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Comparing the effect of local injection of combined morphine, triamcinolone and lidocaine and lidocaine injection on pain intensity after mastoidectomy-tympanoplasty; a triple-blind clinical trial

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Abstract

Introduction: Postoperative pain control is one of the patient's rights and the challenges of surgeons and anesthesiologists since about 20% of patients experience severe pain in the first 24 hours after surgery. Mastoidectomy and tympanoplasty are common surgeries in the head and neck area, in which profound and long-term analgesia is essential.

Objectives: The present study investigated the effect of the combination of topical morphine, triamcinolone, and lidocaine compared to the control group.

Patients and Methods: In the current clinical trial, 68 patients' candidates for mastoidectomy-tympanoplasty surgery were included and randomly divided into intervention and control groups. The variables of demographic, pain, hemodynamics, extubation time, and received opioids were measured.

Results: The results of the current study indicated a significant reduction in the patient's pain scores in both groups ($P=0.001$), while the patients of group 1 had significantly lower pain scores than group 2 after 8, 12, and 24 hours in the ward ($P<0.05$). Moreover, a significant reduction was observed in systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) in all patients during surgery ($P<0.001$). However, in patients who received morphine, triamcinolone, and lidocaine (group 1), SBP and MAP were significantly lower than group 2 after 40, 80, 100, 120, 140, and 160 minutes during surgery ($P<0.05$).

Conclusion: The present study indicated that the combination of morphine, triamcinolone, and lidocaine compared to the control group could lead to better pain control, further reduction of SBP and MAP, reduction of post-operative opioid use, and delay during the first opioid administration.

Trial Registration: The trial protocol was approved by the Iranian Registry of Clinical Trials (identifier: IRCT20200825048515N39; https://irct.ir/trial/57931, ethical code; IR.MUI.MED.REC.1400.064).

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Introduction

Postoperative pain is a significant concern of anesthesiologists and their patients, yet surgical patients often experience inadequate postoperative pain control. Approximately 20% of patients experience severe pain in the first 24 hours after surgery that has remained almost fixed for the past 30 years (1). The intensity of this pain varies depending on the type of surgery, the patient's age, and the patient's tolerance to pain. The goal of post-operative pain relief is to reach an acceptable level of pain and accelerate the patient's return to normal individual and social functioning (2). Postoperative pain control is mainly done by relying on drug interventions including intramuscular, intravenous, local anesthetics, and non-steroidal anti-inflammatory drugs according to the needs of patients (3).

Key point

The results of this study showed that the pain score after 8, 12, and 24 hours of hospitalization in the ward in group 1 was significantly lower than group 2.

Among the drugs used in anesthesia and analgesia is lidocaine, which by binding to voltage-gated sodium channels in the nerve membrane, causes hyperpolarization and blocks the conduction of electrical impulses by the nerve membrane (4). The most sensitive nerve fibers to the effect of local anesthetics are thinly myelinated fibers Aʒ and Aɣ, which are responsible for guiding the sense of touch, heat, and pain, and unmyelinated C fibers have the least sensitivity (5).

Opioids have long been the cornerstone of moderate and severe acute pain relief. However, there is a challenge between their benefits and threats to optimal postoperative recovery (6). Morphine is one of the derivatives of alkaloids found in opium, which has analgesic and narcotic properties and is used as an analgesic in the pain of heart diseases, sickle cell disease, post-operative and severe chronic pain (7).

Triamcinolone is a long-acting steroid conducted in chronic pain as a local injection. Due to its anti-inflammatory properties, it is helpful in controlling pain after ophthalmic and orthopedic surgeries (8). Moreover, its local use in tonsillectomy is effective in head and neck surgery (9). Deep and long-term anesthesia is necessary for mastoidectomy-tympanoplasty surgery (10).

Objectives

Since no documented study has been conducted to investigate the effect of morphine, triamcinolone, and topical lidocaine combination in mastoidectomy-tympanoplasty surgery, it was attempted to study the impact of adding morphine and triamcinolone to topical lidocaine in reducing pain after mastoidectomy-tympanoplasty surgery and compare it with the control group.

Patients and Methods

Study design

This triple-blind clinical trial was conducted in Al-Zahra and Ayatollah Kashani hospitals in Isfahan. The research population included patients referred to these two hospitals due to mastoidectomy-tympanoplasty surgery and were willing to participate in the study.

The research inclusion criteria were 15 to 65 years of age, the patient indicating mastoidectomy-tympanoplasty, and consent to participate. Exclusion criteria include a history of drug and alcohol addiction, a history of seizures and mental problems, the existence of kidney disease, the prolongation of surgery for more than 2.5 hours, and the impossibility of following up with the patient until the end of the intervention due to various reasons, such as the death.

The non-probability sequential sampling method was used in this study, which means that all samples qualified for the research were included in the study until the sample volume was completed.

