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Comparative Evaluation of Butorphanol Versus Nalbuphine for Postoperative Epidural Analgesia in Lower Limb Orthopaedic Surgeries

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Abstract

Background: Epidural opioids acting through the spinal cord receptors improve the quality and duration of analgesia along with dose-sparing effect with the local anesthetics. The present study compared the efficacy and safety profile of epiduraly administered butorphanol and nalbuphine combined with ropivacaine. *Materials and Methods:* A total of 60 adult patients of either sex of American Society of Anesthesiologist physical status I and II, aged 18-60 years, undergoing lower limb orthopaedic surgeries under combined spinal epidural anaesthesia were enrolled into the study. Patients were randomly divided into three groups of 20 each: 0.2% Ropivacaine (group 1), 0.2% ropivacaine + 2 mg butorphanol (group 2), 0.2% ropivacaine + 10 mg Nalbuphine (group 3). The hemodynamic parameters as well as onset of pain relief and duration of analgesia were noted. Adverse events and sedation scores were also noted. *Results:* We found that haemodynamics were comparable in all the three groups. Onset of analgesia was earliest in Nalbuphine group (group 3) 1.45±0.51 min) followed by butorphanol group - group 2 (4.45±0.61 min) and maximum in ropivacaine plain group 1(8.30±0.97 min. The duration of analgesia was significantly prolonged in group 3 (6.40±0.821 hr) followed by butorphanol group - group 2 (4.45±0.605 hr) and shortest in plain group - group 1 (2.30±0.470 hr). Sedation was observed markedly in butorphanol group. No serious cardio respiratory side effects were observed in any group. *Conclusions:* Butorphanol and Nalbuphine as epidural adjuvants are equally safe and provide comparable stable hemodynamics, early onset and establishment of sensory anesthesia. Nalbuphine provides a significantly prolonged post-operative analgesia.

Keywords: Ropivacaine; butorphanol; epidural anesthesia; nalbuphine; lower limb orthopaedic surgery.

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Introduction

One of the primary aim of an anesthesiologist is to render the patient pain free during a surgical procedure. However the patient's problem does not end with the surgical procedure, as pain following surgery is a universal problem. So pain during post-operative period is a cause of concern for both the patient and the physician.

Routine practice employed for pain management still remains the administration of a non-steroidal anti-inflammatory drug intramuscularly to the patient whose pain tolerance has been exceeded. However with the introduction of regional

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anaesthesia in the modern era, anaesthesia as well as pain management is towards revolution.

Recent trends suggests that regional anaesthesia is replacing general anaesthesia in all most all the surgeries below umbilicus mainly because its benefits such as avoidance of poly pharmacy, airway manipulation, misplacement of endotracheal tube, hypo or hyper ventilation, vomiting and pulmonary aspiration. Also it reduces surgical stress and attenuates increase in plasma catecholamines and other hormones [1]. Along with this the main advantage of regional anaesthesia is that it provides intra and postoperative pain relief with full preservation of mental status and normal reflexes, unlike general anaesthesia.

When it comes to regional anaesthesia & pain relief, epidural anaesthesia is considered far better to spinal anaesthesia. It is the most commonly used technique for providing not only peri-operative surgical anaesthesia but post-operative analgesia in lower limb surgeries. Early postoperative mobilization and rehabilitation with minimally associated pain and discomfort is the most desirable feature in modern orthopaedic surgery [2].

The role of epidural anaesthesia and analgesia in reducing the incidence and severity of perioperative physiologic derangements, in addition to relieving pain has been reported in several studies [3,4].

Drugs commonly used for epidural based analgesia techniques include local anesthetics [5], Opioids [6], local anesthetic-opioid combinations [7] and other adjuvants: like clonidine [8], epinephrine [9], ketamine [10], sodium bicarbonate [11], Magnesium [12] etc.

It has been demonstrated that combination of the local anaesthetic agents and other adjuvants improves the onset & intensity of the epidural block [13,14].

Opioids are most popular epidural adjuvants. Butorphanol and Nalbuphine, opioid agonist - antagonists (K analgesics) provide an equipotent perioperative analgesia as compared to pure agonist opioids such as morphine and fentanyl with lesser incidence of respiratory depression and other opioid related side effects.

