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Hyoscine and Lidocaine-Prilocaine Cream for Prevention of Postoperative Catheter-Related Bladder Discomfort: A Prospective Randomized Trial

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Abstract

Catheter-related bladder discomfort is an uncomfortable complication for patients undergoing urinary catheter placement during surgery. Hyoscine and lidocaine-prilocaine cream affect catheter-related bladder discomfort, but it is not clear which is more effective. This study aimed to evaluate the effects of two drugs on the prevention of catheter-related bladder discomfort. In this triple-blinded prospective randomized clinical trial, 105 patients undergoing non-urological surgery that required intraoperative urinary catheterization were selected by convenience sampling and divided into three groups using random methods. The hyoscine group (n=35) received 20 mg of intravenous hyoscine immediately before the end of anesthesia. The catheter was dipped in 3 g lidocaine-prilocaine cream for catheterization in the lidocaine-prilocaine group (n = 35). Routine interventions were performed in the control (lidocaine) group (n = 35). The catheter was dipped in 3 g lidocaine cream for catheterization in the hyoscine and control groups. The incidence and severity of catheter-related bladder discomfort were assessed one, two, three, and four hours after the end of anesthesia. In the first hour after anesthesia, the incidence of catheter-related bladder discomfort in the hyoscine group was lower than that in the other groups ($p=0.028$), but 2, 3, and 4 h after anesthesia didn't differ ($p>0.05$). The severity of catheter-related bladder discomfort wasn't significantly different among the three groups ($p<0.05$). According to the results, intravenous hyoscine is more effective than lidocaine and lidocaine-prilocaine creams in preventing catheter-related bladder discomfort. Therefore, this drug could be used for preventing catheter-related bladder discomfort.

Keywords: *hyoscine, lidocaine, prilocaine, bladder discomfort.*

Introduction

Today, urinary catheters are commonly used (Lachance & Grobelna 2019). In hospitals, about 15 to 25% of patients undergo bladder catheterization (Clarke et al. 2020; U.S. Centers for Disease Control and Prevention 2020). Bladder catheterization is a high-risk procedure commonly used for patients during surgery (Rostami Nouri et al. 2016). The catheter causes severe bladder irritating symptoms as a foreign body in the bladder like urinary tract infection, urethral and bladder damage, and Catheter-Related Bladder Discomfort (CRBD) (Park et al. 2019). This complication is associated with symptoms of pain and discomfort in the suprapubic area, burning sensation and severe need to urinate, restlessness, muscle tension, crying for help, and trying to remove the urinary catheter (Xiaoqiang et al. 2017; Sabetian et al. 2017).

Most patients who undergo surgery for urinary catheterization complain of CRBD (Hu et al. 2016) and it is a well-known problem in the post-anesthesia ward (Bach et al. 2020). Discomfort from urinary catheterization is a concern for the patient on which, and analgesics are ineffective (Agarwal et al. 2006). The rate of CRBD during postoperative recovery is reported to be 47-90% (Li et al. 2020). Some reports have reported the rate as 17-61% after non-urological surgery (Bai et al. 2015).

There are various methods for the prevention and treatment of CRBD, including topical creams and medication (Xiaoqiang et al. 2017; Bach et al. 2020; Bai et al. 2015; Zhou et al. 2017; Mu et al. 2017), but it remains unclear which intervention is more effective as a definitive method for its prevention and treatment. Various drugs have been used to manage CRBD, but some drugs like ketamine and tramadol, cause sedation, dry

mouth, hallucination, and diplopia (Akça et al. 2017; Mu et al. 2017). Hyoscine has sedative and antispasmodic effects on smooth muscle as studies have shown (Davis, 2020), and reduces the severity and incidence of CRBD and the need for analgesics during the hospitalization of patients during recovery (Sabetian et al. 2017). Another method to prevent CRBD is to use topical anesthetic creams such as lidocaine-prilocaine, which has been shown to reduce CRBD (Mu et al. 2017). But the difference between the two drugs in the prevention and treatment of CRBD is not clear; therefore, this study was conducted to compare the effects of hyoscine and lidocaine-prilocaine cream on CRBD.

