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Wound Infiltration Using Bupivacaine Versus Bupivacaine with Ketamine for Postoperative Analgesia Improvement in Cesarean Section Operations.

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ABSTRACT

A common procedure recently used is local anesthetic infiltration of surgical wounds that provides postoperative analgesia for a wide range of surgical operations with a minimum risk of side effects. A total of 60 pregnant women scheduled for elective cesarean section, were divided into 2 equal groups,30 patients each; the control (C) group: received 40 mL of 0.25% bupivacaine in two divided doses; and the ketamine (K) group: received 40ml of 0.25% bupivacaine plus 2 mg/kg ketamine, aiming to evaluate the efficacy of combined bupivacaine with ketamine on postoperative pain control following caesarean delivery. Heart rate, mean arterial blood pressure and respiratory rate were recorded at anaesthesia induction, and then every 10 min until the end of surgery. Mean arterial blood pressure, heart rate, respiratory rate and visual analogue scale were evaluated immediately postoperatively at the recovery room, then at 2,4,6,8,10, 12 and 24 hours postoperatively. Recording the time of the first painkiller request. (the time from recovery until VAS greater than 3) Collection of total doses of morphine requirement in 1st 24 hrs. VAS monitoring at the recovery room immediately postoperatively and then at 2, 4, 6, 8, 10, 12, and 24 hours postoperatively, patient satisfaction, 0 = no satisfaction and 10= full satisfaction. Data was then imported into Statistical Package for the Social Sciences (SPSS version 23.0) software for analysis. The ketamine group had a significantly longer duration before they needed analgesia ($P < 0.001$) as compared to the control group. opioid consumption in the ketamine group was much less than in the control group. ($P< 0.001$). patient in the ketamine group is more satisfied as compared to those in the control group ($P < 0.001$). We concluded that adding ketamine to bupivacaine in wound infiltration has a better effect than bupivacaine alone in controlling the hemodynamic parameters, a longer time for requesting analgesia postoperatively, patients' satisfaction, and a smaller number of opioids needed on the first postoperative day.

1. INTRODUCTION

Pain is considered the highest among undesirable clinical outcomes associated with cesarean section. Appropriate post-operative pain control in obstetric patients is important as they have many post-operative needs like breast and, newborn care which can be affected if the pain is not controlled. The ideal postoperative pain control regime should be efficient without affecting the ability of the mother to take care of her baby with less drug transfer to breast milk. Kerai. et al 2017. recently, techniques of local infiltration and continuous infusion of wounds with local anesthetics have been re-introduced as parts of multimodal analgesia for postoperative pain control. (Goerig M and Gottschalk A. 2017)

The various analgesic regimens used in the cesarean section include transversus abdominis plane (TAP) block, infiltration of the wound with local anesthetic, use of non-steroidal anti-inflammatory drugs (NSAIDs), blocks of ilio-inguinal- ilio-hypogastric nerve, epidural analgesia and ketamine. (Kerai. et al.2017), Bupivacaine is frequently used because it provides a longer duration of action and a preferred ratio of sensory to motor neural block. Bupivacaine has receptors on the inner side of the sodium channels, acting by blocking the influx of sodium into nerve cells and preventing depolarization. (Jonnavithula. et al.2015). Ketamine is an N-methyl-D-aspartate (NMDA) receptor non-competitive antagonist that blocks central sensitization, and its analgesic effect relieves pain postoperatively. (Mohamed. S. et al.2018), infiltration of bupivacaine Subcutaneously relieves pain in the first hour postoperatively and thereby decreases opioid consumption. epidural analgesia had less pain control and patient satisfaction as compared with Wound infiltration. Incisional infiltration with local anaesthetics is an easy, low-cost, with fewer side effects efficient way of pain control postoperatively, without local anaesthetic toxicity, and allows early mobilization and recovery. (Khalaf. et al.2018) Cesarean delivery is the most frequently performed abdominal operation globally (Pyykönen, A et al.2017). many women reported moderate to severe pain lasting at least 48 hours after cesarean section. (Nanji, J et al.2019) Pain relief is a highly significant factor for adequate mother-baby caring, breastfeeding, early mobilization, and short hospital stays. (Garmi, G et al.2022), Control of pain related to cesarean section involves many strategies. Nonopioid systemic analgesic agents are widely used in different regimens. use of large amounts of opioids being prescribed to women after cesarean section has been reported by several studies. These drugs have many side effects, and the risk of addiction after a cesarean section is of great concern. (Badreldin, N et al.2018), (Schmidt, P et al.2018). Wound infiltration after surgery is an easy method for pain relief, as the wide tissue dissection in cesarean section leads to severe pain which is far beyond incisional margins, which makes local anaesthetic infiltration more desirable. Using drains and catheters for wound installation with local anaesthetic agents after cholecystectomy, cardiac surgery, abdominal hysterectomy and splenectomy, reported good pain control in the postoperative period. After checking proper homeostasis, injection of local anaesthetics in the subcutaneous tissue in patients undergoing caesarian section is known and widely used. It improves patient satisfaction, optimizes analgesia and promotes early return to daily activities. (Chhatrapati et al.2019)

