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Original Research Article

Management of sickle cell disease patients presenting to the emergency department with vaso-occlusive crisis: a retrospective study

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ABSTRACT

Background: Sickle cell anemia (SCA) is a hereditary disease of the hemoglobin, characterized by recurring vaso-occlusive crises (VOC) leading to severe pain. VOCs constitute the primary cause for emergency department (ED) visits among sicklers. Frequent VOC episodes are associated with greater mortality. This study aimed to evaluate pain treatment trends regarding admission, discharge, length of stay in the ED, and early ED revisits among SCA patients.
Methods: A cross-sectional study was conducted from January 2020 to January 2023 at the ED of King Abdulaziz medical city in Riyadh. SCA patients who presented with VOC episodes were included in this study. Demographic and clinical data of each patient were retrieved from the electronic medical file.
Results: Total of 144 patients were included in the analysis. Out of the total population, 34% were admitted to hospital. Compared to those patients who were not admitted, the number of VOC was more among patients who had been admitted. Around 34% had ED revisit within 30 days and those patients had higher frequency of VOC attacks compared to those who did not revisit the ED. Only 45% of the population received appropriate dosing, 30% received an insufficient dose, and 25% received over the appropriate dose. Receiving the correct dose of morphine reduced the likelihood of ED revisits within 30 days.
Conclusions: This study explores trends in VOC among sticklers, highlighting that adequate analgesia is associated with better outcomes. Addressing these variables may lead to improved care and better outcomes for SCA patients.

Keywords: SCA, VOC, Better outcomes

INTRODUCTION

Sickle cell anaemia (SCA) is the commonest inherited haemoglobin disorder.[1] It is caused by an autosomal-recessive single gene defect in the beta chain of haemoglobin (HbA), which results in production of sickle cell haemoglobin (HbS).[2]

Abnormal haemoglobin (HbS), predisposes to polymerization and the consequent deformation ("sickling").[3]

According to WHO, 83% of the 330 000 infants who are born annually with haemoglobin disorders have sickle cell disease (SCD).[4] In Saudi Arabia the prevalence of the disease differs in the vast area of the kingdom, ranging from 2% to 27%, mostly concentrated in the eastern province followed by the south-western province.[5]

The most common clinical manifestation of SCD is VOC; where patients experience recurrent pain episodes. These episodes are characterized by having an abrupt onset and are associated with severe pain.[6,7]

Acute vaso-occlusive pain crisis is the most common reason for ED visits for SCD patients and frequent pain episodes are associated with an increased risk of mortality.[8] The severe pain is often managed in the ED requiring parenteral opioid administration, most commonly morphine.[9]

Using opioids and addiction are of particular concern in treating acute pain episodes. A result of a survey showed 53% of ED physicians and 23% of haematologists thought that more than 20% of patients with SCD were addicted.[10] Commonly, physicians fail to distinguish between addiction and tolerance or physical dependency, so they usually under-treat those patients.[11]

Several studies have shown that the majority of SCD patients rated their ED experience as ‘‘very poor, ’’ demonstrating a need for improvement in the care of SCD patients in the ED. This suboptimal pain management results in mistrust and dissatisfaction from the patients toward ED physicians.[12]

The issue of oligoanalgesia and delay to analgesia administration for SCD patients has been addressed in many studies.[13-15] However, few studies have addressed the effect of under-treatment of pain on SCD patients presented to ED with VOC. Therefore, the aim of the present study is to assess the impact of proper management and under-treatment of pain on SCD patients ’rates of admission, discharge, length of stay in ED and early ED revisit rates.

METHODS

Study design and setting

A cross-sectional study was carried out between January 2020 to January 2023 at the ED of the King Abdul Aziz medical city (KMAC), Riyadh, Saudi Arabia. This medical facility is located in the Central region of country and has a bed capacity exceeding 1200. Its primary focus is to provide healthcare services to the Saudi national guards, hospital employees, and their families.

Study population and variables

All NGHA eligible patients above age of 14 years with confirmed diagnosis of SCD were included in the study. Patients who were transferred to another hospital or SCD patients who were admitted for other reasons than VOC were excluded from the analysis. Based on feasibility report from ED, it was estimated that at least 114 patients were required to detect differences in pattern of treatment used with 80% power and 95% confidence level.