Methods

Study design

This triple-blind prospective randomized clinical trial study was conducted on patients who undergo non-urologic operations and were referred to Bohlool Hospital in Gonabad from Avril to August 2021. The study protocol was approved on February 20th, 2021 by the ethics committee of Gonabad University of Medical Sciences (protocol approved ID: IR.GMU.REC.1399.125). Before taking part, written informed consent was obtained from all patients. The study was registered at the Iranian Clinical Trial System (IRCT code: IRCT20210228050530N1). This clinical trial included two intervention groups and a control (lidocaine) group. The random allocation to these three groups was proportional (random assignment ratio: 1.1.1).

Eligibility criteria

In this study, the inclusion criteria were: age 18-60 years, general anesthesia with class one and two American Society of Anesthesiologists classification, and non-urological elective surgery. Exclusion criteria were a history of bladder obstruction, overactive bladder, severe kidney and liver disease, chronic pain, cerebrovascular disorders, psychosis, neurological bladder, untreated closed-angle glaucoma, bleeding, ileus paralysis, pulmonary chronic disease, and chronic sedative abuse.

Interventions

Electrocardiography, pulse oximetry, and blood pressure measurements were performed in all three groups. Midazolam 0.02 mg/kg and fentanyl (2 µg/kg) was injected intravenously into all patients. Using 5 mg/kg sodium thiopental, general anesthesia was induced. Atracurium 0.5 mg/kg was injected for muscle relaxation. Intubation was then performed. Propofol 0.1-0.2 mg/kg/min and remifentanil 0.5 g/kg/min were prescribed with 100% oxygen and the atracurium 0.15 mg/kg was repeated every 20 minutes for maintenance of anesthesia. The mechanical ventilator was adjusted to maintain the exhaled carbon dioxide in the range of 30-40 mmHg. 6 mg morphine was prescribed to all patients to induce intraoperative analgesia. To reverse muscle relaxation, neostigmine (0.05 mg/kg) and atropine (0.03 mg/kg) were prescribed at the end of the surgery. After the patient had adequate spontaneous ventilation and responded to all instructions, the chip tube was removed. In cases where the need arose, 50 mg of intravenous pethidine was injected as rescue analgesia in the recovery room. All analgesics used were recorded during the first 4 h after anesthesia. The urinary catheter was impregnated with 3g of 2% lidocaine gel made by Iran, Iran Darou Company, after induction of anesthesia in the hyoscine and control groups. In the lidocaine-prilocaine cream group, before urinary catheterization, the urinary catheter was impregnated with 3g of lidocaine-prilocaine cream made by Iran, Iran Darou Company. Catheterization was performed with Foley catheter number 14 for men and 12 for women by a nurse of the same gender as the patient and with full observance of sterilization tips. The catheter balloon was filled with 10 ml of distilled water. The catheter was fixed in the proper position without traction. In the hyoscine group, 20 mg of hyoscine n-butyl bromide was injected intravenously one minute before the removal of the endotracheal tube.

Outcome Measures

Baseline variables included age, sex, height, weight, level of education, and type and duration of surgery. The incidence and severity of CRBD were considered the primary outcomes. The use of analgesics was considered a secondary outcome. Patients were evaluated for analgesic use and the incidence and severity of CRBD at one, two, three, and four hours after the end of anesthesia. Patients were classified into four categories according to the severity of CRBD: no discomfort, mild, moderate, and severe.

1. If a patient had no physical or behavioral symptoms, she/he was classified as having no discomfort.
2. If it was possible to diagnose the physical symptoms of CRBD by asking the patients if there were no behavioral symptoms, they were classified as having mild discomfort.
3. If it was possible to diagnose physical symptoms of CRBD without asking the patient, but the patient had no behavioral symptoms, they were classified as having moderate discomfort.
4. If the patient expressed physical symptoms of CRBD along with behavioral symptoms, such as restlessness and muscle tension, crying for help, and trying to remove the urethral catheter, they were classified as having severe discomfort (Sabetian et al. 2017).