2. AIM OF THE STUDY

The aim of our study was to compare the efficacy of adding ketamine to bupivacaine used in wound infiltration on post-operative analgesia quality in cesarean section.

3. METHOD

An interventional comparative prospective randomized double-blinded controlled clinical study was carried out in Benghazi Medical Centre in the Department of Surgery Unit of Anesthesia after approval of the Institutional Review Board (IRB).

Inclusion criteria: All patients eligible for the study met the criteria for ASA physical status I, II, aged 18-45 years old, BMI of (18-25kg/m2) scheduled for elective cesarean section.

Exclusion criteria: patients with high-risk pregnancies, emergency, hepatic diseases, renal diseases, cardiac patients, and a history of allergy to study medications were excluded from the trial.

Study groups: The study comprised 60 patients asking for general anesthesia for elective cesarean section. All selected patients were allocated into two equal groups (30 patients each).

Control group (Group C) (n= 30 patients): Patients received local wound infiltration with a total of 40 mL of 0.25% bupivacaine (20 mL for each side of the incision line). Ketamine group (Group K) bupivacaine plus ketamine group (n= 30 patients): Patients received local wound infiltration with a total volume of 40 ml of 0.25% bupivacaine plus 2 mg/kg ketamine (20 mL for each side of the incision lines).

Randomization: The patients were randomly allocated by computer randomization table into two equal groups according to the study drugs used (30 patients each).

Study procedure: History was taken regarding age, drug allergy, medical, and surgical history, and land laboratory investigations were collected, Patients were kept fast for hours; 6-8 hours, an IV line was inserted, and data of blood pressure, heart rate, ECG, respiratory rate, and oxygen saturation monitoring was recorded. In all patients, general anaesthesia was induced with intravenous 2 mg/kg propofol, controlled mechanical ventilation was initiated utilizing a tidal volume of 7 ml/kg and respiratory rate finely adjusted to maintain an end-tidal carbon dioxide value of 30–35 mmHg, meanwhile rapid sequence intubation was facilitated with 0.6-1.2 mg/kg IV rocuronium.

