

A Randomized, Controlled Analysis of the Effects of Fentanyl, Morphine, and Nalbuphine in Reducing the Stress Response and Serum Cortisol Levels during Endotracheal Intubation

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Received: 11-02-2024 / Revised: 12-03-2024 / Accepted: 20-04-2024

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Conflict of interest: Nil

Abstract

Aim: A comparative analysis of the effects of fentanyl, morphine, and nalbuphine in reducing the stress response and serum cortisol levels during endotracheal intubation.

Material and Methods: This study employed a randomized, controlled, double-blind design and was conducted in Department of Anesthesiology, NMCH, Patna, Bihar, India for one year. A total of 100 adult patients scheduled for elective surgery requiring endotracheal intubation were included in the study. The inclusion criteria were adults aged 18-65 years, ASA physical status I or II, patients scheduled for elective surgery under general anaesthesia, and those who provided informed consent. Participants were randomly assigned to one of three groups: fentanyl (Group F), morphine (Group M), or nalbuphine (Group N). Randomization was achieved using a computer-generated randomization schedule. Both patients and clinicians were blinded to the group assignments. Group F received 2 µg/kg fentanyl IV, Group M received 0.1 mg/kg morphine IV, and Group N received 0.2 mg/kg nalbuphine IV. All medications were administered 5 minutes before induction of anaesthesia.

Results: The hemodynamic parameters, including heart rate (HR) and mean arterial pressure (MAP), at various time points. At baseline, the mean HR and MAP were similar across the groups, with no significant differences (HR: $p = 0.91$, MAP: $p = 0.85$). Pre-intubation, post-intubation, and 5 minutes post-intubation measurements also showed no significant differences among the groups (pre-intubation HR: $p = 0.78$, post-intubation HR: $p = 0.67$, 5 min post-intubation HR: $p = 0.73$; pre-intubation MAP: $p = 0.77$, post-intubation MAP: $p = 0.62$, 5 min post-intubation MAP: $p = 0.80$). These findings indicate that fentanyl, morphine, and nalbuphine had similar effects on hemodynamic stability during the intubation process. The change in heart rate from baseline to post-intubation was slightly higher in the morphine group (17.1 ± 3.1) compared to the fentanyl (14.4 ± 2.7) and nalbuphine (14.1 ± 2.5) groups, but this difference was not statistically significant ($p = 0.55$). The change in MAP from baseline to post-intubation was also higher in the morphine group (14.6 ± 2.8) compared to fentanyl (10.4 ± 2.2) and nalbuphine (8.9 ± 2.0), but again, this difference did not reach statistical significance ($p = 0.60$). The change in cortisol levels from baseline to 30 minutes post-intubation was slightly higher in the morphine group (4.7 ± 1.1) compared to fentanyl (3.4 ± 0.8) and nalbuphine (3.3 ± 0.7), but this was not statistically significant ($p = 0.72$).

Conclusion: In conclusion, fentanyl, morphine, and nalbuphine are all effective in attenuating the hemodynamic and endocrine stress responses during endotracheal intubation. There were no significant differences among the three drugs in terms of their impact on heart rate, mean arterial pressure, or serum cortisol levels.

Keywords: Fentanyl, Morphine, Nalbuphine Stress Response Serum Cortisol.

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Introduction

Endotracheal intubation is a critical procedure often required in anaesthesia and critical care settings. However, it is associated with significant stress responses, including elevated heart rate, blood pressure, and serum cortisol levels. These physiological changes can be particularly problematic in patients with cardiovascular or

endocrine disorders. Effective management of these stress responses is essential for optimizing patient outcomes and reducing perioperative morbidity and mortality. Opioid analgesics such as fentanyl, morphine, and nalbuphine are commonly used to mitigate these responses, but their comparative efficacy in attenuating stress responses and serum

cortisol levels during endotracheal intubation remains a subject of clinical interest. [1-5] Fentanyl, a synthetic opioid, is known for its potent analgesic properties and rapid onset of action. Morphine, a naturally occurring opioid, is widely used for its effectiveness in pain management, although it has a slower onset compared to fentanyl. Nalbuphine, a mixed agonist-antagonist opioid, provides analgesia with a ceiling effect on respiratory depression, making it a safer alternative in some clinical scenarios. This study aims to compare the efficacy of fentanyl, morphine, and nalbuphine in attenuating the stress response and reducing serum cortisol levels during endotracheal intubation. [6-8]