Sample size and randomization

The sample size was calculated based on the results of the study by Mu et al. study (2017) for the variable of CRBD incidence and the study by Akça et al. (2017) for the variable of pain incidence in CRBD. Using a confidence coefficient of 95% and a test power of 80% in each group, the sample size was estimated to be 24 for the CRBD incidence and 32 for the pain variable. Thus, a sample size of 32 was considered for each group and was increased to 35 in each group, considering a possible drop rate of 10%.

$$n = \frac{2\left(z_{1-\alpha/2}\right)^2 \bar{P}(1-\bar{P})}{(P_1 - P_2)^2} = \frac{2(1.96)^2 0.4(1-0.4)}{(0.52-0.28)^2} = 32$$

One thousand eighty-one patients were enrolled in this study. Finally, one hundred and five subjects among the enrollment population, who met the inclusion criteria, were selected by the convenience sampling method (Fig 1). The balanced blocking randomization method with three permutation blocks was used to assign patients to the three study groups. For this purpose, letter A was considered for the control group, letter B for the lidocaine-prilocaine cream group, and letter C for the hyoscine group. There are six possible states in the triple-permutation block: CBA, CAB, BCA, BAC, ACB, and ABC. Using a table of random numbers, 35 numbers were selected from one to six. The letters in the 35 blocks were numbered from one to 105. Two separate lists of blocks were prepared for both genders to homogenize the three groups in terms of gender. The selected patients were divided into three groups.

Blinding

All patients were fully informed about the processes related to the three study groups before anesthesia. It was also explained that they would be randomly assigned to one of the three groups, but the subjects did not know which study groups they belonged to. Furthermore, considering the catheterization time (after anesthesia induction) when the patient was not conscious, the patient was not aware of the group to which they had been assigned. The results were evaluated by a trained nurse who was blinded to the patient groups. In addition, the statistical analyst did not know the study group to which each patient belonged. For the evaluator and analyst, the group statistics were determined using codes.

Statistical analysis

First, the quantitative variables of natural distribution were evaluated using the Kolmogorov-Smirnov test. To analyze the data, a one-way ANOVA test, Kruskal-Wallis test, and Chi-square test, and in cases where Chi-square test conditions were not met, the likelihood test was used, or exact p was reported. In all tests, a significance level of 0.05 was considered.

Results

Participant flow

Fig 1.

Baseline data

One hundred and five patients (male and female) were included in the study. The groups were homogeneous in terms of baseline variables ($p < 0.05$) (Table 1).

Table 1.

Primary outcomes

The primary outcomes were the incidence and severity of CRBD. The incidence of CRBD was not significantly different between the groups at the second, third, and fourth hours after the end of anesthesia. However, in the first hour, the incidence of CRBD in the hyoscine and lidocaine-prilocaine groups was significantly lower than that in the control group ($p = 0.028$) (Table 2).

Table 2.

CRBD severity did not differ between groups at any time point statically ($p > 0.05$). However, the numerical value of the severity of CRBD at the severe level in the first hour after the end of anesthesia indicates that it was lower in the hyoscine group than in the other two groups. (hyoscine 2.9%, lidocaine-prilocaine 8.6%, and lidocaine 20% group). (Table 3).

Table 3.

Secondary outcomes

The number of analgesics used in the first hour after the end of anesthesia in the hyoscine group was less than that in the other two groups ($p = 0.01$). No significant differences were observed at two, three, or four hours after the end of anesthesia ($p > 0.05$) (Table 4).

Table 4.

Discussion

The present study showed that the incidence of CRBD in the first hour after the end of anesthesia was lower in the hyoscine group than in the other two groups. This is consistent with the results of the Sabetian and Nam study (Sabetian et al. 2017; Nam et al. 2018) The results also showed that the incidence of CRBD decreased significantly in the intervention and control groups by the fourth hour after the end of anesthesia, which is in line with the results of the Sabetian et al. (2017) and Nam et al study. The findings of the study by Zhou et al. (2021) also showed that anti-muscarinic, such as hyoscine, could reduce the incidence of CRBD without significant side effects, which is consistent with the findings of the present study.