Anesthesia maintained with inhalational anaesthesia of 0.5 MAC isoflurane and 0.1-0.2 mg/kg IV rocuronium when needed. In a sterile manner, the study drugs were prepared in sterile syringes by an anesthesiologist for local wound infiltration at the end of skin closing. Reversal of muscle relaxant done with neostigmine 0.05 mg /kg and atropine 0.01 mg /kg. All patients received 1 gm IV paracetamol immediately post operative then every 8 hours. Data collection: Demographic data: age, weight, height, ASA, and BMI. Heart rate, mean arterial blood pressure and respiratory rate were recorded at induction of anaesthesia, and then every 10 min until the end of surgery. Mean arterial blood pressure, heart rate, respiratory rate and visual analogue scale were evaluated at the recovery room immediately postoperatively, then at 2,4,6,8,10, 12 and 24 hours postoperatively. Recording the time of the first painkiller request. (the time from recovery until VAS greater than 3) Collection of total doses of morphine requirement in 1st 24 hrs. VAS monitoring (ranges from 0 = no pain to 10 = worst imaginable pain) at the recovery room immediately postoperatively and then at 2, 4, 6, 8, 10, 12, and 24 hours postoperatively, patient satisfaction questionnaire (10-point scale to assess the patient's satisfaction about analgesia postoperatively, 0 = no satisfaction and 10= fully satisfaction) Microsoft Excel software is used for coding and analyzing the data collected throughout history, examination, laboratory investigations and outcome measures. Data was then imported into Statistical Package for the Social Sciences (SPSS version 23.0) software for analysis. The following tests were used to test differences for significance; difference and association of qualitative variable by Chi-square test (X2)., multiple by ANOVA or Kruskal Wallis, P value was set at <0.05 for significant results and <0.001 for high significant result.

4. RESULT

Table (1): Demographic data and clinical state of the studied groups

			Group C(N=30)	Group K(N=30)	X^2/ F	P
Age (years)			29.36±4.23	27.45±4.12	1.702	0.182
Weight (kg)			72.52±12.63	75.85±16.32	0.965	0.325
Height (cm)			167.16±17.25	167.01±9.36	0.885	0.412
BMI			23.95±3.02	25.19±3.85	2.354	0.125
ASA	I	N	20	23		
		%	66.7%	76.7%		
	II	N	10	7	2.28	0.31
		%	33.3%	23.3%		
Total		N	30	30		
		%	100.0%	100.0%		

Table (2): The mean arterial blood pressure at scheduled times in the studied groups

	Group C(N=30)	Group K(N=30)	F	P
MBP basal mmHg	128.41±6.47	124.22±7.41	2.074	0.134
MBP_10 min	124.26±7.72	121.34±6.47	1.305	0.278
MBP_15 min	123.64±11.78	120.90±8.51	1.427	0.213
MBP_30 min	121.12±7.82	120.55±15.32	1.294	0.281
MBP_45 min	117.30±5.22	116.77±16.33	1.195	0.322
MBP_60 min	113.74±10.98	110.90±14.08	2.216	0.117
Immediately post operative	116.17±14.56	115.64±15.09	0.229	0.796
MBP_post2H	117.30±8.75	115.63±12.20	2.800	0.068
MBP_post4H	123.79±5.42	121.51±9.08	1.150	0.323
MBP_post6H	123.89±5.32	121.41±9.18	1.160	0.342
MBP_post8H	124.66±5.42	122.38±9.08	1.150	0.323
MBP_post10H	122.03±4.56	121.34±4.15	0.996	0.355
MBP_post12H	124.03±4.86	122.34±4.25	0.996	0.375
MBP post 24H	123.58±4.86	121.89±4.25	0.996	0.375

