Original Article

Comparison of Low-dose Dexmedetomidine and Fentanyl in General Anesthesia: A Randomized Study

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Abstract

Background: The general anesthetic agents pose significant challenges to the cardiovascular and respiratory systems. Hence, the safety profile of these agents must be carefully studied and monitored. The present study aimed to compare the effects of low-dose dexmedetomidine and fentanyl in general anesthesia. **Materials and Methods:** This randomized and cross-sectional study was conducted on 100 patients belonging to both genders aged between 20 and 50 years, comprising 65 males and 35 female subjects. The ethical committee approval by the Ethics Committee of Mahavir Institute of Medical Sciences and Hospital, Bhopal, was obtained, following which informed written consent was taken from all the study subjects. The patients were randomly categorized into two groups: (a) Group I: This group comprised 50 patients receiving dexmedetomidine and (b) Group II: This group comprised of patients (n = 50) who received fentanyl. Dexmedetomidine (30–50 μg) and fentanyl (100 μg) were used as premedication agents. All obtained values were noted as descriptive statistical values, i.e., mean ± standard deviation (SD). Obtained data were compared to analyze any alterations. **Results and Observations:** On analyzing different parameters associated with dexmedetomidine in male subjects, blood pressure levels in 20–40 years, 40–60 years, and 60–80 years of age groups were found to be 120/80 ± 10, 110/70 ± 10, and 100/70 ± 10 mmHg, respectively. On comparison of heart rates, the mean ± SD values were found to be 68 ± 10 (20–40 years), 60 ± 10 (40–60 years), and 50 ± 10 mmHg (60–80 years). In female subjects who were administered dexmedetomidine, the mean ± SD blood pressure was found to be 120/70 ± 10 (20–40 years), in 40–60 years of age group, it was observed as 100/70 ± 10, and in 60–80 years of age group, the mean ± SD was obtained as 96/60 ± 10. On analysis of heart rate in females of 20–40 years of age range, mean ± SD heart rate was observed as 60 ± 10, whereas in 40–60 years, it was recorded as 55 ± 10. In the 60–80 years of age group, the mean ± SD heart rate was obtained as 50 ± 10. On analyzing blood pressure and heart rate in male study participants who were administered Fentanyl observations made were as follows: Blood pressure analysis showed in 20–40 years of age range, it was found to be 130/80 ± 10 mmHg, in 40–60 years of age range, it was observed as 120/80 ± 10 mmHg whereas in 60–80 years of age group, it was observed as 110/70 ± 10 mmHg and (b) Heart rate: Mean ± SD values of heart rate were – 74 ± 10, 68 ± 10, and 65 ± 10 beats/min in 20–40 years, 40–60 years, and 60–80 years of age ranges, respectively. In female subjects who received fentanyl, they were found to be 130/70 ± 10 mmHg in 20–40 years of age group, 120/70 ± 10 mmHg in 40–60 years of age group, and 110/70 ± 10 mmHg in 60–80 years of age range. On studying heart rate, in 20–40 years of age group, the mean ± SD values were found to be 76 ± 10 beats/min, 70 ± 10 beats/min in 40–60-year age range, and 65 ± 10 beats/min in 60–80-year age range. **Conclusion:** Dexmedetomidine was found to have a higher safety profile when compared to fentanyl.

Keywords: Blood pressure, dexmedetomidine, fentanyl, heart rate, hemodynamics

Introduction

Induction, trachea intubation, extubation, as well as laryngoscopy for achieving general anesthesia have been linked with specific type of hemodynamic alterations, which are associated with sympathetic nerve stimulation that can cause hypertension along with tachycardia.[1] The alterations in hemodynamics increase the risk of developing myocardial ischemia. Hence, counteractions of such unpleasant responses are required.[2]

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The patient sedation using benzodiazepines, propofol, ketamine, fentanyl, remifentanil, and dexmedetomidine has been used at the time of intubation.[3,4] These medicinal agents have both disadvantages and advantages. For example, propofol, opioids, and benzodiazepines attenuate hemodynamic responsiveness along with sedation, resulting in respiratory depression.[5]