These drugs can be administered either as single top up epidural injection or continuous epidural infusion (via an indwelling catheter in epidural space). Though authors agree that continuous epidural technique is much better technique however continuous infusion may require expensive equipments such as infusion pumps which may also be associated with other hazards such as equipment failure, contamination, catheter displacement: intravascular/ subarachnoid, obstruction/ accidental detachment of epidural infusion.

Single top up technique using adjuvant may provide an equivocal analgesia for immediate post operative period as compared to continuous infusion techniques.

Hence present study was planned to compare post operative analgesic efficacy of addition of Butorphanol and Nalbuphine to standard epidural ropivacaine (0.2%) dose in lower limb orthopedic surgeries.

Material and Methods

Present study was conducted amongst 60 American Society of Anesthesiologist (ASA) status I-II patients of either sex in age group of 18-60 yrs coming to tertiary care hospital for lower limb orthopedic surgeries performed under combined spinal epidural anesthesia. The patients were randomly divided into 3 equal groups of 20 patients each.

Group 1 received drug A (6 ml of 0.2% ropivacaine + 2 ml NS) = 8 ml

Group 2 received drug B (6 ml of 0.2% ropivacaine + 1 ml of 2 mg/ml butorphanol + 1 ml NS) = 8 ml

Group 3 received drug C (6 ml of 0.2 % ropivacaine + 1 ml of 10 mg/ml nalbuphine +1 ml NS) = 8 ml

Patients with Contraindication to regional anesthesia, refusal to consent, obese [Body mass index- (BMI) >30 kg/m2], patients with history of severe cardiac, cerebrovascular, respiratory, hepatic or renal disease, patients with known hypersensitivity to butorphanol or nalbuphine, patients with spinal deformities like kyphoscoliosis and scoliosis etc were excluded from the study.

All patients were evaluated preoperatively and counseled regarding use of Visual Analogue Scale (VAS) for perception of pain. Detailed history, investigations and clinical findings were noted. A written informed consent was obtained from each patient.

On the arrival in the operation theatre, multi-parameter monitor was attached to the patient and baseline values of pulse rate (HR), blood pressure (MAP) and oxygen saturation (SpO_2) were noted were noted. A peripheral venous access was secured and the patients were pre-loaded with normal saline 10 ml/kg.

After proper positioning and under all aseptic precautions, in L2-L3 interspace the epidural space was identified using loss of resistance to air technique with 18G epidural needle and epidural catheter was threaded upto 4 cm inside the epidural space and fixed. A test dose of 3 ml of 1.5% lignocaine with adrenaline was given after confirming proper placement of epidural catheter. Subarachnoid block was then performed in the same space using 26G Quincke needle with 3.0 ml of 0.5% heavy bupivacaine.

Vital parameters including HR, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), RR and SpO_2 were monitored continuously and recorded every 5 min for the first 30 minutes and then every 10 mins until the end of surgery. After one hour of commencement of subarachnoid block, a continuous infusion of 0.75% ropivacaine at 5 ml/hr through epidural catheter was started in all the patients until the end of surgery. Any fall in mean arterial pressure more than 20% below the pre-operative value was treated with intravenous bolus injection mephenteramine 6 mg/cc boluses and noted.

After the surgery patient was shifted to the post-anesthesia care unit (PACU). VAS score and other hemodynamic parameters were observed. All the three groups were given the drug solution diluted to a total of 8 ml with normal saline and top up was given through the epidural catheter when the VAS score reached 3.

The onsets of pain relief and duration of analgesia were noted in all patients. Onset of pain relief is defined as the time interval from administration of the study drug (VAS score of >3) till VAS score came down to <3. Thereafter VAS was observed every hourly till the score reaches 5 and next rescue top up was given and study in that patient was ceased. Duration of analgesia is defined as the time interval between the administrations of study drug (VAS score > 3) till VAS score reverted back to 5.

The patients were continuously observed for respiratory depression with SpO_2 (< 90%) and RR (< 10) and other adverse effects like nausea, vomiting, pruritis, bradycardia and urinary retention. The sedation score was measured with Observer's assessment of alertness/sedation (OAA/S) scale. The hemodynamic parameters and the sedation scores were noted at the same time interval as VAS.