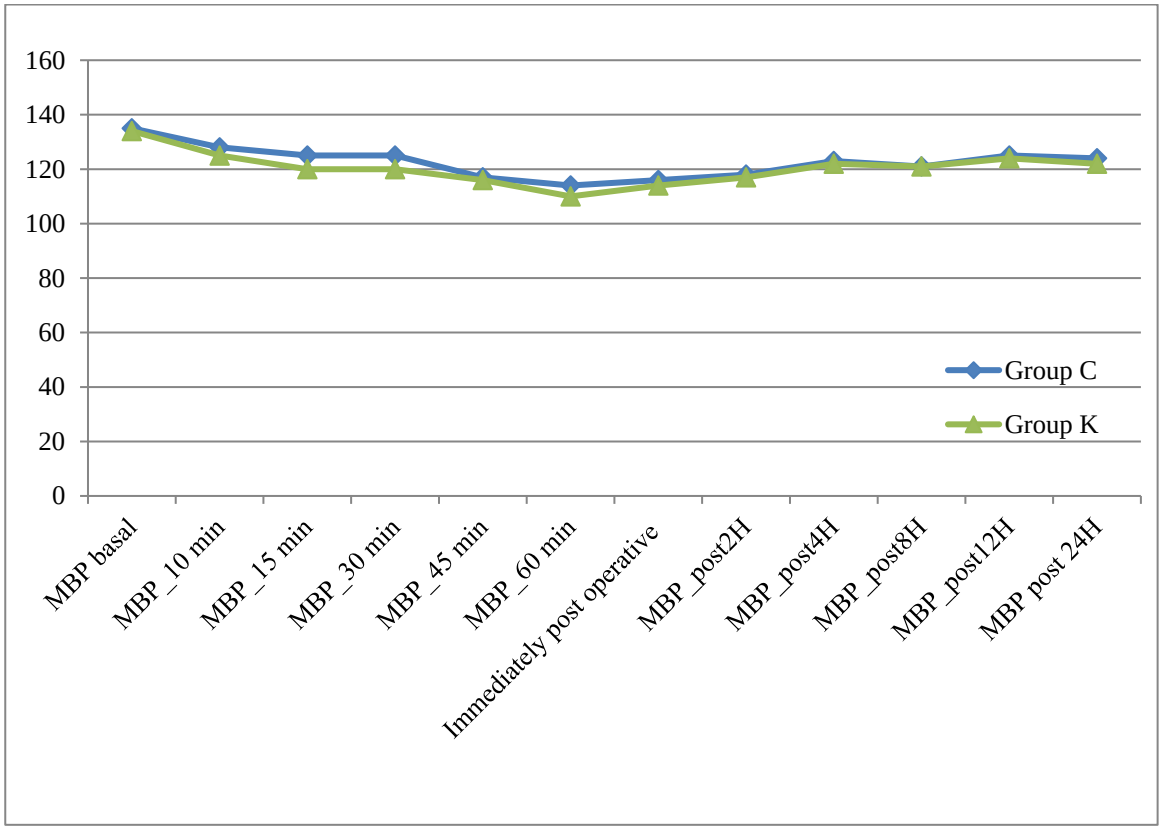

Fig (1) Mean arterial blood pressure among studied groups at different time periods.

Table (3): Heart rate distribution among the studied groups

HR(beat/min)	Group C(N=30)	Group K(N=30)	F	P
HR induction	81.22±2.19	79.21±1.51	1.423	0.211
HR_10 min	74.22±2.41	74.99±7.56	12.856	0.00**
HR_15 min	74.11±3.25	75.63±8.69	16.568	0.00**
HR_30 min	75.21±5.12	76.85±11.32	17.235	0.00**
HR_45 min	74.19±6.21	75.25±5.28	11.541	0.00**
HR_60 min	74.36±7.25	74.36±5.85*	8.388	0.00**
Immediately post operative	74.11±2.4	74.63±8.87*	2.554	0.068
HR_post2H	74.85±2.46	75.85±8.07*	2.452	0.079
HR_post4H	78.36±10.23	76.83±7.52	1.884	0.212
HR_post6H	77.36±7.43	76.73±7.62	1.574	0.312
HR_post8H	77.33±3.58	76.87±7.52	1.454	0.289
HR_post10H	77.36±10.43	77.83±7.62	1.784	0.232
HR_post12H	77.55±6.25	77.37±5.85	0.125	0.895
HR post 24H	76.54±1.95	76.15±3.06	0.085	0.902