In this trial, after obtaining the code of ethics from the vice president of research and statistical consulting, 68 patients with American Society of Anesthesiology (ASA) 1 and 2 who were candidates for mastoidectomy-tympanoplasty surgery assigned to the two groups of 34. In group, I, 0.15 mg/kg of morphine and 10 mg of TriamHexal were added to 100 mg of 2% lidocaine and epinephrine with a concentration of 1.100000 and injected by the surgeon at the surgical site before surgery. In group II, 100 mg of lidocaine 2% and epinephrine with a concentration of 1.100000 were injected preoperatively in the surgical incision site.

Due to the need for controlled hypotension in this type of surgery, patients in both groups were given nitroglycerin infusion at the rate of 5 mcg/kg/min, and in case of pressure control or increased heart rate, labetalol infusion at the rate of 0.5 mg/kg was used.

Before the induction of anesthesia, both groups of patients received 6-8 cc/kg of liquid and underwent full monitoring, including electrocardiography (ECG) , pulse oximetry, and blood pressure measurement. Then, in both groups, after the induction and maintenance of anesthesia with the same method, the changes in systolic and diastolic blood pressure, mean arterial pressure and heart rate, Spo2 during the operation and every 10 minutes until the end of the operation, the mean length of stay in recovery, and the time to discontinue the drug until Extubation time were recorded in two groups. After surgery, the pain level was measured and recorded on the basis of a visual analog scale (VAS) from time zero (when the patient regained full consciousness) and one hour later in recovery and at 2, 8, 12, and 24 hours after the operation. In addition, the amount of opioid used in the first 24 hours after the operation was calculated in two groups, and in case of a visual analog scale above 4, pethidine was injected at the dose of 0.5 mg/kg. The time of anesthesia induction, duration of surgery, time of discontinuing anesthetic, time of entering recovery and extubation, the length of stay in recovery, and the time of first request for painkillers were carefully recorded for each patient.

The patient's information was registered in a form that specifically prepared for this purpose. Before the anesthesia induction, the researcher went to the patient's bedside at the specific times in the operating room, recovery room, and the ward to complete the information.

Statistical analysis

The data was analyzed using SPSS software version 26. Independent samples *t* test and chi-square test were used to compare the mean of quantitative data and distribution of qualitative data respectively. Repeated measures analysis was used to compare the average changes of quantitative variables over time in each of the two groups. The significance level of less than 0.05 was considered in all analysis.

Results

In the present research, 68 patients were included in the study and were randomly assigned into two groups of 34 and the data were analyzed. The CONSORT diagram of the patients was shown in Figure 1.

The analysis of the demographic information between the two groups indicated no significant difference ($P=0.39$) in terms of age ($P=0.33$), gender ($P=0.47$), weight ($P=0.24$), body mass index (BMI) ($P=0.27$), ASA classification ($P=0.13$), and presence of any accompanying

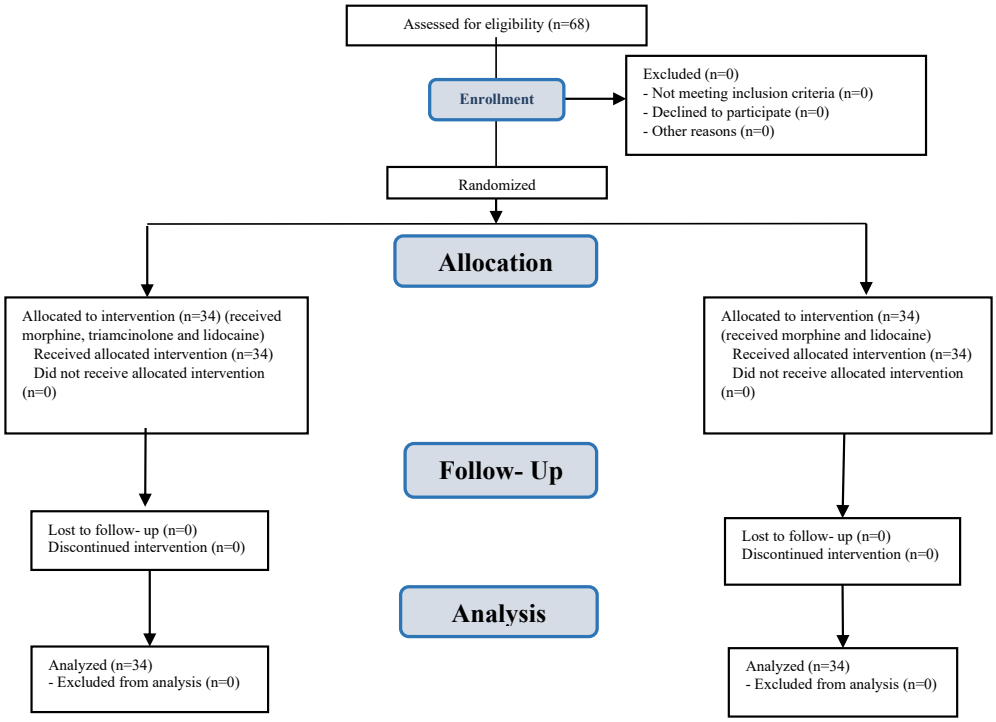

Figure 1. Consort flowchart of patients.

disease. The data are summarized in Table 1.

