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COMPARISON BETWEEN PROPOFOL AND DEXMEDETOMIDINE AS AN AGENT OF CONSCIOUS SEDATION IN PATIENTS UNDERGOING TYMPANOPLASTY: A RANDOMISED CONTROLLED TRIAL

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ABSTRACT

Objective: In this study our main goal is to Evaluation of conscious sedation in patient undergoing tympanoplasty by intravenous propofol and intravenous dexmedetomidine. **Method:** This Randomised prospective clinical trial study was carried out with the patients who underwent tympanoplasty conducted at ENT operation theatre in BSMMU, Dhaka according to inclusion & exclusion criteria from February 2016 to February 2018. ASA I-II patients aged (18-45) years undergoing tympanoplasty were enrolled. Patients were randomized as Group I and Group II by computer-gerenated randomization where there was 30 patients in each group (n=30). **Results:** During the study, a computer-generated randomization table was used to allocate the patients into 2 equal groups, 30 in each where Group I received dexmedetomidine and Group II received propofol. Observations were made during perioperative period for conscious sedation effectiveness on haemodynamics SBP, MAP,DBP,HR,SpO2 on different time intervals, surgical field bleeding status, patient satisfaction, surgeon satisfaction, intraoperative rescue sedation, intraoperative rescue analgesics, postoperative rescue analgesics, time to achieve target Ramsay sedation scale (RSS) after induction, intra and postoperative pain intensity level, and adverse effects. **Conclusion:** From our results we can conclude that, dexmedetomidine with local anaesthetic lignocaine infiltration provides better outcome of conscious sedation in terms of patients satisfaction, surgeons satisfaction, reduce per operative surgical site bleeding for patients undergoing tympanoplasty.

KEYWORDS: Propofol, Dexmedetomidine, haemodynamics. Tympanoplasty.

INTRODUCTION

Middle ear surgeries pose a different set of challenges for patients, surgeons and anaesthesiologist. There are various types of surgeries done in ears including external, middle and internal ear either individually or simultaneously. This procedure done under different types of anaesthetic technique like general anaesthesia, local infiltration, local infiltration with sedation, regional blocks and or combination all above procedures. Each of technique has its own advantages and disadvantages.

Using local anaesthesia only comparison to general anaesthesia in terms of patient recovery, patient turnover, avoidance of intubation and elimination of possibility of laryngotracheal complicaiton is as well as removal of cardiovascular, respiratory, renal, and neurological complications.

Local anaesthesia with sedation may be an better alternative to general anaesthesia and local anaesthesia to overcome and prevention of disadvantages and better patient satisfaction. Surgical field free of blood is important for membrane placement, patient to lie still is important. Movement of patient and sympathetic stimulation increase surgical field bleeding, disturb the microscopic nature of surgery may leads to graft failure so local anaesthesia with sedation may be an better alternative for general anaesthesia and or local anaesthesia.

Good patient selection, proper preoperative counseling, use of appropriate drugs for sedation are important factors for tympanoplasty.[1] Local anaesthesia with sedation well tolerated by the patient.

Conscious sedation involves administration of different types of drugs either alone or combination for anxiolysis, hypnosis, amnesia and analgesic effects.[2] Commonly used drugs for conscious sedation are benzodiazepines, opioids, propofol, ketamine, neuro leptics, alpha.2 asonist.[3] Each of the drugs has several advantages and disadvantages either individually or combination. Among the sedative drugs opioids cause reduction of minute ventilation, periodic breathing, apnoea, drowsiness ,lethergy, nausea, vomiting, hypotension, bronchospasm and prolong recovery.[4] Ketamine used for sedation causes tachycardia, hypertension, hallucination, hypersalivation, in adequate sedation, agitation.[5] Neuroleptics have anti dopaminergic, anti-cholinergic, cardiac arrythmia effect.[4]

Propofol is a newer drug has been used for conscious sedation have narrow therapeutic index, risk of progression to deep sedation. It has no analgesic effect and must be used with adequate pain relief.[6] Profopol causes hypotension, apnoea required intervention during conscious sedation.[7] It also causes hypoxia, vomiting, deep sedation, caughing, agitation, airway obstruction, desaturation, higher recall.