Dexmedetomidine, a twin receptor agonist, can cause respiratory depression.[6,7] It has 8 times higher selectivity as well as affinity for presynaptic α-1 receptor.[8] Dexmedetomidine has a lowered incidence of cardiovascular events during the induction of anesthesia.[9] In addition, it increases the stabilization of heart rate during surgery along with a reduction and suppression of intraocular pressure.[10,11]

These anesthetic agents act on both pre- and postsynaptic sympathetic neural terminals and the central nervous system, thereby decreasing sympathetic nerve outflow and release of norepinephrine, which results in sympatholytic, sedative, anti-anxiety, analgesic, and hemodynamic effects.[12]

Dexmedetomidine has been reported to cause hypotension and bradycardia; however, opioid related side effects such as nausea, vomiting, pruritic, and respiratory depression.[13]

Fentanyl, an opioid anesthetic agent has short duration of action and fast onset of action and can be used as a balance to the effects of general anesthesia. It causes a reduction of the sympathetic system and causes mitigation of the hemodynamic stress response through opioid receptors.[10]

Fentanyl, a synthetic opioid agonist phenyl pyridine derivative, is used for reducing the hemodynamic responses toward intubation as well as laryngoscopy.[9] This agent acts as an intraoperative analgesic agent. Due to its categorization as a narcotic agent, obtaining fentanyl is difficult and is regulated under the national drug control policy and international treaties.[10]

Fentanyl is used as an adjunctive agent for epidural administration when combined with a lower local anesthetic dosage for achieving the desired effects of anesthesia.[14] The addition of opioids has dose-sparing effect associated with local anesthetic agents and provides superior analgesia. However, side effects such as higher incidence of nausea, vomiting, pruritus, urinary retention, and respiratory depression are noted.[15,16] There is approximately 4%–12% incidence of motor block following epidural analgesia using amide local anesthetic agents.[17] Hence, the present study aimed to compare low-dose dexmedetomidine and fentanyl in general anesthesia.

Materials and Methods

Study participants and sampling

A total of 100 patients belonging to both genders aged between 20 and 50 years were randomly categorized into two study groups. The study sample comprised 65 males and 35 female subjects.

Study design

After the ethical approval by the Ethics Committee of Mahavir Institute of Medical Sciences and Hospital, Bhopal, informed written consent was obtained from the patients before including them in the study. The patients were randomly categorized into two groups: (a) Group I: This group comprised 50 patients who received dexmedetomidine and (b) Group II: This group comprised of patients (n = 50) who received fentanyl.

Inclusion criteria were: (a) Physical status according to the American Society of Anaesthesiologists I and II, and (b) those who consented to participate in the study. Exclusion criteria for participant selection were: (a) those suffering from diabetes mellitus, cardiac diseases, hypertension, chronic obstructive respiratory disease (COPD), coagulation pathway abnormalities, spinal deformities and (b) patients allergic to amide local anesthetic agents.

All the selected study participant patients were provided premedication with ranitidine orally (150 mg) along with alprazolam 0.25 mg one night before and 2 h before the surgery. All subjects were provided counseling during presurgical evaluation and were thoroughly explained about the nature of the study before informed written consent. Dexmedetomidine (30–50 μg) and fentanyl (100 μg) were used as premedication agents.

Intraoperative details

Within the operation theater, adequate venous accessibility was obtained using an 18G cannula. All study participants were prehydrated with 10 ml/kg of Lactated Ringer's solution. Baseline parameters, including electrocardiography, heart rate, noninvasive blood pressure, and pulse oximetry (SpO2), were observed and then recorded. Lumbar epidural anesthesia was then induced using an 18GTouhy needle in the sitting position in L3-L4interspace using "loss of resistance" technique. The test dosage of 3 ml 2% lidocaine with adrenaline was then administered within the epidural space, after which the epidural catheter was secured up to 3–5 cm within the epidural space. After this, the subjects were positioned in the supine position.

1 μg/kg of dexmedetomidine was administered in Group A (n = 50) whereas 1 μg/kg of fentanyl was administered in Group B (n = 50) at a rate of 1 ml/s. The parameters observed immediately following epidural block administration were: (a) time for analgesia onset at T10, (b) achievement of maximum sensory level, (c) time required for achieving maximum sensory level, (d) time for completion of motor blockade, (e) time taken for 2 segmental dermatomal regression, (f) regression till S2, (g) first sensation of pain or rescue analgesia, and (h) total dosage consumption of local anesthetic agent used for more than 24 h.