Data on demographic and clinical data were extracted from each patient's electronic medical records. Demographic data include age, gender, body mass index (BMI), while the clinical data include co-existing comorbidity, previous medical history, vital signs at emergency admission, and lab results. The medication records were reviewed for each patient to extract data on treatment patterns that have been received in the ED. The study outcomes were the admission to the medical words and ED re-visit within 30 days from date of discharge. The data were collected using standardized data collection sheets by trained data collectors, in which the data were double checked for outlier and accuracy prior the analysis. All patients aged under 14 years, admitted for non-VOC-related diagnoses, or with missing data in documentation were excluded. This study had been approved by the ethical committee at King Abdullah international medical research centre.

Data analysis

Descriptive analyses were performed using frequencies and percentages for categorical variables. For the continuous variables, Shapiro–Wilk test was carried out to test for normality, and based on this, the variables were described using mean and standard deviation (SD) if normally distributed or median and interquartile range (IQR) if otherwise. The association of the clinical variables and the study outcomes (admission, ED revisit) was examined using Chi-square test (or Fisher exact test if appropriate), student t-test or non-parametric test (Kruskal-Wallis equality-of-populations rank test, and Wilcoxon rank-sum test). The association between different medication regimen and study outcome were examined using logistic regression. A p value of less than 0.05 was set as a cut-off for statistical significance. All analyses were done with the Stata 12 software system (Stata Corp L.P., college station, TX).

RESULTS

Description of the study population

A total of 144 patients were included in the analysis of this study after reviewing the electronic medical records and applying the study’s inclusion criteria. Table 1 presents the demographic and clinical data of the study population. The participants had a median age of 27 years (IQR 22-32). Approximately half of the population were female (n=73, 50%). For the BMI, 20.8% (n=30) classified as underweight, 45.8% (n=66) as a normal weight, 22.2% (n=32) as overweight, and 11.1% (n=16) as obese. Around 47% of our patients experienced three or more attacks in the year preceding the current episode.

Study outcome

During the study period, out of the patients who visited the ED, 49 individuals (34%) were admitted to the hospital. A comparison was made between the admitted group and the non-admitted group, and it revealed no significant differences in age, gender, BMI, or comorbidities between the two groups. Compared to those patients who were not admitted, the number of VOC was more among patients who had been admitted

(57% of admitted patients had more than three attacks vs 42% among the non-admitted group, p=0.07). The vital signs at ED admission were similar for both the admitted and non-admitted patients. For the retic count, it was lower in the admitted group (median of 71 IQR 0.99-188, p=0.008). Furthermore, the initial pain score among admitted patients was 4.8±1.6, which was statistically different from the mean score of non-admitted patients (4.1±2.2, p=0.032).

In terms of revisits to the ED within 30 days from the date of the last VOC attack, approximately 34% of the study population (50 patients) had a 30-day re-visit. A comparison between those who had an ED revisit and those who did not showed that the number of previous attacks was significantly higher in group with ED revisit (Table 2). Specifically, 70% of patients with ED revisit had experienced 3/ more previous attacks, compared to only 35% of those without an ED revisit (p<0.001). Regarding medication usage, significant majority (84%) of study participants received morphine. Among those who received morphine, 61% were given the medication two to three times during their treatment (Table 3).

When comparing medication usage between patients who were admitted and those who were not, there were no differences in the combination of medications used, except for the number of morphine doses administered. Non-admitted patients received a higher number of morphine doses compared to the admitted patients. Specifically, 55% of non-admitted patients received two to three doses of morphine, while only 44% of the admitted group received the same dosage (p=0.009).

Regarding the outcome of ED revisits within 30 days, it was observed that among the patients who received morphine, 69% did not have subsequent ED revisits within the 30-day period, while 30% did revisit the ED within this time frame (p=0.017, as indicated in Table 3). Furthermore, among those who received Diclofenac, 66% had subsequent ED revisits within 30 days. Regarding different medication combinations, 83% of the patients who received only NSAID, and paracetamol had an ED visit within 30 days (p=0.015). Conversely, the percentages of patients who had no subsequent ED revisits within 30 days for the following combinations were as follows: (morphine and NSAID) 63%, (morphine and paracetamol) 67%, and (morphine, paracetamol, and NSAID) 68% (Table 3).