During the study, a significant reduction was observed in pain scores in all patients of both groups ($P=0.001$). However, patients in group I showed significantly lower pain scores than group II after 8, 12, and 24 hours in the ward ($P<0.05$) (Table 2).

A significant reduction was observed in systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) in all patients during surgery ($P<0.001$). By comparing the two groups, it was found that the patients who received morphine, triamcinolone, and lidocaine (group I) had significantly lower SBP after 40, 80, 100, 120, 140, and 160 minutes during surgery compared to group II. Additionally, group I showed lower MAP after 80, 100, 120, 140, and 160 minutes during surgery compared to group II ($P<0.05$); However, no difference was observed between the two intervention groups regarding DBP ($P>0.05$; Table 3).

Furthermore, it was observed that the combination of morphine, triamcinolone, and lidocaine compared to the control group led to a significant decrease in the opioid received in the first 24 hours after surgery, as well as a delay in the first opioid intake of the patient ($P<0.05$). There was no difference between the groups in terms of extubation time ($P>0.05$; Table 4).

Discussion

One of the challenges of mastoidectomy-tympanoplasty surgery is post-operative pain relief. The present study aimed to investigate the effectiveness of morphine,

Table 1. Analysis of demographic information between the two groups

Variables		Group 1 (n= 34)	Group 2 (n= 34)	*P* value
Age (y)		34.66 ± 10.52	35.72 ± 11.36	0.33
Weight (kg)		76.24 ± 8.07	74.62 ± 9.45	0.24
Height (m)		168.21 ± 10.21	170.92 ± 11.32	0.30
Body mass index (kg/m^2)		24.91 ± 4.23	25.67 ± 3.54	0.27
ASA	1	28 (82.3%)	26 (76.5%)	0.13
	2	6 (17.7%)	8 (23.5%)	
Gender	Female	19 (55.8%)	18 (53%)	0.47
	Male	15 (44.2%)	16 (47%)	
Underlying disease	Yes	4 (11.7%)	3 (8.8%)	0.39
	No	30 (88.3%)	31 (91.2%)	

Data are shown as mean ± SD or No. (%)
AMA, American Society of Anesthesiology.

Table 2. Comparison of pain between the two groups

Pain	T1	T2	T3	T4	T5	*P* value 1	*P* value 2
Group 1	7.63 ± 1.21	6.25 ± 1.27	5.72 ± 1.78	4.21 ± 1.63	3.98 ± 1.07	0.001	0.001
Group 2	7.59 ± 1.70	6.62 ± 1.34	6.44 ± 1.28	5.82 ± 1.97	5.23 ± 1.08	0.001	
P value 3	0.15	0.08	0.02	0.01	0.01		

Data are shown as mean ± SD.
T1: immediately after gaining consciousness, T2: after 2 hours in the ward, T3: after 8 hours in the ward, T4: after 12 hours in the ward, T5: after 24 hours in the ward, P1 (Time), p2 (interaction), p3 (at a significant level of repeated measure test) at a significance level of 5%.

Table 3. Comparison of systolic, diastolic, and mean blood pressure between the two groups

Variables			T1	T2	T3	T4	T5	T6	T7	T8	T9	*P* value 1	*P* value 2
SBP	Group 1	Mean	138.05	120.25	113.10	110.54	104.80	100.70	99.21	94.32	96.28	0.001	0.32
		SD	19.50	16.59	12.64	18.41	14.51	14.20	16.58	14.77	15.60		
	Group 2	Mean	141.24	123.27	119.06	117.59	112.98	110.62	108.36	105.52	105.21	0.001	
		SD	16.96	10.01	14.12	12.54	9.51	11.30	14.92	12.72	11.74		
	P value 3		0.43	0.07	0.03	0.01	0.01	0.01	0.01	0.01	0.01		
DBP	Group 1	Mean	93.40	88.24	80.10	78.28	76.13	75.30	76.27	75.96	74.32	0.001	0.08
		SD	16.21	14.14	11.38	11.27	13.83	12.08	12.62	13.28	13.69		
	Group 2	Mean	94.87	87.94	79.26	79.47	75.57	74.23	76.15	75.61	75.11	0.001	
		SD	13.68	10.94	12.92	9.64	9.06	10.36	11.21	10.44	9.38		
	P value 3		0.27	0.37	0.41	0.28	0.25	0.28	0.33	0.21	0.21		
MAP	Group 1	Mean	128.01	118.54	110.94	106.36	96.07	92.23	91.39	88.20	88.39	0.001	0.37
		SD	14.93	9.40	11.81	9.70	9.53	11.22	12.08	10.34	11.42		
	Group 2	Mean	124.87	117.98	114.87	110.34	108.45	105.47	100.77	96.08	95.31	0.001	
		SD	16.95	17.97	12.39	13.215	11.04	10.54	11.46	11.39	10.95		
	P value 3		0.66	0.07	0.06	0.04	0.01	0.01	0.01	0.01	0.01		