Therefore, suitable drugs and adequate doses for sedation have been debated and variety of drugs used around the world used and consequently search for appropiate newer drugs continues. The alpha 2 agonist dexmedetomidine now a day's widely used for its sedative analgesic and sympatholytic properties in the perioperative and critical care. It was approved by FDA 1999 for used as a sedative agents.[8] It has shorter half life and eight fold greater sensitivity and selectivity for the receptor than clonidine.[9] It also attenuates the stress response to surgery, provides opioid sparing effect, stable haemodynamics.[12] A metaanalysis of the use of dexmedetomidine for tonsillectomy, adenoidectomy found effective in preventing postoperative pain.[10] It prevents post operative nausea, vomiting, shivering and potential benefits of cardio, neuro and renal protection. It can be used in perioperative period as an analgesic adjunct. Dexmedetomidine used significantly less tramadol in FESS and septoplasty.[11] It is better drug for conscious sedation with better haemodynamic stability, reduce analgesic requirements fentanyl about 44%.[13]

Dexmedetomidine has been used for various surgical procedures, preserved muscle tone and spontaneous ventilation and awaken by external stimulus.[14] EEG study demonstrated sedative effects of dexmedetomidine mimics second stage of non REM sleep.[15] In USA dexmedetomidine approved for sedation of non intubated patient or during surgical procedure. A Conchrane review 2009 examined benefits of alpha 2 agonist in obtunding the perioperative stress induced sympathetic activity.[16] In CNS dexmedetomidine stimulates brainstem reduce heart rate and decrease blood pressure. It has selective alpha 2 agonist with properties of analgesia, sympatholysis and can titrate sedation without respiratory depression. It reduces opioid requirements and stress response to surgery ensuring a stable haemodynamics. The use of dexmedetomidine in other ENT surgeries like FESS, septoplasty, thyroplasty under conscious sedation has also documented. Atipamazole very specific antagonist to alpha 2 receptor. It can be safely and effectively used for surgeries under conscious sedation.[17]

In our country few articles published on dexmedetomidine shows that dexmedetomidine infusion reduces the NT-Pro BNP level has better cardiac outcome for patients undergoing ORIF for fracture shaft of femur. But no such study yet done on tympanoplasty at Bangladesh. We assume that conscious sedation with dexmedetomidine may be an better alternative to other sedative drugs for patient undergoing tympanoplasty.

For this perspective, our study is designed to determine whether dexmedetomidine with local anaesthetics lidocaine infiltration have better outcome in comparison to propofol.

OBJECTIVE

General objective

Evaluation of conscious sedation in patient undergoing tympanoplasty by intravenous propofol and intravenous dexmedetomidine.

Specific objective

- To compare intra operative haemodynamics.(SBP,DBP,MAP,SPO2,HR).
- To compare operative field bleeding by bleeding scale.
- To compare surgeon satisfaction by Likert scale.
- To compare intra operative adverse effects. (Hypotension, bradycardia, hypoxia).
- To compare postoperative adverse effects. (Hypotension, bradycardia, hypoxia, PONV).

METHODOLOGY

Study type

- This was an Randomised prospective clinical trial**.**

Study place and period

This study was carried out with the patients who underwenttympanoplastyconducted at ENT operation theatre in BSMMU, Dhaka according to inclusion & exclusion criteria from February 2016 to February 2018.

Sampling method

- The sample was collected by computer generated random sampling.

Study population

- Total 30 patients were included in this study.

Selection criteria

Inclusion criteria

- All Patients (both male and female) underwent tympanoplasty.
- Aged between 18-45 years of age.
- ASA physical status I and II

Exclusion criteria

- Patient (both male & female) refused to be included in the study.
- COPD, asthma, Cardiac, renal, hepatic dysfunction or disease.
- History of difficult intubation.
- Coagulopathy or coagulation disorder.
- Obesity (20% of ideal body weight).
- History of drug allergy.
- Patients requiring endotracheal intubation.
- Sleep apnoea.

Procedure of data collection

ASA I-II patients aged (18-45) years undergoing tympanoplasty were enrolled. Patients were randomized as Group I and Group II by computer-gerenated randomization where there was 30 patients in each group (n=30). Patients were interviewed for detailed medical and drug history and underwent a physical examination before the surgery to verify whether fulfill inclusions criteria. All investigations were reviewed and optimization was done if required. Before the surgery, patients were instructed clearly about anaesthetic technique, NRS pain scale.