Statistical Analysis

After completion of the study, the results were compiled and statistically analyzed using Chi Square test for non-parametric data and ANOVA for parametric data. Post hoc students paired t test was applied wherever indicated using SSPS 22.0 software. We have used means and standard deviations to represent the average and typical spread of values of variables and median to represent various scores. Power of the study was calculated on the basis of duration of analgesia (hrs), with a sample size of 20 each for 3 groups and confidence interval of 95%. Power of study came out to be 96%. p value of less than 0.05 was considered significant and less than 0.001 as highly significant.

Results

The present study was conducted on 60 patients in the age group of 18-60 years of ASA grade I and II scheduled for lower limb orthopaedic surgeries under combined spinal epidural anesthesia. Demographic parameters are shown in Table 1. Postoperative heart rate and systolic and diastolic blood pressure (SBP and DBP) are shown in Figure 1, 2 and 3. Postoperative VAS scores, onset of analgesia and duration of analgesia and observer sedation score is shown in Table 2, 3 and 4.

Table 1: Demographic parameters

Parameters	Group 1 (n=20)	Group 2 (n= 20)	Group 3 (n=20)	P value
Age in years (mean ± SD)	50.75 ± 7.338	46.00 ± 12.222	48.25 ± 13.17	0.459
BMI in kg/m^2 (mean ± SD)	26.01 ± 2.27	25.83 ± 2.30	25.55 ± 2.17	0.806
Gender (Male: Female)	10:10	13:7	16:4	0.138
ASA grade (I : II)	11: 9	10:10	10:10	0.935

Table 2: Onset of pain relief and Duration of analgesia in three groups

Parameters	Group 1		Group 2		Group 3		
	Mean	SD	Mean	SD	Mean	SD	p-value
Onset of pain relief (minutes)	8.30	.979	4.45	.605	1.45	.510	<.001**
Duration of Analgesia (hours)	2.30	.470	4.45	.605	6.40	.821	<.001**