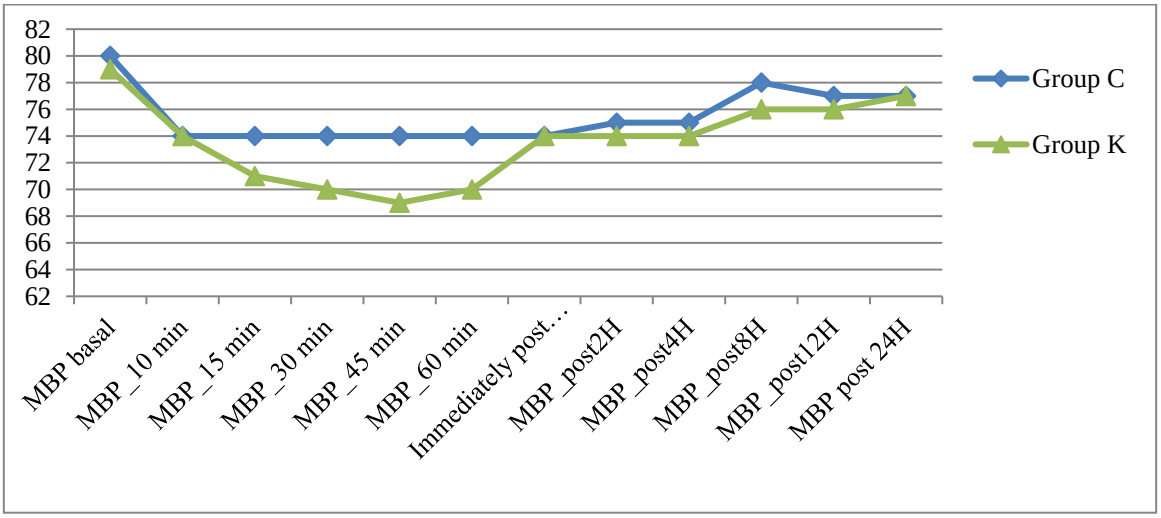

Fig (2) heart rate distribution among the studied groups at different time periods.

Table (4): Oxygen saturation distribution among the studied groups

SPO2% /minute	Group C(N=30)	Group K(N=30)	F	P
SPO2 basal	97.45±2.2	97.84±1.98	0.001	0.999
SPO2_10 min	97.56±2.63	97.5±1.63	0.067	0.932
SPO2_15 min	97.88±1.66	97.83±0.7	0.195	0.823
SPO2_30 min	97.83±1.71	96.83±1.76	1.600	0.282
SPO2_45 min	97.25±1.85	96.91±1.3	0.257	0.774
SPO2_60 min	97.75±1.72	97.83±1.8	0.464	0.631
Immediately post operative	97.58±1.88	96.83±1.43	2.046	0.137
SPO2_post2H	97.5±1.74	97.35±1.6	0.355	0.802
SPO2_post4H	97.75±1.7	97.22±1.19	0.434	0.666
SPO2_post10H	97.53±1.81	97.73±1.66	1.510	0.393
SPO2_post8H	97.83±1.57	97.29±1.03	1.162	0.326
SPO2_post10H	97.63±1.71	97.83±1.76	1.610	0.292
SPO2_post12H	98.5±1.47	97.9±0.88	1.039	0.358
SPO2 post 24H	98.87±0.99	98.5±0.88	1.239	0.312

Table (5) : Visual Analogue Scale during scheduled times in the studied groups

	Group C(N=30)	Group K(N=30)	Kruskal Wallis	P
Immediately post-operative	4.0 (1-6) *	0.0 (0-1)	58.63	0.00**
VAS2	3.0 (1-5) *	0.0 (0-1)	54.411	0.00**
VAS4	3.0 (2-6) *	1.0 (0-2)	27.663	0.00**
VAS6	3.0 (2-7) *	1.0 (0-3)	24.362	0.00**
VAS8	4.0 (2-5) *	2.0 (1-4)	35.186	0.00**
VAS10	4.0 (3-5) *	2.0 (0-4)	34.176	0.00**
VAS12	4.0 (3-5) *	2.0 (0-3)	28.271	0.00**
VAS24	3.0 (2-4)	2.0 (1-4)	2.034	0.154