The group I received dexmedetomidine and group II received propofol. After taking the patient on the operation table, a monitoring device was attached and baseline haemodynamics (SBP, DBP, MAP, SpO2, HR) were noted. An intravenous cannula was inserted for giving intravenous fluids and drugs. All patients were monitored with an automated non invasive blood pressure device, pulse oximetry, and an electrocardiogram. Drugs were prepared and two 50 ml syringes were labeled as loading and maintainence syringe for each patient.

Patients in Group I were get injection dexmedetomidine loading dose 1µgm/kg over 10 minute followed by continuous infusion 0.4 µgm/kg/hr. Patients in the Group II were get injection propofol loading dose 75 µgm/kg intravenously over 10 minute than 50µgm/kg/min continuous infusion was started.

Patients were observed for the depth of sedation throughout the period of surgery and sedation both intraoperatively and postoperatively. Light sedation was assumed from the observation of haemodynamics, somatic (movement, eye opening or grimacing) or autonomic (lacrimation, sweating) changes. Light sedation symptoms were treated by administering a bolus of fentanyl (0.5 µgm/kg) followed by titration of doses of propofol and dexmedetomidine. Hypotension is treated with intravenous fluids and titrating the infusion rate of drugs. Vasopressor drugs are administered if hypotension persist. Bradycardia is treated with anticholinergic drugs. At the end of the surgery, infusion are discontinued. After the completion of surgery patients were shifted to the recovery ward and were monitored for hemodynamic parameters, degree of analgesia, and adverse events also were noted for 2 h. Drug trial registration is under processing. Applied to clinical trial .gov. PRS registration and password was created.

Statistical analysis

All relevant collected data was compiled on a master data sheet first. Then organized. Statistical analyses was carried out by using the Statistical Package for Social Sciences version 16.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The mean values were calculated for continuous variables. The quantitative observations will be indicated by frequencies and percentages. Chi-Square test was used to analyze the categorical variables like sex, ASA status and surgical satisfaction, patient satisfaction which was shown with cross tabulation. Un paired t-test was used for continuous variables like systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), heart rate (HR), percent saturation of oxygen (SpO2) at different interval. Unpaired t-test was also be used for age, weight, height, duration of surgery. P values <0.05 was considered as statistically significant.

RESULTS

A computer-generated randomization table was used to allocate the patients into 2 equal groups, 30 in each where Group I received dexmedetomidine and Group II received propofol. Observations were made during perioperative period for conscious sedation effectiveness on haemodynamics **SBP, MAP, DBP, HR, SpO2** on different time intervals, surgical field bleeding status, patient satisfaction, surgeon satisfaction, intraoperative rescue sedation, intraoperative rescue analgesics, postoperative rescue analgesics, time to achieve target Ramsay sedation scale (RSS) after induction, intra and postoperative pain intensity level, and adverse effects.

Both groups were almost similar in respect to age, weight, height, BMI. Mean age of the patient group-I was 30.93 $\pm$ 7.11 and 29.03 $\pm$ 7.36 in group-II and among them maximum age was 50 years and minimum age was 19 years in group-I and 44,14 years in group-II.