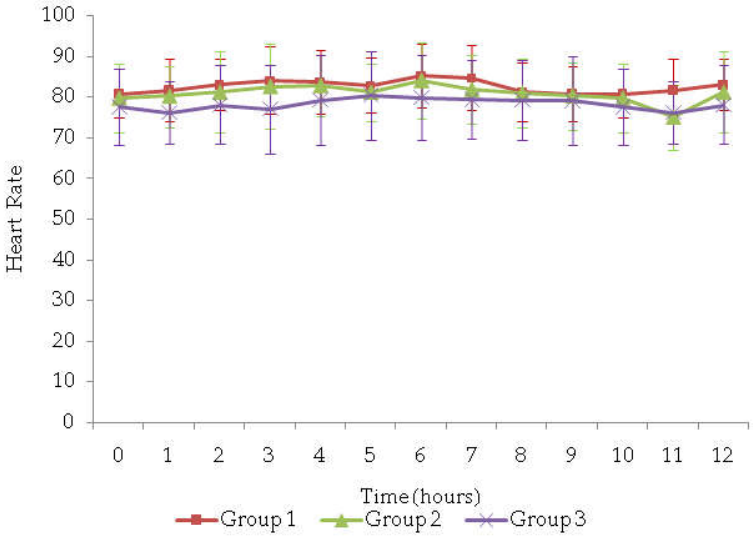

Fig. 1: Post operative heart rate (/min) at various time intervals

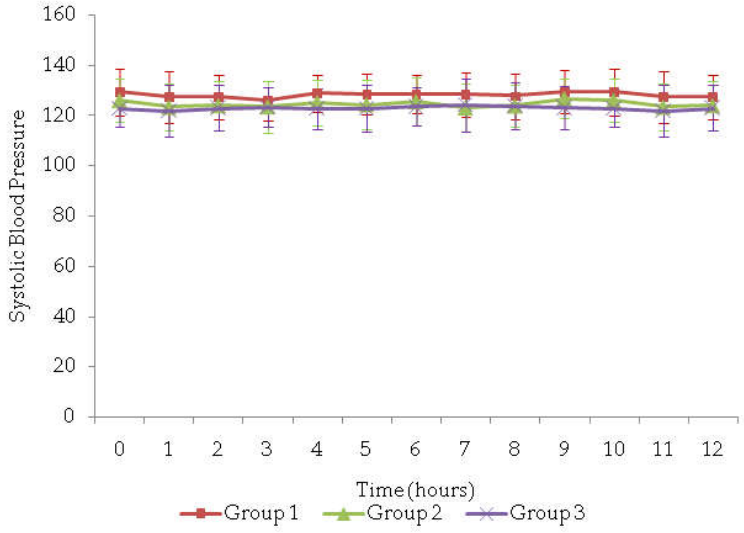

Fig. 2: Post operative mean systolic blood pressure (in mm of Hg) at various time intervals

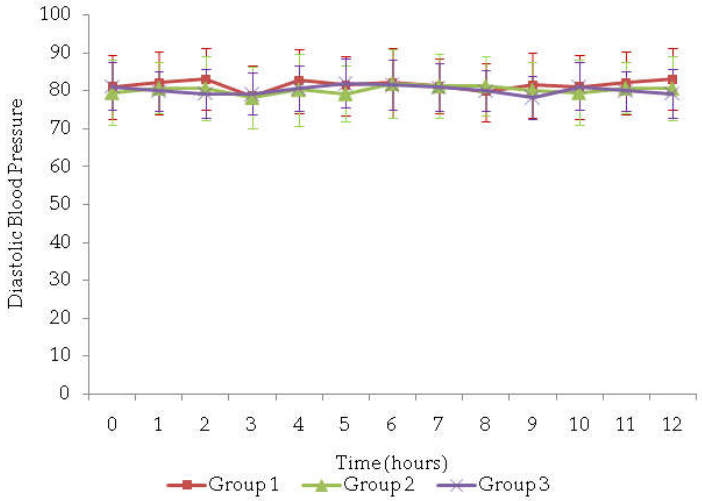

Fig. 3: Post operative mean diastolic blood pressure (in mm of Hg) at various time intervals

Table 3: VAS Scores in three groups at various time intervals

	Group 1			Group 2			Group 3			p-value
VAS Score	Median	Range	IQR	Median	Range	IQR	Median	Range	IQR	
0	0.00	0–0	–	0.00	0–0	–	0.00	0–0	–	1.000
1 hr	0.00	0–1	–	0.00	0–1	–	0.00	0–1	–	.529
2 hr	1.00	0–2	1–1	1.00	0–2	1–1	1.00	1–2	1–1	.937
3 hr	1.00	1–2	1–2	1.50	1–3	1–2	2.00	1–2	1–2	.440
4 hr	2.00	1–3	2–3	2.00	0–3	2–2	2.00	1–3	2–3	.134
5 hr	3.00	0–3	1–3	3.00	0–3	0–3	3.00	0–3	0–3	.940
6 hr	2.00	0–5	0.25–3	0.00	0–4	–	0.00	0–0	–	<.001**
7 hr	5.00	0–5	4.5–5	1.50	1–5	1–2	1.00	0–1	0–1	<.001**
8 hr	5.00	5–5	5–5	3.00	2–5	2–3.25	1.00	1–3	1–2	<.001**
9 hr	–	–	–	5.00	2–5	4.25–5	2.00	1–4	2–2.75	<.001**
10 hr	–	–	–	5.00	5–5	5–5	4.00	2–5	2–4	.002**
11 hr	–	–	–	–	–	–	5.00	2–5	4–5	
12 hr	–	–	–	–	–	–	5.00	5–5	5–5	