In contrast, Al-Shawi et al. (2018) examined the effect of hyoscine on CRBD in male patients undergoing urological surgery and found that hyoscine injection before the end of anesthesia did not affect the incidence of CRBD during the first hour after anesthesia. These results were not consistent with the results of the present study. One of the reasons for this is the difference in the types of research units and surgery. In this regard, it should be mentioned that male sex and urological operations are effective in reducing the incidence of CRBD (Mitobe et al. 2023), and in the Al-Shawi study et al. (2018), only male patients underwent urological surgery.

To justify the effect of hyoscine on CRBD, it has been argued that hyoscine is a muscarinic antagonist. Ant-muscarinic can block the muscarinic receptors of the detrusor muscle and reduce its contraction intensity, effectively preventing or reducing CRBD (Zhou et al. 2021). Hyoscine has a high affinity for M2 and M3 muscarinic receptors, which are responsible for contractions of the bladder detrusor muscles. The mechanism by which hyoscine relieves CRBD may be its anti-muscarinic and antispasmodic effects, as well as its relaxing effect on the bladder (Nam et al. 2018).

The present study also showed that lidocaine-prilocaine cream can reduce the incidence of CRBD compared to the control.

This finding was consistent with the results reported by Etezadi et al. (2018). They applied urethral lubrication gel with 5 mL of 2% lidocaine hydrochloride gel in conjunction with 100 mg of ketamine and examined the incidence of CRBD after surgery. The results showed that a combination of lidocaine gel with other drugs could be more effective in reducing CRBD than lidocaine gel alone. This finding is consistent with the results of the Mu study (2017) because it showed that lidocaine-prilocaine cream can reduce CRBD in patients undergoing elective surgery. These results are consistent with the results of the present study.

To justify the reduction in CRBD due to the use of lidocaine-prilocaine cream, it can be argued that local anesthesia using local anesthetic cream reduces the patient's anxiety and discomfort. When lidocaine-prilocaine cream is applied to the mucous membrane, the anesthetic penetrates rapidly and absorption from the mucosa occurs within 5 to 7 min. Lidocaine and prilocaine reduce CRBD by acting on pain receptors and nerve endings (Mu et al. 2017).

The results of the present study showed that the severity of CRBD was not significantly different among the three groups. However, according to the numerical value of CRBD severity in the hyoscine, lidocaine-prilocaine, and control groups, the CRBD severity was the lowest in the hyoscine group and was lower in the lidocaine-prilocaine group than in the control group. This finding is consistent with that of Al-Shawi et al. (2018), Salama et al. (2017), and Sabetian et al. (2017). The results of a study by Ryu et al. (2013) showed that hyoscine could reduce the severity of CRBD and increase heart rate within six hours after hyoscine injection. This was inconsistent with the results of the present study because, in the present study, the effect of hyoscine on reducing the severity of CRBD was not significant during the two to fourth hours after anesthesia and had no effect on heart rate. Since masculinity and urological surgeries affect CRBD (Mitobe et al. 2023), one of the reasons for inconsistency is the male sex and urological surgery in Ryu's study (2013).

The results of the present study showed no significant difference in CRBD severity between the lidocaine-prilocaine and control groups. Meanwhile, the results of the study by Etezadi et al. (2018) showed that ketamine-lidocaine gel can reduce the severity of CRBD within two hours after anesthesia compared to the control group. The results of the study are not consistent with the present study. In Etezadi et al.'s study (2018), ketamine was used in combination with lidocaine, which is one of the reasons for the inconsistency in the results of the present study and Etezadi et al. This may have been due to the effects of ketamine. The findings of the present study were also inconsistent with the results of Mu et al. (2017) which showed that lidocaine-prilocaine cream can reduce the severity of CRBD. Since the male gender is effective on CRBD,(Mitobe et al. 2023) one of the reasons for the inconsistency of the results is the masculine samples in the study of Mu et al. (2017).