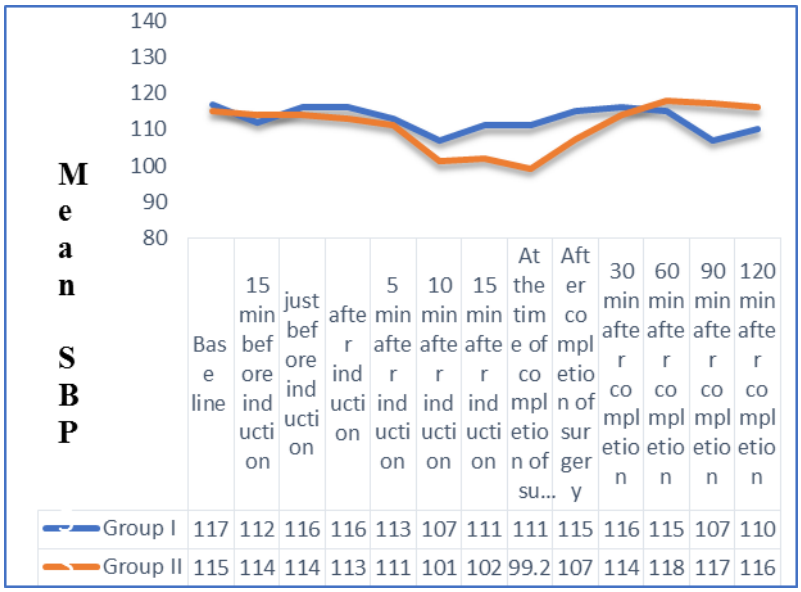
Mean weight of the patient group-I was 58.43 $\pm$ 6.88 and 57.50$\pm$ 5.52 group-II and among them maximum weight was 72 kg and minimum weight was 45 kg in group-I and 67,49 years in group-II. Mean height of the patient group-I was 1.60 $\pm$0.06 and 1.59 $\pm$ 0.06 group-

II and among them maximum height was 1.73 and minimum height was 1.49 in group-I and 1.79,1.49 meter in group-II. Mean BMI of the patient group-I was 22.72 ± 2.60 and 22.52 ± 2.18 group-II. Demographic data between the two groups were not statistically significant.

Table I: Demographic data and clinical data (n = 30 each group).

parameter	Groups		P value
(n = 30 each group)	Group I	Group II	
Age	30.93±7.11	29.03±7.36	$^{a}0.31^{ns}$
Range	19,45	14,44	
Weight	58.43±6.88	57.50±5.52	$^{a}0.56^{ns}$
Range	45,72	49,67	
Height	1.60±0.06	1.59±0.06	$^{a}0.72^{ns}$
Range	1.49,1.73	1.49,1.79	
BMI	22.72± 2.60	22.52±2.18	$^{a}0.75^{ns}$
ASA grade			
I	28(93.3%)	26(86.7%)	$^{b}0.38^{ns}$
II	2(6.7%)	4(13.3%)	
Marital status			
Married	24(80%)	17(56.7%)	$^{b}0.09^{ns}$
Unmarried	6(20%)	13(43.3%)	

Significant ^{s}, non-significant ^{ns}
Values were expressed as number and percentages.
^{b}p was derived from chi square test, ^{a}p was derived from unpaired t test.

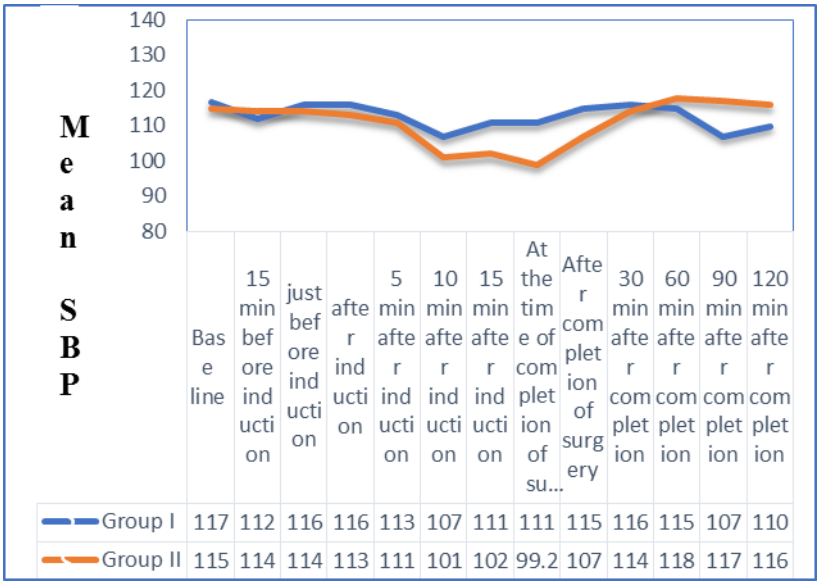


Time - Minute

Figure I: Line diagram showing comparison of SBP of two groups in different time intervals throughout the perioperative period.(mean)

Systolic blood pressure (SBP)

Base line mean± SD value of SBP in Group I was 117 ± 7.78 mm of Hg. On the other hand base line SBP of Group II was 115± 8.80 mm of Hg and during different evaluation period ranged from 114± 8.67 mm of Hg to 116± 9.02 mm of Hg. The changes were similar most of the observation and showed no significant differences between groups.