Sedation assessment was done at 20 min intervals intraoperatively at 1 h interval during postoperative period by the use of subjective sedation scale as follows: (a) Grade 0 = awake, conscious, no sedation to slight restlessness; (b) Grade 1 = calm and composed, (c) Grade 2 = awake following verbal

command; (d) Grade 3 = awaken on gentle tactile stimulation; Grade 4 = awake on vigorous shaking; Grade 5 = cannot be aroused. The motor nerve blockade assessment was done by employing "modified Bromage scale" according to which 0 = no block, 1 = not able to raise extended leg, 2 = unable to flex knee, and 3 = unable to flex ankle as well as foot.

Statistical analysis

All the obtained values were noted as descriptive statistical values, i.e., mean ± standard deviation (SD). The obtained data were then compared to analyze any alterations.

Results

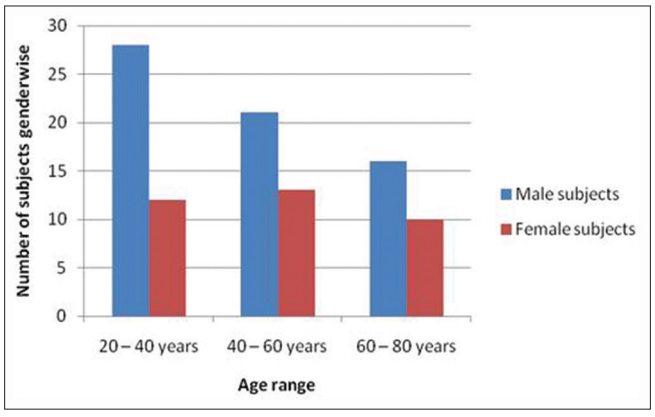
On analyzing the gender distribution in different age groups, it was noted that there were 28 male and 12 female subjects in the age group of 20–40 years, in the age group between 40 and 60 years, there were 21 male and 13 female subjects and in age group ranging from 60 to 80 years, 16 male and 10 female patients were administered dexmedetomidine [Table 1 and Graph 1].

In patients who were administered fentanyl, there were 28 male and 12 female subjects belonging to 20–40 years of age group, whereas in 40–60 years of age group, there are 21 male and 12 female subjects. In 60–80 years of age group, there were 16 male and 10 female subjects [Table 2 and Graph 2].

On analyzing different parameters associated with dexmedetomidine in male subjects, blood pressure levels in 20–40 years, 40–60 years, and 60–80 years of age groups were found to be 120/80 ± 10, 110/70 ± 10, and 100/70 ± 10 mmHg, respectively. On comparison of heart rates, the mean ± SD values were found to be 68 ± 10 in 20–40 years, 60 ± 10 in 40–60 years, and 50 ± 10 in 60–80 years of age group [Table 3 and Graph 3].

On analysis of bodily parameters (blood pressure and heart rate) in female subjects who were administered dexmedetomidine, the following observations were made:

a. Blood pressure: In 20–40 years of age group, the mean ± SD blood pressure was found to be 120/70 ± 10 while in 40–60 years of age group, it was observed as 100/70 ± 10 and in 60–80 years of age group, the mean ± SD was obtained as 96/60 ± 10



Graph 1: Gender distribution in patients treated with dexmedetomidine

b. Heart rate: In 20–40 years of age range, the mean ± SD heart rate was observed as 60 ± 10, whereas in 40–60 years of age range, it was recorded as 55 ± 10. In the 60–80 years of age group, the mean ± SD heart rate was obtained as 50 ± 10 [Table 4 and Graph 4].

On analyzing blood pressure and heart rate in male study participants who were administered fentanyl observations made were as follows: (a) blood pressure (mean ± SD): In 20–40 years of age range, it was found to be 130/80 ± 10 mmHg, in 40–60 years of age range, it was observed as 120/80 ± 10 mmHg whereas in 60–80 years of age group, it was observed as 110/70 ± 10 mmHg and (b) heart rate: Mean ± SD values of heart rate were- 74 ± 10, 68 ± 10 and 65 ± 10 beats/min in 20–40 years, 40–60 years, and 60–80 years of age ranges, respectively [Table 5 and Graph 5].