T1: immediately after anesthesia, T2: after 20 minutes, T3: after 40 minutes, T4: after 60 minutes, T5: after 80 minutes, T6: after 100 minutes, T7: after 120 minutes, T8: After 140 minutes, T9: after 160 minutes, P1 (Time), p2 (interaction), p3 (at a significant level of repeated measure test) at a significance level of 5%.

Table 4. Comparison of opioid intake, first request, and extubation time between the two groups

Variable	Group 1 (n= 34)	Group 2 (n= 34)	*P* value
Narcotic injection in the first 24 hours after surgery (mg)	7.26± 2.69	9.34± 3.07	0.02
First request for narcotics after surgery (min)	132.14± 14.29	92.37± 12.84	0.01
Extubation time (min)	74.63± 11.28	77.28± 12.02	0.34

Data are shown as mean± SD.

triamcinolone, and lidocaine combination in comparison with the control group in a clinical trial on 70 patients referred to Al-Zahra and Ayatollah Kashani hospitals in Isfahan. There was no difference in terms of demographic information ($P > 0.05$).

The current work indicated that the combination of morphine, lidocaine, and triamcinolone and the use of lidocaine along with morphine can lead to a reduction in postoperative pain, with the difference that the combination of morphine, lidocaine, and triamcinolone could significantly reduce pain compared to the control group ($P < 0.05$). It suggested the higher efficacy of several local drugs the combination compared to one drug.

Several studies have shown the favorable results of opioids the combination with local drugs, such as lidocaine and fentanyl, in increasing the effect and depth of local anesthesia. In the study of Cabral et al on local anesthesia for cataract surgery, adding clonidine to lidocaine for sub-tenon anesthesia increased the duration of anesthesia and immobilization of the eye and analgesia (11).

In another study by Pobereskin and Sneyd on 95 adults who underwent back surgery, triamcinolone was injected immediately after the operation at the site of operation, which reduced the pain after spine surgery and the length of hospitalization (12).

In another study by Mullaji et al, the effect of

methylprednisolone along with bupivacaine and fentanyl in a peri-articular injection on improving the quality of function and relieving pain after total knee arthroplasty was investigated. In this study, these drugs could considerably improve the recovery of joint function and reduced the pain level in patients (13).

Mastoidectomy and tympanoplasty surgery require induced hypotension during the operation, which was developed by nitroglycerin in this study. Although a significant reduction was observed in both groups in terms of SBP, DBP, and MAP in all patients during surgery ($P<0.001$), this reduction was more distinctive in the intervention group. SBP and MAP were significantly lower in the morphine, triamcinolone, and lidocaine groups, which can help the operation progress ($P<0.05$). It is worth noting that uncontrolled hypotension did not occur in any of the patients in the two groups.

Conclusion

The present study showed that the combination of morphine, triamcinolone, and lidocaine compared to the control group can lead to better pain control, more reduction of SBP and MAP, reduction of postoperative opioid use, and delay in the time of first opioid administration.

Limitations of the study

The small size of the sample and the lack of a control group can be regarded as weaknesses of this study.

Authors' contribution

Conceptualization: Reihanak Talakoub.
Data curation: Hoda Sadat Rohani.
Formal analysis: Hoda Sadat Rohani.
Funding acquisition: Reihanak Talakoub.
Investigation: Hoda Sadat Rohani.
Methodology: Reihanak Talakoub.
Project administration: Reihanak Talakoub.
Resources: Hoda Sadat Rohani.
Supervision: Reihanak Talakoub.
Validation: Gholamreza Khalili.
Visualization: Gholamreza Khalili.
Writing–original draft: Hoda Sadat Rohani.
Writing–review and editing: Gholamreza Khalili.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

The research was conducted in accordance with the tenets of the Declaration of Helsinki. The Ethics Committee of Isfahan University of Medical Sciences approved this study (Ethical code #IR.MUI.MED.REC.1400.064). Accordingly, written informed consent was taken from all participants before any intervention. This study was part of the anesthesiology residential thesis of Hoda Sadat Rouhani at this university. The trial protocol was approved by the Iranian Registry of Clinical Trials (identifier: IRCT20200825048515N39; https://irct.ir/trial/57931).

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