The results of the present study showed that the number of analgesics used in the first hour after anesthesia in the hyoscine group was less than that in the control group but was not significantly different at two, three, or four hours after anesthesia. The results of studies by Sabetian et al.(2017), Zhou et al. (2021), and Ryu et al. (2013) showed that hyoscine can reduce the number of analgesics in patients, which is consistent with the present study. The results of the studies by Nam and Salama showed that there was no significant difference in the number of analgesics used between the hyoscine group and other groups(Nam et al. 2018; Salama et al. 2017) which is inconsistent with the present results.

In the present study, the side effects of hyoscine resulting from its anti-muscarinic properties were not significant. Anti-muscarinic can cause side effects, including nausea, vomiting, and dry mouth. (Zhou et al. 2021) In some studies, the side effects of hyoscine were reported more frequently than in the control group, and in other studies, these side effects were not significant (Sabetian et al. 2017; Ryu et al. 2013). In the present study, lidocaine-prilocaine cream had no side effects. Various studies have confirmed that local anesthetics, such as lubricant gels, do not have significant side effects (Mu et al. 2017; Imai et al. 2020).

Limitations and advantages

A limitation of the present study is that it was performed on patients with non-urological surgeries, and the results of the study are not generalizable to urological surgeries. One of the advantages of the present study is its triple-blind structure, with two intervention groups and a control group, which makes the results more robust.

Conclusion

According to the results, the hyoscine (combination of lidocaine-hyoscine) was more effective than lidocaine-prilocaine creams and lidocaine (control) in preventing or reducing the incidence of CRBD. Therefore, hyoscine could be used to prevent CRBD.

Ethical and financial statements

The study protocol was approved on February 20th, 2021 by the ethics committee of Gonabad University of Medical Sciences (protocol approved ID: IR.GMU.REC.1399.125).

The authors declare that they have no financial support and sponsorship.

Contribution: Study conception and design by [**Faezeh Khajeh**], [**Mahdi Basiri Moghadam**], [**Arash Hamzei**], and [**Hosein Ajamzibad**]. Material preparation, data collection, and analysis were performed by [**Faezeh Khajeh**], [**Mahdi Basiri Moghadam**], and [**Hosein Ajamzibad**]. The first draft of the manuscript was written by [**Faezeh Khajeh**], [**Mahdi Basiri Moghadam**], and [**Hosein Ajamzibad**]; Commented on previous versions of the manuscript by [**Faezeh Khajeh**], [**Mahdi Basiri Moghadam**], and [**Hosein Ajamzibad**]. Read

and approved the final manuscript [**Faezeh Khajeh**], [**Mahdi Basiri Moghadam**], [**Arash Hamzei**], and [**Hosein Ajamzibad**].

CRediT taxonomy: Conceptualization: [**Faezeh Khajeh**], [**Mahdi Basiri Moghadam**], [**Arash Hamzei**], and [**Hosein Ajamzibad**]; Methodology: [**Faezeh Khajeh**], [**Mahdi Basiri Moghadam**], [**Arash Hamzei**], and [**Hosein Ajamzibad**]; Formal analysis and investigation: [**Faezeh Khajeh**], [**Mahdi Basiri Moghadam**], and [**Hosein Ajamzibad**]; Writing - original draft preparation: [**Faezeh Khajeh**], and [**Hosein Ajamzibad**]; Writing - review and editing: [**Faezeh Khajeh**], [**Mahdi Basiri Moghadam**], [**Arash Hamzei**], and [**Hosein Ajamzibad**]; Funding acquisition: [**Faezeh Khajeh**], and [**Hosein Ajamzibad**]; Resources: [**Faezeh Khajeh**]; Supervision: [**Hosein Ajamzibad**].

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Declaration of Competing Interest

The authors declare that they have no competing interests.