Table 1: Subject distribution according to gender being treated with dexmedetomidine (Group A)

Age group (years)	Male subjects	Female subjects
20–40	28	12
40–60	21	13
60–80	16	10

Table 2: Gender distribution in patients administered with fentanyl (Group B)

Age group (years)	Male subjects	Female subjects
20–40	28	12
40–60	21	13
60–80	16	10

Table 3: Studied parameters with dexmedetomidine administration in male subjects

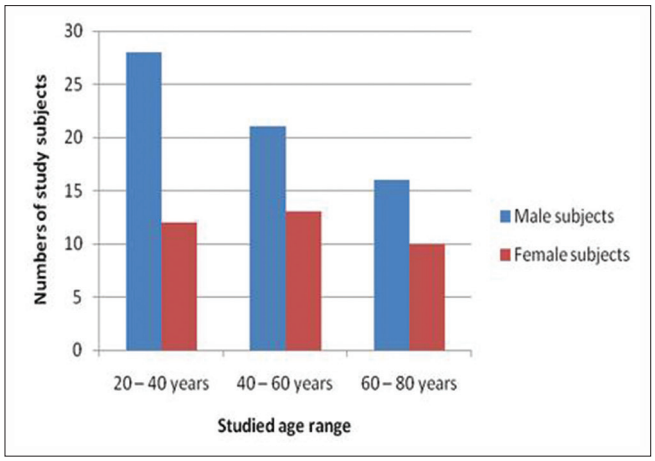
Age group (years)	Blood pressure	Heart rate
20–40	120/80±10	68±10
40–60	110/70±10	60±10
60–80	100/70±10	50±10

Table 4: Studied parameters with dexmedetomidine administration in female subjects

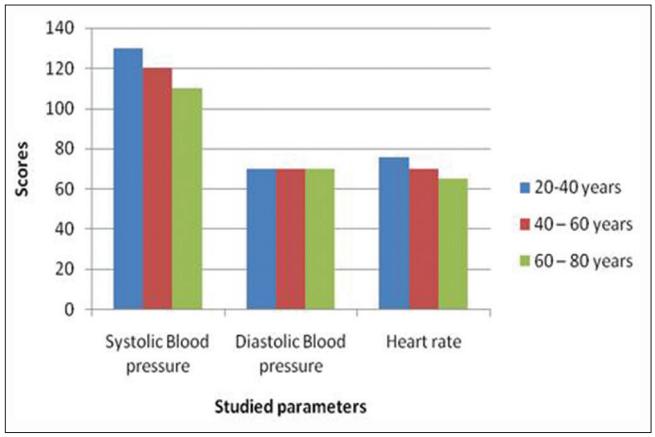
Age group (years)	Blood pressure	Heart rate
20–40	120/70±10	60±10
40–60	100/70±10	55±10
60–80	96/60±10	50±10

Table 5: Studied parameters with fentanyl administration in male subjects

Age group	Blood pressure	Heart rate
20–40	130/80±10	74±10
40–60	120/80±10	68±10
60–80	110/70±10	65±10



Graph 2: Graph demonstrating subject distribution based on gender



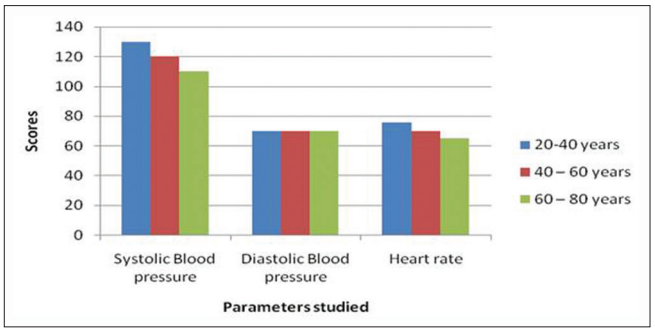
Graph 4: Graph showing parameters studied in female subjects with dexmedetomidine administration

On studying mean ± SD blood pressure values in female subjects who received fentanyl, they were found to be – 130/70 ± 10 mmHg in 20–40 years of age group, 120/70 ± 10 mmHg in 40–60 years of age group, and 110/70 ± 10 mmHg in 60–80 years of age range. On studying heart rate, in 20–40 years of age group, the mean ± SD values were found to be 76 ± 10 beats/min, 70 ± 10 beats/min in 40–60 years of age range and 65 ± 10 beats/min in 60–80-year age range [Table 6 and Graph 6].