For the morphine dosage, the study found that only 45% of the entire study population received the appropriate dose, while 30% received a suboptimal dose, and 25% received over the appropriate dose of morphine. The mean morphine dose was significantly lower among the patients who were admitted compared to those who were not. Thus, admitted patients received an average of 0.12 mg/kg of morphine, while non-admitted patients received 0.15 mg/kg (p=0.008). Additionally, patients who had ED revisits within 30 days received a lower morphine dose, as 51% of those who received suboptimal morphine doses had ED revisits within 30 days, compared to 35% of those who received the appropriate dose.

The risk of admission and ED revisits within 30 days were compared between those who received morphine and those who did not. The results indicated that receiving morphine reduced the risk of ED revisits within 30 days by 33%, with a confidence interval of 95% (0.13-0.84). Additionally, patients who received suboptimal doses were twice as likely to be admitted to the hospital compared to those who received the appropriate dose. Furthermore, those who received suboptimal doses were three times more likely to have ED revisits within 30 days, with a 95% confidence interval of (1.45-9.53).

Regarding the time to receive the medication, the median time was two hours (IQR 1-3.2 hours), with the minimum being thirty minutes and the maximum twelve hours. Interestingly, younger patients (≤twenty five years), those with a history of more than three previous attacks, and those with the previous hospital admission tended to receive the medication more quickly (as shown in supplement file 1).

Table 1: Descriptive, clinical, and laboratory parameters of the study population based on admission status.

Variables	Total population, n=144 (%)	Not admitted, n=95 (65%)	Admitted, n=49 (34%)	P value
Age (In years) (median IQR)	27 (22-32)	26 (21-32)	29 (23-35)	
Age categories (In years)				
≤25	61 (42.3)	41 (43.1)	20 (40.8)	0.719
26-35	56 (38.8)	38 (40.0)	18 (36.7)	
>35	27 (18.7)	16 (16.8)	11 (22.4)	
Gender				
Female	73 (50.6)	49 (51.5)	24 (48.9)	0.768
Male	71 (49.3)	46 (48.4)	25 (51.1)	
BMI categories				
Underweight	30 (20.8)	19 (20.0)	11 (22.4)	0.734
Healthy weight	66 (45.8)	44 (46.3)	22 (44.9)	
Overweight	32 (22.2)	23 (24.2)	9 (18.3)	
Obese	16 (11.1)	9 (9.4)	7 (14.2)	

Continued.

Variables	Total population, n=144 (%)	Not admitted, n=95 (65%)	Admitted, n=49 (34%)	P value
Co-existing comorbidities				
Diabetes mellitus	13 (9.0)	8 (8.4)	5 (10.2)	0.724
Hypertension	8 (5.5)	5 (5.2)	3 (6.1)	0.552
Previous medical history				
Splenectomy	15 (10.4)	7 (7.3)	8 (16.3)	0.095
Number of attacks in previous year				
None	32 (22.2)	20 (21.1)	12 (24.4)	0.070
1-2 attacks	44 (30.5)	35 (36.8)	9 (18.3)	
≥3 attacks	68 (47.2)	40 (42.1)	28 (57.1)	
Required blood transfusion in the previous year				
None	83 (57.6)	57 (60.0)	26 (53.1)	0.566
Once-twice	30 (20.8)	20 (21.1)	10 (20.4)	
More than 3 times	31 (21.5)	18 (18.9)	13 (26.5)	
Pain site at the current attack				
Generalised	67 (46.5)	40 (42.1)	27 (55.1)	0.202
Specific to the upper body	28 (19.4)	18 (18.9)	10 (20.4)	
Specific to the back and lower body	49 (34.1)	37 (38.9)	12 (24.4)	
Vitals at emergency admission				
Heart rate /min (mean ±SD)	96±19.1	95.7±18.3	97±20.5	0.691
Respiratory rate/ min (median, IQR)	20 (19-20)	20 (19-20)	20 (19-20)	0.261
Oxygen saturation (percenatges) (median, IQR)	98 (96-100)	98 (96-99)	98 (96-99)	0.628
Temperature C^0 (median, IQR)	36.9 (36.7-37)	36.9 (36.7-37)	36.9 (36.7-37.1)	0.294
Systolic blood pressure (mean, SD)	115±22	118±12.7	118.5±16.5	0.561
Diastolic blood pressure (mean, SD)	71 (12.1)	71.9±12.4	70±11.7	0.266
Lab results [DFMO1]				
Haemoglobin level (median, IQR)	99 (85-110)	100 (85-111)	95 (83-104)	0.736
Retics count (median, IQR)	147.2 (0.13-257)	180 (52-276)	71 (0.99-188)	0.008*
WBC (median, IQR)	10 (6.8-14.1)	10.5 (6.3-18.2)	11.2 (7.5-14.1)	0.387
Initial pain score (mean ± SD)	4.3±2.1	4.1±2.2	4.8±1.6	0.032

P<0.05 considered significant.