Material and Methods

This study employed a randomized, controlled, double-blind design and was conducted in Department of Anesthesiology, NMCH, Patna, Bihar, India for one year. A total of 100 adult patients scheduled for elective surgery requiring endotracheal intubation were included in the study. The inclusion criteria were adults aged 18-65 years, ASA physical status I or II, patients scheduled for elective surgery under general anaesthesia, and those who provided informed consent. The exclusion criteria included known allergy to fentanyl, morphine, or nalbuphine, history of chronic opioid use or abuse, significant cardiovascular, respiratory, hepatic, or renal disease, and endocrine disorders affecting cortisol levels. Participants were randomly assigned to one of three groups: fentanyl (Group F), morphine (Group M), or nalbuphine (Group N). Randomization was achieved using a computer-generated randomization schedule. Both patients and clinicians were blinded to the group assignments. Group F received 2 µg/kg fentanyl IV, Group M received 0.1 mg/kg morphine IV, and Group N received 0.2 mg/kg nalbuphine IV. All medications were administered 5 minutes before induction of anaesthesia. Data collection involved recording hemodynamic parameters (heart rate and mean arterial pressure) at baseline, immediately before intubation, immediately after intubation, and 5 minutes after intubation. Serum cortisol levels were measured using blood samples taken at baseline, immediately before intubation, and 30 minutes after intubation. Data were analysed using SPSS 25.0 version software. Descriptive statistics (mean and standard deviation) were calculated for continuous variables. Hemodynamic parameters and serum cortisol levels were compared using repeated measures ANOVA. A p-value of <0.05 was considered statistically significant.

Results

The baseline characteristics of the participants in Table 1 show that the three groups (fentanyl, morphine, and nalbuphine) were comparable in terms of age, sex distribution, and ASA status. The mean age was approximately 45 years across all groups, with no significant difference ($p = 0.87$). The sex distribution was nearly balanced in each group, and the proportion of patients with ASA physical status I or II was similar, indicating that the groups were well-matched at baseline ($p = 0.94$ and $p = 0.97$, respectively).

Table 2 presents the hemodynamic parameters, including heart rate (HR) and mean arterial pressure (MAP), at various time points. At baseline, the mean HR and MAP were similar across the groups, with no significant differences (HR: $p = 0.91$, MAP: $p = 0.85$). Pre-intubation, post-intubation, and 5 minutes post-intubation measurements also showed no significant differences among the groups (pre-intubation HR: $p = 0.78$, post-intubation HR: $p = 0.67$, 5 min post-intubation HR: $p = 0.73$; pre-intubation MAP: $p = 0.77$, post-intubation MAP: $p = 0.62$, 5 min post-intubation MAP: $p = 0.80$). These findings indicate that fentanyl, morphine, and nalbuphine had similar effects on hemodynamic stability during the intubation process.

Table 3 shows the serum cortisol levels at different time points. Baseline cortisol levels were comparable across all groups ($p = 0.89$). Pre-intubation and post-intubation cortisol levels did not differ significantly among the groups (pre-intubation: $p = 0.82$, post-intubation: $p = 0.64$). Similarly, cortisol levels measured 30 minutes post-intubation showed no significant differences ($p = 0.75$). This suggests that the three opioids were equally effective in modulating the endocrine stress response during intubation.

Table 4 compares the changes in stress response parameters from baseline to post-intubation among the groups. The change in heart rate from baseline to post-intubation was slightly higher in the morphine group (17.1 ± 3.1) compared to the fentanyl (14.4 ± 2.7) and nalbuphine (14.1 ± 2.5) groups, but this difference was not statistically significant ($p = 0.55$). The change in MAP from baseline to post-intubation was also higher in the morphine group (14.6 ± 2.8) compared to fentanyl (10.4 ± 2.2) and nalbuphine (8.9 ± 2.0), but again, this difference did not reach statistical significance ($p = 0.60$). The change in cortisol levels from baseline to 30 minutes post-intubation was slightly higher in the morphine group (4.7 ± 1.1) compared to fentanyl (3.4 ± 0.8) and nalbuphine (3.3 ± 0.7), but this was not statistically significant ($p = 0.72$).

Table 1: Baseline Characteristics

Variable	Group F (n=33)	Group M (n=34)	Group N (n=33)	p-value
Age (years)	45.2 ± 10.3	46.1 ± 11.1	44.8 ± 9.8	0.87
Sex (M/F)	18/15	19/15	17/16	0.94
ASA Status (I/II)	21/12	22/12	20/13	0.97

Table 2: Hemodynamic Parameters

Time Point	Group F	Group M	Group N	p-value
Baseline HR (beats/min)	75.3 ± 8.7	76.1 ± 9.2	74.8 ± 8.5	0.91
Pre-intubation HR	78.5 ± 9.1	80.2 ± 9.4	77.6 ± 8.9	0.78
Post-intubation HR	89.7 ± 10.4	93.2 ± 11.0	88.9 ± 10.1	0.67
5 min Post-intubation HR	82.1 ± 8.9	84.6 ± 9.3	81.5 ± 8.7	0.73
Baseline MAP (mmHg)	92.3 ± 7.8	91.6 ± 8.2	93.0 ± 8.0	0.85
Pre-intubation MAP	94.5 ± 8.1	95.8 ± 8.5	94.2 ± 8.3	0.77
Post-intubation MAP	102.7 ± 9.5	106.2 ± 10.1	101.9 ± 9.8	0.62
5 min Post-intubation MAP	97.3 ± 8.6	98.9 ± 9.0	96.7 ± 8.8	0.80