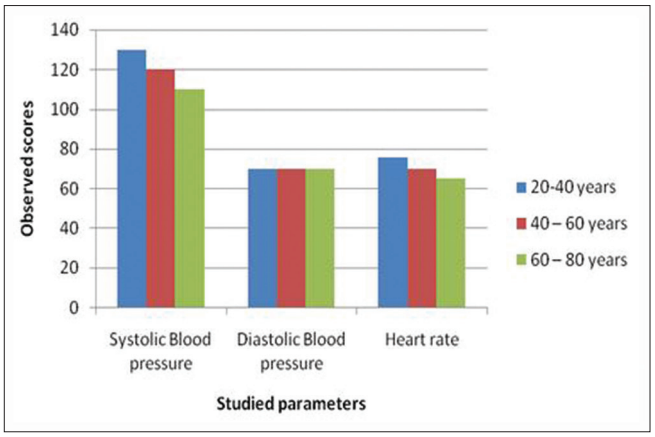
Discussion

Fentanyl is a synthetically derived opioid agonist "phenyl pyridine" derivative, which is used for reducing hemodynamic responsiveness toward tracheal intubation and laryngoscopy.[9] In addition, fentanyl also has an intraoperative analgesic action. However, this anesthetic agent comes under the narcotic category hence, there are regulatory guidelines for procuring this agent.[10]

Dexmedetomidine efficiently decreases stress-associated response while causing a reduction in the hemodynamic effects, especially following intubation and laryngoscopic procedures.[18] This drug increases the stabilization of the



Graph 3: Graph showing studied parameter in male subjects administered with dexmedetomidine



Graph 5: Graph showing parameters in male study participants administered with fentanyl

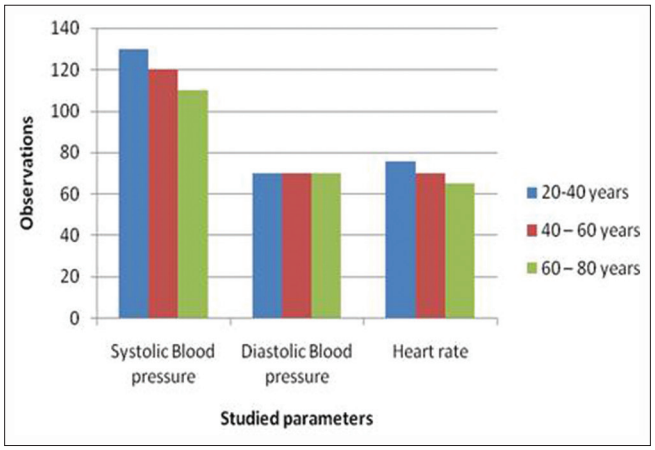
heart rate during surgery. This agent causes a decrease as well as suppression of intraocular pressure, which might occur as a result of intubation and/or laryngoscopy.[11] Dexmedetomidine produces analgesia as well as sedation without any hemodynamic and/or respiratory depression, especially during a difficult endotracheal intubation.[19]

The present study divided the study subjects into three broad groups: (a) 20–40 years, (b) 40–60 years, and (c) 60–80 years. The numbers of study participants in each group were kept similar to avoid any age-associated bias. Physiological parameters: (a) blood pressure and (b) heart rate were compared between the study groups. In Group A male subjects, the mean ± SD blood pressure was found to be 120/70 ± 10 mmHg (20–40 years), 100/70 ± 10 mmHg (40–60 years), and 96/60 ± 10 mmHg (60–80 years). Thereby, demonstrating steadily lowering levels of blood pressure as the age advanced. On the other hand, on comparing heart rates, mean ± SD value was noted as 60 ± 10 (20–40 years), 55 ± 10 (40–60 years), and 55 ± 10 (60–80 years), demonstrating a negligible reduction in heart rate with dexmedetomidine use.