Table 2: Study population based on ED revisit within 30 days from the date of VOC attack date.

Variables	ED revisit within 30 days		P value
	No, n=94 (65%)	Yes, n=50 (34%)	
Age (In years)	29 (22-32)	26 (21-34)	0.956
Age categories			
≤25	41 (43.6)	20 (40.0)	0.630
26-35	34 (36.1)	22 (44.0)	
>35	19 (20.21)	8 (16.0)	
Gender			
Female	50 (53.1)	23 (46.0)	0.411
Male	44 (46.8)	27 (54.0)	
BMI (kg/m^2)			
Underweight	20 (21.2)	10 (20.0)	0.318
Health weight	39 (41.4)	27 (54.0)	
Overweight	25 (26.6)	7 (14.0)	
Obese	10 (10.6)	6 (12.0)	
Previous medical history			
Splenectomy	7 (7.4)	8 (16.0)	0.151
Number of attacks in previous year			
None	27 (28.7)	5 (10.0)	<0.001
1-2 attacks	34 (36.1)	10 (20.0)	
≥3 attacks	33 (35.1)	35 (70.0)	

Continued.

Variables	ED revisit within 30 days		P value
	No, n=94 (65%)	Yes, n=50 (34%)	
Required blood transfusion in the previous year			
None	59 (62.7)	24 (48.0)	0.188
Once-twice	16 (17.1)	14 (28.0)	
More than 3 times	19 (20.1)	12 (24.0)	
Admission	33 (35.1)	16 (32.0)	0.708
discharge pain score (median IQR)	0 (0-2)	1 (0-3)	0.121

Table 3: Medication regimen and dose of morphine received by the patients and its association with hospital admission and ED revisit.

Type of medication received	Total, n (%)	Admission			ED revisit within 30 days		
		Not admitted, n=95 (65%)	Admitted, n=49 (34%)	P value	No, n=94 (65%)	Yes, n=50 (34%)	P value
Morphine	121 (84.1)	78 (64.4)	43 (35.5)	0.381	84 (69.4)	37 (30.5)	0.017
Nonopioid medication							
Paracetamol	117 (81.2)	75 (64.1)	42 (35.9)	0.324	74 (63.2)	43 (36.7)	0.287
NSAID							
Ketorolac	33 (22.9)	21 (63.6)	12 (36.3)	0.835	21 (63.6)	12 (36.3)	0.822
Diclofenac	12 (8.3)	8 (66.6)	4 (33.3)	0.958	4 (33.3)	8 (66.6)	0.024
Medication combination vs morphine							
NSAID +paracetamol	6 (4.7)	3 (50.0)	3 (50.0)	0.667	1 (16.6)	5 (83.3)	0.015
Morphine + NSAID	36 (29.7)	23 (63.8)	13 (36.2)	0.932	23 (63.8)	13 (36.1)	0.390
Morphine+paracetamol	102 (84.3)	65 (63.7)	37 (36.2)	0.695	69 (67.6)	33 (32.3)	0.326
Morphine+ paracetamol+ NSAID	34 (38.1)	21 (61.7)	13 (38.2)	0.698	21 (61.7)	13 (38.2)	0.253
Fluids	126 (87.5)	81 (64.2)	45 (35.7)	0.258	86 (68.2)	40 (31.7)	0.047
0.9NACL	119 (92.2)	77 (64.7)	42 (35.2)	0.962	80 (67.2)	39 (32.7)	0.731
D5%0.45NACL	11 (8.7)	7 (63.6)	4 (36.3)		7 (63.6)	4 (36.3)	
Morphine dose							
Number of morphine dose received							
Once	25 (20.6)	22 (88.0)	3 (12.0)	0.021	18 (72.0)	7 (28.0)	0.052
Twice to three times	74 (61.1)	41 (55.4)	33 (44.5)		48 (64.8)	26 (35.1)	
More than three times	22 (18.1)	15 (68.1)	7 (31.8)		18 (81.1)	4 (18.1)	
Mean dose (SD)	0.14 (0.06)	0.15 (0.05)	0.12 (0.06)	0.008	0.15 (0.06)	0.12 (0.05)	0.003
Dose categorization							
Suboptimal	35 (28.9)	17 (48.5)	18 (51.4)	0.066	16 (45.7)	19 (54.2)	0.001
Appropriate dose	55 (45.4)	39 (70.9)	16 (29.1)		42 (76.3)	13 (23.6)	
Over the appropriate dose	31 (25.6)	22 (70.9)	9 (29.1)		26 (83.8)	5 (16.1)	

The percentage shown for admission and ED revisit category is row percentage.