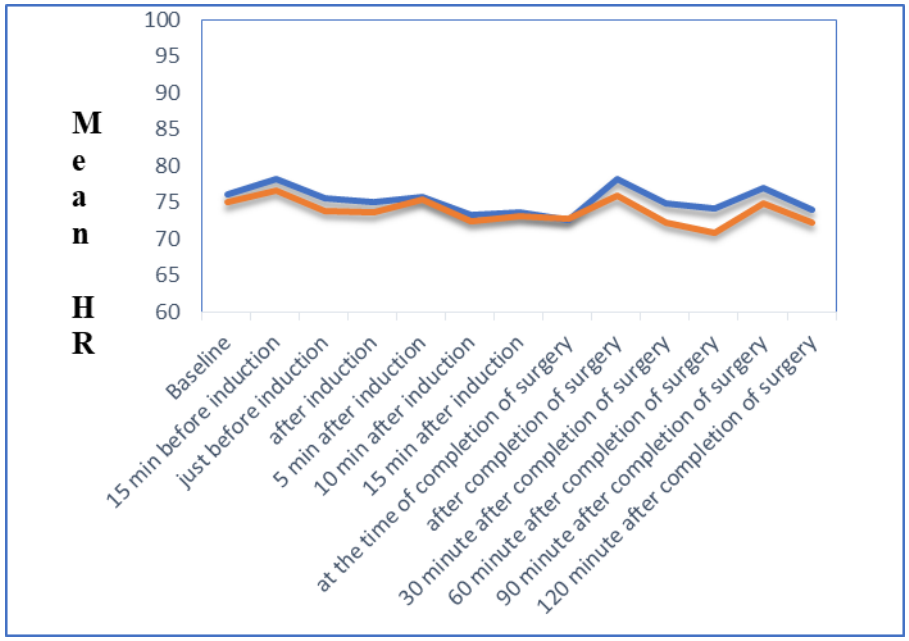


Time – Minute

Figure II: Line diagram showing comparison of SBP of two groups in different time intervals throughout the perioperative period. (mean)

Diastolic blood pressure (DBP)

Base line mean± SD value of DBP in Group I was 68.7 ± 3.88 mm of Hg. On the other hand base line DBP of Group II was 67.1 ± 4.49 mm of Hg. The changes were similar most of the observation and showed no significant differences between groups.



Time –Minute

Figure III: Line diagram showing comparison of DBP of two groups in different time intervals throughout the perioperative period. (mean)

Time to achieve target RSS

Time to achieve target RSS after induction. Among group I, 24(80%) patient achieves target sedation (RSS = 3) within (8-10) minutes and 3(10%) within (5-8) minutes and 3(10%) patients needs more than 10 minutes to achieve target RSS .On the contrary among group II, 25(83.3%) patient achieves target sedation (RSS = 3) within (1-5) minutes and 4 (13.3%)within (5-8) minutes and 1 (3.3%) patients needs.

Table II: Ramsay sedation score (n = 30 each group).

Groups	(1-5) minute	(5-8) minute	(8-10) minute	Above10 minute	[b]pvalue
Group I	0%	10%(3)	80%(24)	10%(3)	
Group II	83.3%(25)	13.3%(4)	0%	3.3%(1)	0.01[s]

Significant [s]
Values were expressed as number and percentages.
[b]p was derived from chi square test.

Intraoperative pain intensity

Intraoperative pain intensity score at different grade in intraoperative period. Among group I, 23 (76.7%) patients have no pain, 4(13.3%) have mild pain 3(10%) have moderate pain with the anaesthesia technique .On the contrary 21(70%) have no pain, 3 (10%) have mild pain and 6(20%) have moderate pain with the anaesthesia technique in group II respectively. Study revealed Group II found statistically significant (P<0.05).

Table III: Pain intensity (n= 30 each group).