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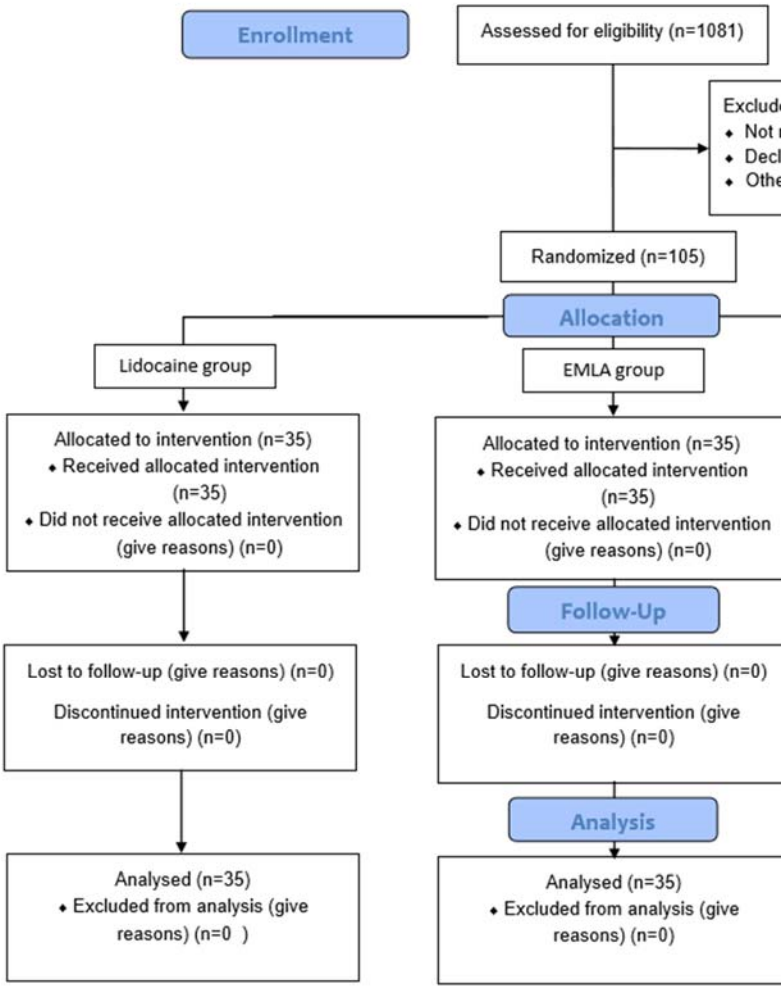
Fig 1. Flowchart of the randomized clinical trial.



Group

Table 1: Baseline characteristics of the subjects

Variable	Variable Level	**Hyoscine (n=35)**	Lidocaine-prilocaine	**Control (n=35)**	**P value**
Age (year)		41.45 ± 11.26	43.28 ± 12.47	48.43 ± 17.12	0.74*

Gender	**Male**	17(31.5)	19(35.2)	18(33.3)	0.89**
	Female	18(35.3)	16(31.4)	17(33.3)	
Height (cm)		171.91 ± 10.88	172.02 ± 9.61	171.57 ± 10.01	0.98*
Weight (kg)		75.97 ± 13.60	77.28 ± 12.86	76.42 ± 10.67	0.90*
Education level	**Elementary School**	8(33.3)	9(37.5)	7(22.9)	0.98**
	Middle and High school	9(34.6)	8(30.8)	9(34.6)	
	Diploma and Collegiate	18(32.7)	18(32.7)	19(34.6)	
Type of surgery	**Neurosurgery**	19(35.2)	16(29.6)	19(35.2)	0.91**
	Gynecological surgery	8(33.3)	8(33.3)	8(33.3)	
	General surgery	8(29.6)	11(40.8)	8(29.6)	
Duration of surgery (Minute)		207.71 ± 68.07	201.42 ± 56.62	220.85 ± 59.67	0.41*