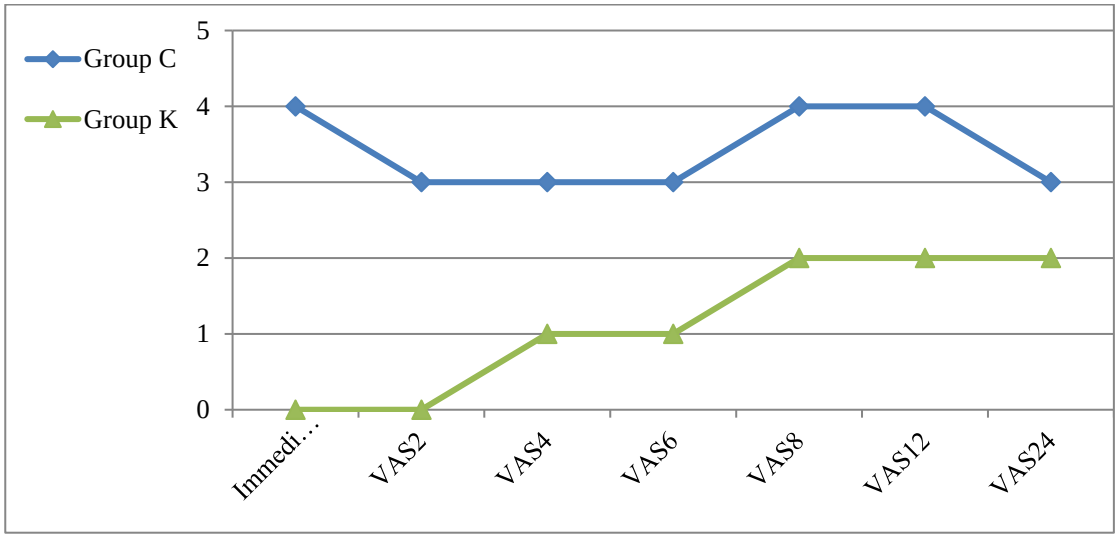

Fig (3) Visual Analogue Scale during scheduled times periods among the studied groups

Table (6): The time to the first analgesic request, morphine consumption, and patient satisfaction among the studied groups

			Group C(N=30)	Group K(N=30)	F	P
time of the first analgesic request (h)			5.13±0.81#	9.20±1.21*	228.66	0.00**
dose of morphine /24 hours (mcg)			75.66±31.62*	35.50±13.85#	21.34	0.00**
Patient satisfaction	Not	N	10	3		
		%	33.3%	10.0%		
	Average	N	15	5	23.011	0.00**
		%	50.0%	16.7%		
	Good	N	5	22		
		%	16.7%	73.3%		
Total		N	30	30		
		%	100.0%	100.0%		

Table (7): Complications distribution among the studied groups

		Group C (N 30)	Group K (N 30)	X^2	P
Nausea	N	4	8	3.36	0.18
	%	13.3%	26.7%		
Vomiting	N	5	5	3.31	0.19
	%	16.7%	16.7%		
Shivering	N	2	5	3.56	0.16
	%	6.7%	16.7%		
Bradycardia	N	3	4	7.91	0.19
	%	10.0%	13.3%		
Hypotension	N	3	4	0.22	0.89
	%	10.0%	13.3%		
Total	N	30	30		
	%	100.0%	100.0%		

5. DISCUSSION

Cesarean delivery represents about 54% of all obstetric operations and causes moderate to severe postoperative pain. Infiltration of the wound site might be used to improve postoperative pain control. Ryu, C. et al.2022

Treatment of pain related to cesarean delivery involves different strategies. Non-opioid systemic analgesic agents are widely used in different regimens. Nonetheless, opioid-sparing agents are occasionally not potent enough to achieve adequate pain control after cesarean delivery, and opioids are universally used Garmi, et al 2022 Consequently, several studies have reported that excessive amounts of opioids are being prescribed to women after cesarean delivery. These agents are associated with numerous adverse effects, and the risk of chronic use after cesarean delivery is of great concern Badreldin, N et al2018, Bateman, B. et al.2017