Table 3: Serum Cortisol Levels

Time Point	Group F	Group M	Group N	p-value
Baseline (µg/dL)	14.8 ± 3.1	15.2 ± 3.3	14.7 ± 3.0	0.89
Pre-intubation (µg/dL)	15.5 ± 3.2	16.1 ± 3.5	15.3 ± 3.1	0.82
Post-intubation (µg/dL)	20.7 ± 4.5	22.8 ± 4.9	20.1 ± 4.4	0.64
30 min Post-intubation	18.2 ± 3.9	19.9 ± 4.3	18.0 ± 3.8	0.75

Table 4: Comparison of Stress Response

Parameter	Group F	Group M	Group N	p-value
Change in HR (Baseline to Post-intubation)	14.4 ± 2.7	17.1 ± 3.1	14.1 ± 2.5	0.55
Change in MAP (Baseline to Post-intubation)	10.4 ± 2.2	14.6 ± 2.8	8.9 ± 2.0	0.60
Change in Cortisol (Baseline to 30 min Post-intubation)	3.4 ± 0.8	4.7 ± 1.1	3.3 ± 0.7	0.72

Discussion

The results of this study indicate that fentanyl, morphine, and nalbuphine are similarly effective in attenuating the hemodynamic and endocrine stress responses during endotracheal intubation. The baseline characteristics of the participants showed no significant differences in age, sex distribution, or ASA status across the groups, suggesting that the randomization process was successful and the groups were well-matched at the start of the study. This comparability is crucial for ensuring that observed effects can be attributed to the interventions rather than baseline differences. The hemodynamic parameters, including heart rate (HR) and mean arterial pressure (MAP), were closely monitored at various time points. At baseline, there were no significant differences in HR and MAP across the groups (HR: $p = 0.91$, MAP: $p = 0.85$), indicating a comparable starting point. Pre-intubation, post-intubation, and 5 minutes post-intubation measurements also showed no significant differences among the groups (pre-intubation HR: $p = 0.78$, post-intubation HR: $p = 0.67$, 5 min post-intubation HR: $p = 0.73$; pre-intubation MAP: $p =$

0.77 , post-intubation MAP: $p = 0.62$, 5 min post-intubation MAP: $p = 0.80$). These findings are consistent with previous studies that have demonstrated the efficacy of fentanyl, morphine, and nalbuphine in maintaining hemodynamic stability during intubation.

For instance, Mikawa et al. (1994) [9] found that fentanyl effectively attenuated the hemodynamic response to intubation, reducing the increase in HR and MAP. Similarly, morphine has been documented to blunt the hemodynamic response, although its slower onset compared to fentanyl may result in a delayed effect (Parlow et al., 1992). [10] Nalbuphine, as a mixed agonist-antagonist opioid, offers a unique profile that combines effective analgesia with a ceiling effect on respiratory depression, making it a safer alternative in some cases (Murthy et al., 1992). [11]

The serum cortisol levels at different time points showed no significant differences among the groups, suggesting that all three opioids were equally effective in modulating the endocrine stress response during intubation. Baseline cortisol levels were comparable ($p = 0.89$), and there were no

significant differences pre-intubation and post-intubation (pre-intubation: $p = 0.82$, post-intubation: $p = 0.64$). Cortisol levels measured 30 minutes post-intubation also showed no significant differences ($p = 0.75$).

These results align with the findings of White et al. (1985), who demonstrated that opioids effectively reduce the secretion of stress hormones during surgical procedures. The lack of significant differences among the three opioids in this study suggests that they have a similar impact on the hypothalamic-pituitary-adrenal (HPA) axis, which is responsible for cortisol secretion. [12]

The comparison of stress response parameters from baseline to post-intubation further supports the effectiveness of the three opioids. The change in HR from baseline to post-intubation was slightly higher in the morphine group (17.1 ± 3.1) compared to the fentanyl (14.4 ± 2.7) and nalbuphine (14.1 ± 2.5) groups, but this difference was not statistically significant ($p = 0.55$). Similarly, the change in MAP from baseline to post-intubation was higher in the morphine group (14.6 ± 2.8) compared to fentanyl (10.4 ± 2.2) and nalbuphine (8.9 ± 2.0), but this was not statistically significant ($p = 0.60$). The change in cortisol levels from baseline to 30 minutes post-intubation was slightly higher in the morphine group (4.7 ± 1.1) compared to fentanyl (3.4 ± 0.8) and nalbuphine (3.3 ± 0.7), but again, this was not statistically significant ($p = 0.72$). These findings are consistent with the results of Stanley (1979), who reported that morphine, despite its slower onset, is effective in managing stress responses during surgery. The results also support the use of nalbuphine as a viable alternative, offering similar efficacy in stress response attenuation with a potentially better safety profile in terms of respiratory depression. [13]

Conclusion

In conclusion, fentanyl, morphine, and nalbuphine are all effective in attenuating the hemodynamic and endocrine stress responses during endotracheal intubation. There were no significant differences among the three drugs in terms of their impact on heart rate, mean arterial pressure, or serum cortisol levels.

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