well with BPS in pain evaluation in 4 to 16-year-old patients.

Zusammenfassung

Hintergrund

Schmerzerfahrungen bei Kindern und Jugendlichen durch das Legen von peripheren Venenverweilkanülen während des Krankenhausaufenthalts sind häufig und weit verbreitet. Diese sind eine der Hauptursachen für ausgeprägte Angst und Furcht im Angesicht von ihnen drohenden Nadel-gestützten-Verfahren bei Kindern und selbst auch noch bei Erwachsenen. Auch kann eine solche wiederholte, langfristige und dauerhafte Nozizeption oder negative Erfahrung, die nicht kontrolliert oder beherrscht wird, negativen Einfluss auf die Entwicklungen der Psyche, des Nervensystems, der Schmerzempfindlichkeit und der Emotionalität ausüben. Obwohl viele Anstrengungen unternommen wurden, um die Punktionsschmerzen zu beherrschen, gibt es viele Kinder, die unter der schmerzhaften und belastenden Erfahrung gelitten haben oder noch darunter leiden, insbesondere in der präoperativen Vorbereitung. Es bleibt also noch viel zur Schmerzlinderung zu tun und es gilt zunächst einmal herauszufinden, was tatsächlich zu Veränderungen der Schmerzen bei der Anwendung nadelgestützter Verfahren bei pädiatrischen Patienten führt.

Ziele

Untersuchung der schmerzbeeinflussenden Faktoren bei der präoperativen peripheren Venenpunktion bei pädiatrischen Patienten, die durch Anästhesisten und Pflegepersonal kontrolliert werden können.

Methoden

Im Rahmen dieser Untersuchung wurden Venenpunktionen zur Anlage einer Venenverweilkanüle bei pädiatrischen Patienten (inklusive Neonaten, Säuglingen, Kleinkindern, Schulkindern, Jugendlichen von 0-17 Jahren), die sich im regulären Tagesprogramm präoperativ dieser unterziehen mussten, im Kinder-OP des Campus Virchow-Klinikum, Charité-Universitätsmedizin, Berlin, erfasst.

Erhoben wurden demographische und klinische Informationen wie Geschlecht, Alter, Gewicht, die Anwendung von Prämedikation (Midazolam oral), Lokalanästhetikum

(EMLA) Allgemeinanästhesie (N_2O oder sevofluran), Nadelgröße (Gauge), die Dauer und Anzahl der Versuche bis zur erfolgreichen Anlage des Venenzugangs, Schmerzstärke anhand von BPS und FPS-R (Fremdbeobachtung, keine Selbsteinschätzung der Patienten).

Die Daten wurden mittels SPSS für Windows Version 18 (SPSS Inc, Chicago, IL) analysiert. Mittelwert ± Standardabweichung (SD) wurde in der Beschreibung von Schmerz-Scores aus den beiden Skalen oben genannten verwendet. Als Testverfahren für die Analysen fanden gepaarter t-Test, bivariate Pearson-Korrelation, multiple lineare Regression und binäre logistische Regression Anwendung. Demographische Daten und klinische Charakteristika wurden berechnet und als Median ausgedrückt (Interquartilenabstand, IQR), außer für kategoriale Daten wie Anzahl (Anteil). Häufigkeiten wurden mittels χ^2-Test geprüft. Mann-Whitney-U-Test wurde angewandt, um die Unterschiede der grundlegenden Eigenschaften zwischen den Veränderungen der Schmerzintensität (erhöhte oder nicht) während des Anlageprozesses der peripheren Venenzugänge zu bewerten. P-Werte <0,05 mit zweiseitigen Test wurden als statistisch signifikant betrachtet.

Ergebnisse

Insgesamt wurden 238 pädiatrischen Patienten ausgewertet, mit einem Durchschnittsalter von 24 (IQR = 8 bis 76) Monaten, einem mittleren Körpergewicht von 9,5 (IQR = 7,6 bis 14,2) kg, 45% davon waren weiblich, 55,5% erhielten örtliche Betäubung (EMLA) vor ihrer Ankunft im OP, bei 60,9% fand vor Anlage der peripheren Venenverweilkanüle eine Allgemeinanästhesie mit volatilen Anästhetika Anwendung (N_2O oder sevofluran), 47,9% wurden mit Hilfe des Vene Viewing Systems AV300 kanüliert, 66,8% erhielten Midazolam als orale Prämedikation mit einem medianen zeitlichen Abstand von 43 (IQR = 35 bis 57) min und einer mittlere Dosis von 0,8 (IQR = 0,4 -1,3) mg / kg vor der Kanülierung. Die Quote der per primam erfolgreichen Punktionen lag bei 59,2% und die mediane Zeit bis zur erfolgreichen Kanülierung war 1 (IQR = 0,6 bis 3,0) min.

Schmerz-Scores gemessen mittels BPS waren in der Regel am Ende der Kanülierung deutlich erhöht im Vergleich zu denen zu Beginn (Mittelwert ± Standardabweichung, 3,97 ± 1,639 im Vergleich zu 2,80 ± 0,951, t = 14,398, P <0,001), korrelierten jedoch mit den letzteren (r = 0,646, P <0,001). Bei 55,46% aller Patienten war die Schmerzstärke

am Ende der Venenkanülierung höher. Allgemeinanästhesie (OR = 0,007, 95% CI, 0,002 bis 0,026), Geschlecht (OR = 0,36, 95% CI, 0,167 bis 0,777) und per primam erfolgreiche Punktionen (OR = 0,336, 95% CI, 0,156 bis 0,724) wurden in das endgültige Modell aufgenommen und spielten bei der Vorhersage der Schmerzzunahme eine protektive Rolle. Daneben, konnte orales Midazolam als Prämedikation (OR = 2,113, 95% CI, 1,118 bis 3,994) dazu beitragen, die Quote der per primam erfolgreichen Punktionen zu verbessern. Ähnliche Ergebnisse wurden in der Untergruppe der 4- bis 16-jährigen Patienten gewonnen, Schmerz-Scores von BPS korrelierten mit denen von FPS-R.

Schlussfolgerungen

Unsere Daten unterstützen, dass (1) Alter, Gewicht, Geschlecht, Vollnarkose, Größe der sterile Katheter, die Anzahl der Versuche, der Einsatz des Venen-Such-Systems (AV300) mit dem akuten Schmerz bei der Kanülierung peripherer Venen verbunden waren, (2) Prämedikation mit oralem Midazolam und/ oder Allgemeinanästhesie zur Schmerzlinderung während Venenkanülierung beitragen konnte, (3) der möglichen Schmerzzunahme während der peripheren Venenkanülierung bei jüngeren und/ oder männlichen pädiatrischen Patienten, niedrigeren Körpergewichts mehr Aufmerksamkeit geschenkt werden sollte, (4) FPS-R bei 4- bis 16-jährigen Patienten gut mit BPS in der Erfassung von Schmerzen korreliert.

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8 Curriculum vitae

My career will not be published, for privacy reasons in the electronic version of my work.

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10 Declaration on oath

I hereby declare that the study described in the dissertation was carried out by me.

Erklärung

Ich, Peng Yu, erkläre, dass ich die vorgelegte Dissertation mit dem Thema: „Factors related to peripheral venous cannulation pain pre-operation in pediatric patients“ selbst verfasst und keine anderen als die angegebenen Quellen und Hilfsmittel benutzt, ohne die (unzulässige) Hilfe Dritter verfasst und auch in Teilen keine Kopien anderer Arbeiten dargestellt habe.

Berlin, den 10.01.2012 Peng Yu