Table 4: Postoperative OAA/S Score in three groups at various time intervals

OAA/S Score	Group 1			Group 2			Group 3			p-value
	Median	Range	IQR	Median	Range	IQR	Median	Range	IQR	
0	5.00	5–5	5.00–5.00	5.00	5–5	5.00–5.00	5.00	5–5	5.00–5.00	1.000
1 hr	5.00	3–5	4.00–5.00	5.00	3–5	4.00–5.00	4.00	3–5	4.00–5.00	.292
2 hr	4.00	3–5	3.00–4.00	4.00	3–5	4.00–4.75	4.00	3–5	3.25–4.00	.207
3 hr	5.00	3–5	4.00–5.00	5.00	4–5	4.00–5.00	4.00	3–5	4.00–5.00	.279
4 hr	5.00	3–5	5.00–5.00	5.00	5–5	5.00–5.00	5.00	5–5	5.00–5.00	.368
5 hr	4.00	3–5	3.25–4.00	2.00	1–5	1.25–4.00	4.00	3–5	4.00–4.00	<.001**
6 hr	4.00	3–5	3.00–5.00	2.00	1–5	2.00–4.00	4.50	3–5	4.00–5.00	<.001**
7 hr	5.00	4–5	5.00–5.00	3.00	1–5	2.00–4.75	4.50	4–5	4.00–5.00	<.001**
8 hr	5.00	4–5	4.75–5.00	4.00	1–5	2.50–4.50	4.00	3–5	4.00–5.00	.013*
9 hr	4.50	4–5	3.00–5.00	5.00	2–5	4.00–5.00	4.00	4–5	4.00–5.00	.353
10 hr	5	5–5	–	5.00	5–5	5.00–5.00	5.00	4–5	4.00–5.00	.196
11 hr	5	5–5	–	–	–	–	5.00	4–5	5.00–5.00	.732
12 hr	5	5–5	–	–	–	–	5.00	5–5	5.00–5.00	1.000

Discussion

Acute postoperative pain can cause detrimental effects on multiple organ systems such as cardiovascular stress, autonomic hyperactivity, tissue breakdown, increased metabolic rate, pulmonary dysfunction, fluid retention, dysfunction of the immune system, delayed return of bowel function, and development of chronic pain syndromes. The development of epidural analgesia played a significant role in man's triumph over pain.

Opioids as epidural adjuvants to local anesthetics improve the quality of analgesia and provide a dose-sparing effect. Since both nalbuphine and butorphanol have k-agonist and μ antagonistic properties, we chose to investigate the analgesic efficacy of nalbuphine and butorphanol, as an epidural adjuvant to 0.2% ropivacaine for postoperative analgesia.

We enrolled 60 pateints divided in three groups of 20 each who were comparable with respect to their demographic profile i.e age, ASA grade, body mass index and gender distribution of patients (Table 1).

Intraoperative as well as postoperative HR, SBP and DBP were comparable in all the three groups at all the intervals (Figs. 1, 2 and 3). Our results are in concordance with study done by Palacios, Jones MM et al., in 1991. He compared epidural Butorphanol and morphine for post caesarean section analgesia. Epidural butorphanol 1, 2 and 4 mg were compared with morphine, 5 mg, for postoperative analgesia in 92 patients. He found that no patient developed clinically important change in pulse rate, blood pressure and respiratory rate [15].

Kaur et al. in 2014 compared epidural butorphanol and fentanyl as adjuvants in lower abdominal surgery and concluded that there is no statistically significant change in HR, blood

pressure, Respiratory rate and SpO_2 in any group throughout the study period [16].

Postoperative VAS score, onset of analgesia and duration of analgesia is shown in Table 2 and 3, In present study, time of onset of pain relief (Table 2) was minimum in nalbuphine group - group 3 (1.45 ± 0.51 min) followed by butorphanol group - group 2 (4.45 ± 0.61 min) and maximum in plain group - group 1 (8.30 ± 0.97 min).

N. Swathi et al. compared the effect of addition of 2 mg butorphanol to 0.125% bupivacaine (total volume 10 ml) and subsequent doses 1 mg butorphanol added to 0.125% bupivacaine (total volume 10 ml) with 2 mg/kg tramadol added to 0.125% bupivacaine (total volume 10 ml) and subsequent doses 1 mg/kg tramadol added to 0.125% bupivacaine (total volume 10 ml). They found that onset was faster with butorphanol (8.44 ± 1.158 min) than tramadol (12.80 ± 1.354 min) [17].

Hunt et al. also in his study concluded that addition of 2 mg butorphanol to 0.25% bupivacaine hastens the onset of labor analgesia (6.9 ± 3.6 min) as compared to 0.25% bupivacaine alone (21.3 ± 5.2 min) [18].

Karia S et al. in 2014 in their study concluded that addition of butorphanol 2 mg to 0.75% ropivacaine (9.56 ± 0.20 min) hastens the onset of analgesia in single shot epidural anaesthesia as compared to 0.75% ropivacaine alone (13.83 ± 0.24 min). Their results were in concordance with our study [19].