Table 4: Univariate analysis of the risk of hospital admission and ED revisit within 30 days in relation to different medication regimens received by patients.

Variables	OR, 95% CI	P value
Opioid vs non-opioid		
Admission	1.156 (0.57-4.25)	0.383
ER visit	0.33 (0.13-0.84)	0.020
NSAID+ paracetamol vs opioid		
Admission	1.81 (0.35-9.37)	0.477
ER visit	11.3 (1.28-29.9)	0.029
Opioid NSAID vs opioid		
Admission	1.03 (0.45-2.33)	0.932
ER visit	1.43 (0.62-3.28)	0.391

Continued.

Variables	OR, 95% CI	P value
Opioid + paracetamol vs opioid		
Admission	1.23 (0.43-3.51)	0.695
ER visit	1.79 (0.55-5.82)	0.331
Opioid + paracetamol + NSAID vs opioid		
Admission	1.17 (0.51-2.67)	0.698
ER visit	1.62 (0.70-3.75)	0.255
Dose		
Admission		
Appropriate	Reference	
Underdose	2.58 (1.06-6.23)	0.035
Over the appropriate dose	0.99 (0.37-2.62)	0.995
ER visit		
Appropriate	Reference	
Underdose	3.83 (1.54-9.53)	0.004
Over the appropriate dose	0.62 (0.19-1.94)	0.414

DISCUSSION

The importance of our study lies in highlighting the importance of pain management in patients presenting to the ED with VOC and assessing the factors that led to 30-day ED revisit and admission.

Firstly, our study revealed that 34% of SCD patients with VOC were admitted to the hospital. This admission rate is less than a retrospective review conducted by Jacob et al which reported admission rates ranging from 50% to 60% among SCD patients with VOC.[16] In addition, another retrospective study carried on by Cheng et al) reported an admissions rate of 53%.[17] These findings indicate that a significant proportion of SCD patients presenting with VOC require hospitalization for adequate management and support the results of previous literature in terms of the need for standardized pain management plans, as studied by (Givens et al, Ender et al and Kavanagh et al).[18,19] However, it's importance to note that populations of these studies had relatively lower mean age than ours.

According to current study, 30-day ED revisit rate for patients with VOC found to be 34% (n=50), which is lower compared to rates reported in literature. Prospective study by Matthew examined ED revisits within 3 and 30 days, revealing rates of 16% and 67%, respectively.[20] Another retrospective study conducted by Solmon found an ED revisit rate of approximately 28% within 3 days.[21]

A retrospective cohort study by Glassberg developed a risk score to predict 30-day ED revisits in sickle cell pain patients. The risk score incorporated four variables: age, insurance status, triage pain score, and the amount of opioids administered during the ED visit. This scoring system correctly identified 60% of patients who had ED revisits within 30 days and accurately identified 80% of patients who did not have ED revisits within 30 days.[22]

In a retrospective cohort study conducted by Brousseau et al, an association was observed between ED revisits within 30 days and age. The study found that the 30-day rehospitalization rate was highest among individuals aged 18 to 30 years, with a rate of 41.1% (95% confidence interval, 40.5%-41.7%). For this age group, nearly half of all hospitalizations resulted in a return to the ED for sickle cell-related acute care within 30 days.[23] To the best of our knowledge, there is currently no existing study in our area that has investigated the potential relationship between ED revisits within 30 days and the frequency of vaso-occlusive attacks. The current study investigated variables influencing the 30-day ED revisit rate and found significant associations with certain factors. Patients with a history of previous VOC attacks had a higher likelihood of ED revisits, with 70% of revisiting patients having experienced more than 2 previous attacks. Additionally, 84% of the current study population received morphine, of which 61% of those received morphine twice to three times. The administration of morphine in the ED showed better outcome in terms of ED revisit within 30 days. The results showed that receiving morphine reduce the ED re-visit within 30 days by 33%, 95% CI (0.13-0.84). Furthermore, the appropriate administration of morphine had significant reflection on the outcome in terms of the ED revisit within 30 days and admission rate. Patients receiving suboptimal doses of morphine were three times more likely to have ED revisits within 30 days. Moreover, patients receiving suboptimal morphine doses were twice more likely to get admitted. Another retrospective study by Leslie et al reported a significantly higher frequency of ED revisits in patients prescribed NSAIDs only without opioids (OR=6.9, 95% C=1.3-37.3, p=0.03). [24]In line with these findings, our study observed that 83% of patients who received only acetaminophen and NSAIDs in the ED without opioids had ED revisits within 30 days.