* One-way ANOVA test ** Chi-square test

Table 2: Incidence of CRBD

Time	Incidence of CRBD	Group			p value
		Hyoscine (n=35)	Lidocaine-prilocaine (n=35)	Lidocaine (n=35)	
1	Yes	9(25.7)	14(40.0)	20(57.1)	0.028*
	No	26(74.3)	21(60.0)	15(42.9)	
2	Yes	8(22.9)	12(34.3)	17(48.6)	0.078*
	No	27(77.1)	23(65.7)	18(51.4)	
3	Yes	5(14.3)	8(22.9)	12(34.3)	0.143*
	No	30(85.7)	27(77.1)	23(65.7)	
4	Yes	4(11.4)	3(8.6)	9(25.7)	0.102*
	No	31(88.6)	32(91.4)	26(74.3)	

* Chi-square test

1= One hour after the end of anesthesia; 2= Two hours after the end of anesthesia; 3= Three hours after the end of anesthesia; 4= Four hours after the end of anesthesia.

Table 3: severity of CRBD

Time	Level severity of CRBD Timing	Group			p
		Hyoscine (n=35)	Lidocaine-prilocaine (n=35)	Control (n=35)	
1	None	26(74.3)	21(60.0)	15(42.9)	0.14*
	mild	5(14.3)	6(17.1)	8(22.9)	
	moderate	3(8.6)	5(14.3)	5(14.3)	
	sever	1(2.9)	3(8.6)	7(20.0)	
2	None	27(77.1)	23(65.7)	18(51.4)	0.16**
	mild	7(20.0)	9(25.7)	10(28.6)	
	moderate	1(2.9)	3(8.6)	5(16.3)	
	sever	0(0.0)	0(0.0)	2(5.7)	
3	None	30(58.7)	27(77.1)	23(65.7)	0.31**
	mild	5(14.3)	7(20.0)	10(28.6)	
	moderate	0(0.0)	1(2.9)	2(5.7)	
4	None	31(88.6)	32(91.4)	26(74.3)	0.10*
	Mild	4(11.4)	3(8.6)	9(25.7)	

*Likelihood ** Exact p

1= One hour after the end of anesthesia; 2= Two hour after the end of anesthesia; 3= Three hour after the end of anesthesia; 4= Four hour after the end of anesthesia

Table 4: Incidence of hyoscine side effects, using analgesics, and severity of CRBD pain

Variables		Group			p value
		Hyoscine (n=35)	Lidocaine-prilocaine (n=35)	Control (n=35)	
Nausea and Vomiting	Yes	3(8.6)	6(17.1)	6(17.1)	0.50*

Dry mouth		**No**	32(91.4)	29(82.9)	29(82.9)	
		Yes	31(88.6)	32(91.4)	30(85.7)	0.75**
	1	**No**	4(11.4)	3(8.6)	5(14.3)	
		Yes	6(17.1)	12(36.3)	18(51.4)	0.01*
	2	**No**	29(82.9)	23(65.7)	17(48.6)	
Analgesics		**Yes**	18(51.4)	16(65.7)	11(31.4)	0.22*
	3	**No**	17(48.6)	19(54.3)	24(68.6)	
		Yes	5(14.3)	4(11.4)	3(8.6)	0.75**
	4	**No**	30(85.7)	31(88.6)	32(91.4)	
		Yes	6(17.2)	5(14.3)	6(17.2)	0.93*
		No	29(82.9)	30(85.7)	29(82.9)	
VAS		**1**	3.57 ± 10.53	5.28 ± 13.55	6.94 ± 14.75	0.56***
		2	2.00 ± 6.62	3.00 ± 8.51	4.77 ± 11.12	0.51***
		3	0.34 ± 2.02	1.17 ± 4.82	1.57 ± 6.72	0.79***
		4	0.28 ± 1.69	0.00 ± 0.00	0.82 ± 4.90	0.60***

* Chi-square test ** likelihood Ratio *** One-way ANOVA test *** Kruskal-Wallis test

1= One hour after the end of anesthesia, 2= Two hours after the end of anesthesia, 3= Three hours after the end of anesthesia, 4= Four hours after the end of anesthesia