Babu S et al. in the year 2017 compared the efficacy of butorphanol 2 mg and nalbuphine 10 mg as adjuvant to 0.2% ropivacaine for postoperative pain as thoracic epidural analgesia in emergency laparotomy and concluded that the time of onset of analgesia was faster with nalbuphine than butorphanol [20].

In present study we found that duration of analgesia was longest in nalbuphine group - group 3 (6.40 ± 0.821 hr) followed by butorphanol group - group 2 (4.45 ± 0.605 hr) and shortest in plain group - group 1 (2.30 ± 0.470 hr) (table 2).

Karia S et al. in their study in year 2014 concluded that addition of 2 mg butorphanol to 0.75% ropivacaine (408 ± 4.19 min) prolongs the duration of analgesia as compared to 0.75% ropivacaine alone (275 ± 3.35 min) [19].

Kaur J et al. in 2014 conducted the study comparing the effect of addition of 1 mg of butorphanol to 20 ml of 0.5% bupivacaine (group BB), 100 g of fentanyl to 20 ml of 0.5% bupivacaine (group BF) and 20 ml of plain 0.5% bupivacaine (group B) and concluded that onset of analgesia was faster in group BB (7.64 ± 1.41 hr) followed by group BF (5.96 ± 1.30 hr) as compared to group B (4.74 ± 1.47 hr) [16].

Sharma et al. conducted a study in 2015 for comparison of clonidine and butorphanol as adjuncts to epidural bupivacaine in orthopaedic surgery and concluded that duration of analgesia when butorphanol was used as adjunct to bupivacaine was 3.76 ± .63 hrs [21].

Chatrath V et al. in 2015 compared the effect of addition of nalbuphine 10 mg and tramadol 100 mg to 0.25% bupivacaine in lower limb orthopedic surgeries and concluded that the duration of analgesia with nabupine group was 384 ± 11.29 min and 380 ± 9.8 min with tramadol group and the difference was insignificant in between the two groups but patient satisfaction score was better with nalbuphine group [22].

Babu S et al. in 2016 compared the efficacy of butorphanol 2 mg and nalbuphine 10 mg as adjuvant to 0.2% ropivacaine for postoperative pain as thoracic epidural analgesia in emergency laprotomy and concluded that eight patients in butorphanol group needed rescue analgesic while only one patient needed rescue analgesic in nalbuphine group in the immediate 6 hr postoperative period [20].

Sedation was noted in all the three groups (Table 4). Sedation was comparable (least score grade 4) in nalbuphine group – group 3 and plain group – group 1. However in butorphanol group markedly higher sedation was observed (grade 2). No other adverse effects like nausea, vomiting, pruritis, bradycardia, urinary retention and respiratory depression were observed.

Abboud et al. also found paucity of any side effects with epidural butorphanol given after cesarean section and attributed this to high lipid solubility of butorphanol thus limiting its cephalic spread to the brainstem [23].

Placios et al. also observed sedation in patients receiving epidural butorphanol [15]. Kaur J et al. compared butorphanol and fentanyl for post operative analgesia in lower abdominal surgeries reported similar scores of sedation with butorphanol and quoted that the sedation caused by epidural butorphanol is often desirable in perioperative period [20].

Chatrath V et al. studied the effects of epidural nalbuphine and tramadol for post-operative analgesia in orthopedic surgeries and concluded that patients were more comfortable after nalbuphine epidurally since they complained of lesser side effects [22].

Babu S et al. who compared nalbuphine and butorphanol for post operative analgesia in emergency laparotomy also reported similar results of arousable sedation with both these opioids [20].

Hence, both nalbuphine and butorphanol when added as adjuvant to ropivacaine hastens the onsent as well as prolong the duration of analgesia. Further large population and multicentric studies with extended durations or when used as infusion can add on to the significance of study.

Conclusion

We conclude that addition of Nalbuphine in dose of 10 mg can help in safely providing a faster onset and longer duration of post operative analgesia. Butorphanol also hastens the onset as well as duration but not as effectively as nalbuphine, further higher sedation as observed in Butorphanol group is not a much desired effect.

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