Limitation

It is important to acknowledge the limitations of our study. First, our findings are based on data collected from a single ED in Saudi Arabia, which may limit the generalizability of the results to other populations.

Additionally, the finding of the results need to be interpreted with caution as data on confounders were not comprehensively collected. The retrospective nature of the study design may introduce selection bias and confounding factors. Future prospective studies involving larger and diverse patient populations are warranted to validate our findings and provide more robust evidence.

CONCLUSION

A comprehensive approach is essential to tackle the challenges of managing VOC in the ED for patients with SCD. This approach should encompass personalized pain management techniques and improved compliance with established protocols. By prioritizing effective pain management and optimizing patient care, healthcare providers can make significant strides in enhancing the outcomes and experiences of SCD patients during their ED visits.

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APPENDIX

Table 1: Study population based on time to medication.

Variables	Time to medication in hours		Time to medication categories		P value
			Less than 2 h 78 (54.1%)	More than 2 h 66 (45.8%)	
Age (In years)					
Age categories (In years)					
≤25	1.8 (1.0-3.1)		34 (43.5)	27 (40.9)	
26-35	2.0 (1.0-3.6)	0.613	29 (37.1)	27 (40.9)	0.901
>35	2.0 (1.1-3.2)		15 (19.2)	12 (18.1)	
Gender					
Female	2.0 (1.0-3.6)	0.077	37 (47.4)	36 (54.5)	0.395
Male	1.7 (0.6-3.0)		41 (52.5)	30 (45.4)	
BMI (kg/m^2)					
Underweight	2 (0.5-2.5)		15 (19.2)	15 (22.7)	
Health weight	2.0 (1.1-3.1)	0.566	35 (44.8)	31 (46.9)	0.653
Overweight	2.0 (1.0-3.6)		17 (21.7)	15 (22.7)	
Obese	1.2 (0.5-2.6)		11 (14.1)	5 (7.5)	
Previous medical history					
Splenectomy	2.0 (1.3-2.5)	0.609	7 (8.9)	8 (12.1)	0.538
Number of attacks in previous year					
None	2.0 (1.3-3.0)		20 (25.6)	12 (18.1)	
1-2 attacks	2.3 (1.1-3.2)	0.531	21 (26.9)	23 (34.8)	0.442
≥3 attacks	2.2 (1.3-2.6)		37 (47.4)	31 (46.9)	
Required blood transfusion in the previous year					
none	2.0 (1.0-3.6)		42 (53.8)	41 (62.1)	
Once-twice	1.1 (0.5-4.3)	0.041	23 (29.4)	7 (10.6)	0.015
More than 3 times	2.2 (1.0-4.0)		13 (16.6)	18 (27.2)	
Admission					
No	2.0 (0.5-3.2)	0.201	52 (66.6)	43 (65.1)	0.848
Yes	1.8 (0.5-3.0)		26 (33.3)	23 (34.8)	
Type of medication received					
Paracetamol	2.0 (1.3-3.1)	0.624	63 (80.7)	54 (81.8)	0.872
Morphine	2.0 (1.3-3.5)	0.739	63 (80.7)	58 (87.8)	0.246
Number of morphine dose received					
Once	2.3 (2.0-4.0)		10915.8)	15 (25.8)	
Twice to three times	1.8 (1.3-4.0)	0.152	38 (60.3)	36 (62.1)	0.152
More than three times	1.4 (2.5-1.3)		15 (23.8)	7 (12.1)	
Ketorolac	2.2 (1.0-5.3)	0.296	16 (20.5)	17 (25.7)	0.456
Diclofenac	1.8 (1.4-2.1)	0.997	9 (11.5)	3 (4.5)	0.133
Fluids	2.0 (1.3-3.2)	0.719	66 (84.6)	60 (90.9)	0.255