Whereas in female subjects belonging to Group A, mean ± SD blood pressure was found to be 120/70 ± 10 (20–40 years), age group, it was observed as 100/70 ± 10 (40–60 years) and 96/60 ± 10 (60–80 years). Similar lowering of blood pressure

Table 6: Studied parameters with fentanyl administration in female subjects

Age group	Blood pressure	Heart rate
20–40	130/70±10	76±10
40–60	120/70±10	70±10
60–80	110/70±10	65±10



Graph 6: Graph demonstrating parameters after Fentanyl use in female study participants

levels with increasing age was observed in female subjects. Overall, female study participants were found to have lower blood pressure than males. On comparing heart rates, mean ± SD heart rate was observed as 60 ± 10 (20–40 years age range), 55 ± 10 (40–60 years), and 50 ± 10 (60–80 years). A gradual lowering of heart rate was seen with an increase in age range.

The male subjects belonging to Group B (fentanyl) demonstrated that the analysis of blood pressure and heart rate demonstrated – mean ± SD values of 130/70 ± 10 mmHg in 20–40 years of age range, it was found to be 130/80 ± 10 mmHg, in 40–60 years of age range, it was observed as 120/80 ± 10 mmHg whereas in 60–80 years of age group, it was observed as 110/70 ± 10 mmHg, thereby, demonstrating marginal decrease in blood pressure levels and (b) Heart rate: Mean ± SD values of heart rate were – 74 ± 10, 68 ± 10, and 65 ± 10 beats/min in 20–40 years, 40–60 years and 60–80 years of age ranges, respectively. Here, also a subsequent decrease in heart rate was observed with increasing age. On analysis in female subjects, the mean ± SD blood pressure levels were observed as – 130/70 ± 10 mmHg in 20–40 years group, 120/70 ± 10 mmHg in 40–60 years of age group and 110/70 ± 10 mmHg in 60–80 years of age range. On observing heart rate in 20–40 years of age group, mean ± SD scores were observed as 76 ± 10 beats/min, in 40–60 years of age range, it was found to be 70 ± 10 beats/min and 65 ± 10 beats/min in 60–80 years of age range. Here, a marginal decrease in heart rate was found with increasing age.

Hence, it can be deduced from the present study findings that dexmedetomidine has superior efficacy in terms of effect on heart rate when compared to fentanyl. Our findings are supported by Mohsin *et al*. in their meta-analysis, who demonstrated significantly reduced heart rate in patients who were provided dexmedetomidine when compared with fentanyl at intubation, studied at 1 min, 5 min, and 10 min. Dexmedetomidine was found to have higher efficacy in the prevention of an increase in hemodynamic response to intubation and laryngoscopy in comparison with fentanyl.[20]

Dexmedetomidine inhibits norepinephrine, a neurotransmitter released from the nerve endings, thereby producing stabilization of the cardiovascular system. Although it has less effectiveness, fentanyl reduces hemodynamic response by causing pain suppression thus lowering the central sympathetic tonicity and causing an increase inactivation of vagal tonicity.[21]

The decreased heart rate is well well-documented side effect of opioid agents, which has been observed in the present study as well. Bajwa *et al*. (2011) in their study showed similar findings due to the negative chronotropic effect of dexmedetomidine at approximately 30–35 min following epidural injection. A stable heart rate was observed after 56–70 min.[22] Similar to our findings, Bhana N *et al*. (2000) reported that the mean arterial pressures were observed to decrease from baseline in both patient groups, i.e., those who received dexmedetomidine or fentanyl with maximum decline at 30–50 min after epidural injection, though it never fell <65 mmHg. During the postoperative period, both the heart rates and mean arterial pressures were found to remain stable in both the groups. This gradual decrease in heart rate can be attributed to their central activity, whereby a decrease in sympathetic outflow along with the release of norepinephrine takes place.[12] Hence, in the present study, based on our findings and as supported by other similar studies, dexmedetomidine was found to be a better anesthetic agent when compared with fentanyl.

A limitation of the present study was its small sample size and assessment of only two parameters for the evaluation of the drug effect.

Conclusion

Dexmedetomidine is a better alternative agent than fentanyl since it provides a stable hemodynamic profile, has an early onset, and establishes good sensory anesthesia, prolonged postoperative analgesia with lowered consumption of local analgesics postoperatively, and has better levels of sedation.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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