Infiltration of the wound with local anaesthetics is one of the techniques that has been used in a range of surgical procedures for postoperative pain control. The technique affects somatic pain created by the surgical wound without producing major adverse effects Sedek, A. et al.2015 The results of the present work showed that there was no significant difference among studied groups regards Age, BMI and ASA distribution ($p > 0.05$). which is in agreement with the study of Oham, A. et al.2020. who found that there was no significant difference among studied groups regarding age, body weight and ASA distribution ($p> 0.05$). also, agreed with the study of Shafqat, E et al.2019. who reported that there was no significant difference among studied groups regards Age, or weight between group A (bupivacaine) and group B (bupivacaine plus ketamine). Kazemeini et al.2014 concluded a similar result. Also, Rizk et al.2022 found that Age was distributed respectively with no statistically significant differences among groups. Also, there were no statistically significant differences regards BMI, or ASA distribution ($p > 0.05$). The current results showed that there were no significant differences among both groups regarding as regards the mean arterial blood (MAP), Oxygen saturation and Heart rate at different periods ($P> 0.05$). which is in agreement with the study of Mostafa and Mekki,2018 who found that there was no significant difference among studied groups regarding mean arterial blood at all different times. Also, Oham et al.2020 reported that there were no significant differences among both groups regarding as regards Oxygen saturation and Heart rate at different periods ($P> 0.05$), but in contrast regarding the mean arterial blood (MAP), there was a significant difference between the studied group (63.03 ± 3.83) for bupivacaine plus ketamine group and (65.32 ± 3.16) for bupivacaine alone group. Also, Rizk et al.2022 reported that there was no significant difference between the bupivacaine group versus bupivacaine with ketamine ketamine groups regarding HR at different times. This present study showed significantly lower VAS scores during rest and cough in the ketamine group up to 12 hrs postoperatively compared to the Bupivacaine alone group but there was no significant difference among the studied groups regarding 24 Hrs. These results are under that of Mohamed et al.2018 who reported that there was a reduction in postoperative pain scores in the ketamine group in comparison with the group bupivacaine. Jha et al.2013 noted that subcutaneous ketamine plus bupivacaine infiltration provided a longer favourable pain score state of up to 12 hours with a low pain score of less than 4 and also lower analgesic demand in patients. Also, Javid et al.2012 corroborated the efficacy of low-dose subcutaneous ketamine in achieving low and favourable pain scores in their study. They observed lower pain scores in the ketamine groups compared to the control group.

The current study showed that the time to the first analgesic request, was significantly longer in the K group when compared with the C groups ($p< 0.001$). Also, group K had significantly the lowest dose of morphine consumption during 24 hours postoperatively compared with the C groups ($p < 0.001$). These results are in agreement with that of Mohamed et al.2018 who compared the analgesic and stress-attenuating effects of adding ketamine as an adjuvant to bupivacaine versus bupivacaine alone in local wound infiltration for patients undergoing total abdominal hysterectomy, and showed that time to the first request of rescue analgesia was significantly prolonged in bupivacaine plus ketamine group compared to the bupivacaine alone group alone and found that morphine consumption was significantly less in bupivacaine plus ketamine group than bupivacaine alone group.

Mostafa and Mekki,2018 showed that the time to first request analgesia was longer in the BK group (20.26 ± 0.8 h) as compared to the B group (7.73 ± 1.9 h). Also, total pethidine consumption was also lower in the BK group when compared to the B group (11.58 ± 6 mg versus 53.75 ± 16.8 mg) and that difference was highly statistically significant.

Also, Garcia et al.2019 reported that the addition of ketamine or dexmedetomidine to local anaesthetics wound infiltration increased time to the first analgesia request and decreased total analgesic consumption, but ketamine was found superior. Total postoperative analgesic consumption is also an index of efficacy and quality of analgesia. Oham et al.2020 found that postoperative analgesic consumption was significantly lower in group I who received multimodal analgesic therapy (bupivacaine plus ketamine) than in group II (bupivacaine alone group).