Parameters	Groups	No pain	Mild pain	Moderate pain	Severe pain	[b]pvalue
Intraoperative period	Group I	76.7%(23)	13.3%(4)	10%(3)	0%	
	GroupII	70%(21)	10%(3)	20%(6)	0%	0.04[s]
Postoperative period	Group I	63.3%(19)	20%(6)	16.6%(5)	0%	
	GroupII	66.7%(20)	30%(9)	3.3%(1)	0%	0.2[ns]

Significant s, nonsignificant ns
Values were expressed as number and percentages.
bp was derived from chi square test.

Intra operative rescue sedation

Rescue sedation during intraoperative period. Among group I, 25(83.3%) needs no rescue sedation, and only 5 (16.7 %) patients required rescue sedation with the anaesthesia technique. On the contrary 24(80%) patients not required rescue sedation and only 6(20%) patients required rescue sedation in group II respectively. Study revealed found statistically not significant.

Table IV: Intra operative rescue sedation and analgesics (n = 30 each group).

Parameter	Groups		[b]P value
	Group I	Group II	
Sedation required	16.7 %(5)	20%(6)	
Sedation not required	83.3%(25)	80%(24)	0.73 [ns]
Analgesics required	23.3%(7)	33.3%(10)	
Analgesicsnot required	76.7%(23)	66.7%(20)	0.01[s]

Significant [s], non significant [ns]
Values were expressed as number and percentages.
[b]p was derived from chi square test.

Post operative intervention

Intervention required during post operative period. we found 13 patients needs postoperative interventions, and 47 patients not required postoperative intervention with the anaesthesia technique.

Table V: Requirement of intra operative and postoperative intervention (n= 30 each group).

Parameter	Groups		P value
	Group I	Group II	
required	8	7	
not required	22	23	0.76[ns]
required	6	7	
not required	24	23	0.75[ns]

Significant [s] non significant [ns]
Values were expressed as number and percentages.
[b]p was derived from chi square test.

DICUSSION

Patients for tympanoplasty surgery were recruited into this prospective, randomized clinical trial study with the aim to measure whether intravenous dexmedetomidine with local anaesthetics infiltration would have better outcome in conscious sedation in terms of

haemodynamics, patient satisfaction, surgeon satisfaction, rescue analgesics and sedatives, and intra operative, postoperative adverse effects.

In this current study, it was observed that, almost 93.3 % patients in group I and 86.7 % in group II had ASA Grade I which were almost same between two groups. The present study findings is closely resembled with.[18]

In our study perioperative haemodynamics was stable and it was not statistically significant may be due to patient was well hydrated in both groups and surgery time was short duration. Moreover dexmedetomidine have a direct effect at the postsynaptic vascular smooth muscle to cause vasoconstriction and this alpha 2 adrenoreceptor mediated inhibit sympathoinhibitory action of dexmedetomidine. It was observed that 80% of the patient in group I achieve target RSS within 8-10 minutes and in group II 83.3 % patient within 1-5 minutes corresponds with the results was found by.[19]

In this study, it was observed that intraoperative pain intensity score among group I, 23 (76.7%) patients have no pain, 4(13.3%) have mild pain 3(10%) have moderate pain with the anaesthesia technique .On the contrary 21(70%) have no pain, 3 (10%) have mild pain and 6(20%) have moderate pain with the anaesthesia technique in group II respectively.

It was observed that Among group I, 25(83.3%) needs no rescue sedation, and only 5 (16.7 %) patients required rescue sedation with the anaesthesia technique. On the contrary 24(80%) patients not required rescue sedation and only 6(20%) patients required rescue sedation in group II respectively. The total number of rescue doses of sedatives was lesser in dexmedetomidine group consistent with the findings of.[20]

In conclusion this prospective randomization study demonstrated that compairing the dexmedetomidine and propofol for conscious sedation in tympanoplasty we found that dexmedetomidine have better satisfaction in both patient and surgeon, less bleeding score, less requirements of analgesics both intra operative and postoperative period. Haemodynamic parameters are unremarkable in both groups.

CONCLUSION

Under the conditions of the present study, it is concluded that dexmedetomidine with local anaesthetic lignocaine infiltration provides better outcome of conscious sedation in terms of patients satisfaction, surgeons satisfaction, reduce per operative surgical site bleeding for patients undergoing tympanoplasty. It also decreases intra operative pain intensity and decrease the requirements of rescue analgesics. Hence dexmedetomidine can be safely and effectively used for conscious sedation.

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