In line with our findings, the study by Kazemeini et al. (2014) observed that the group receiving ketamine plus bupivacaine required the least rescue analgesia over a 24-hour period compared to other groups. A longer time until the first analgesic request in the postoperative period indicates better pain control. Oham et al. (2020) found that administering subcutaneous ketamine in conjunction with surgical wound infiltration of plain bupivacaine resulted in an extended time before the first analgesic request. This finding can be attributed to the analgesic properties of ketamine, even at low doses, and its slow release into the bloodstream from the subcutaneous route.

In the current study, there was a highly significant difference in patient satisfaction between the groups, with those in the ketamine group reporting a higher satisfaction rate than those in the control group. The low satisfaction in the control group may be due to an earlier onset of pain. These results align with those of Rizk et al. (2020), who also reported a significant difference in patient satisfaction, indicating higher satisfaction rates in the ketamine group compared to the control group. Furthermore, Oham et al. (2020) noted that the dose of ketamine used was well tolerated, resulting in greater satisfaction among patients in the ketamine group than in the control group. This high level of satisfaction could be attributed to the low dose and the slow release of subcutaneously administered ketamine into the systemic circulation.

The high level of satisfaction expressed by parents and guardians suggests that the patients received adequate anaesthesia and analgesia with minimal side effects. Guardians and parents in the combination group showed higher satisfaction, likely due to the longer time to the first analgesic request and lower postoperative analgesic consumption in this group.

Regarding complications (such as nausea, vomiting, shivering, or hypotension), no significant differences were noted among the studied groups. This finding is consistent with Hala et al. (2018), who reported no significant differences in the incidence of side effects between the groups. Additionally, Javid et al. (2012) corroborated the efficacy of low-dose subcutaneous ketamine, noting minimal side effects. The low incidence of side effects following the administration of low-dose subcutaneous ketamine may be due to the plasma level of ketamine remaining below 150 ng/ml. Mostafa and Mekki (2018) found that an overall analysis indicated that postoperative complications, such as nausea and vomiting, were not statistically significant between the two study groups, except at the 6th hour; however, this difference was not clinically significant. No other side effects were reported.

Menkiti et al.2013 reported that the incidence of complications was similar in both groups. Hypotension was the most common complication followed by shivering. There was no difference in the mean dose of ephedrine given between the groups (P = 0.56). No complication was recorded in 12 patients in Group B and 10 patients in Group BK. Shafqat et al.2019 reported that the addition of preservative-free drugs like ketamine enhanced the time of postoperative analgesic effects in patients below diaphragm surgery. The dose of ketamine caudal block is controversial, many previous studies determine the dose of ketamine but it was not justified properly, 0.5mg per kg is an optimum dose of ketamine for the caudal epidural blockade. Rizk et al.2020 demonstrated that Surgical wound administration of ketamine may reduce the adverse hemodynamic effects of its intravenous administration while still providing postoperative analgesia. Jha et al.2013 reported that surgical site infiltration with either bupivacaine or ketamine provides adequate analgesia and is devoid of major side effects and that the ketamine supplement is superior to bupivacaine in terms of requirement of rescue analgesics, peaceful sleep pattern, and early resumption of feeding. The present study used bupivacaine versus bupivacaine with ketamine in wound infiltration for postoperative analgesia in cesarean section operation and found that adding ketamine with bupivacaine has a better effect than bupivacaine alone as regards hemodynamic stability, the time to the first analgesic request, patients' satisfaction and the total dose of morphine consumption during 24 hours post-operatively.

6.CONCLUSION

The current study concluded that adding ketamine with bupivacaine in wound infiltration has a better effect as regards hemodynamic stability, the time to the first analgesic request, patients' satisfaction and the total dose of morphine consumption during the 24 hours post operatively, compared with the bupivacaine alone group.

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