LOWEST DOSES OF PROPOFOL OR MIDAZOLAM USED IN COMBINATION WITH LOW DOSE FENTANYL INFUSION FOR THE SEDATION OF CRITICALLY ILL PATIENTS

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Introduction: Sedative and analgesic drugs are widely used in the treatment of critically ill patients who require mechanical ventilatory support. With the use of modern partial ventilatory therapies patients are better tolerating mechanical ventilation at light levels of sedation and analgesia.

The aim of this study is to evaluate the hemodynamic response and adequacy of sedation when the lowest doses of propofol or midazolam together with low dose fentanyl are infused to the critically ill, mechanically ventilated patients.

Materials and Methods: This prospective study was approved by the ethical committee of Aegean University and 28 critically ill but fully conscious patients who consequently needed mechanical ventilation with Pressure Support (PS) or SIMV+PS modes were included. The patients were randomly separated into two groups after their hemodynamic and respiratory stabilization was maintained for at least 24 hours. The ventilator settings were not changed during the study period. All the patients had continuous ECG and radial arterial blood pressure monitoring throughout the study. At the beginning of the study and at the end of each hour throughout the study arterial blood gas were analysed and respiratory parameters were recorded as well as the hemodynamic parameters and the Ramsay sedation scores. After the initial records 1.0 mg/kg/h infusion of propofol (Group I) following a bolus dose of 1.0 mg/kg and 2 µg/kg/h infusion of fentanyl following a bolus dose of 2 µg/kg were maintained; for the patients of Group II 10µg/kg/h midazolam infusion was started after a bolus dose of 0.1mg/kg together with fentanyl used at same doses as for Group I. The patients were also observed in terms of their hemodynamic response to tracheal aspirations performed before the infusion (baseline), at the end of the 1st, 3rd, and 6th hours of the study and the peak hemodynamic values during aspirations with their duration to return to preaspiration values were recorded. The drug infusions were stopped at the end of 6th hour and the periods the patients needed to be fully cooperative and oriented were evaluated as their recovery time. The statistical analyses of the data were performed by using Student's t test.

Results: The optimum Ramsay (III) count was higher but recovery was longer in G-II ($p<0.05$), the urea and creatinin show differences ($p<0.05$) but not clinical significance (Table I). All other parameters had no intergroup difference ($p>0.05$). The differences in the same group's values are seen on Table II.

Table I: Patients' Data Group I (Propofol) and II (midazolam) [mean±SD (range)]

	Group I (Propofol)	Group II (Midazolam)
Age (years)	45.1 ± 13.0 (19-58)	53.2 ± 12.4 (30-69)
Sex	11Male / 3Female	13Male / 1Female
Body weight (kg)	70.2 ± 11.2 (50-90)	74.6 ± 11.0 (60-93)
Apache II score	17.6 ± 8.6 (5-34)	19.2 ± 8.7 (1-36)
Blood urea (mg/dl)	29.1 ± 13.5 (13-69)	44.6 ± 10.2 (28-61)*
Blood creatinin (mg/dl)	0.8 ± 0.3 (0.5-1.6)	1.1 ± 0.4 (0.7-1.9)*
SGOT IU/L	57.8 ± 45.0 (12-169)	93.9 ± 65.4 (21-227)
SGPT IU/L	47.6 ± 27.4 (10-100)	64.9 ± 35.1 (24-138)
Ventilation mode	SIMV+PS PS	10 patients 4 patients
Adequacy of Sedation		
Hours Ramsay S.=II-V (%)	79 (%94.0)	81 (%96.4)
Optimum Sedation		
Hours Ramsay S.= III (%)	26 (%31.0)	49 (%58.3)*
Recovery Period (min)	14.3 ± 9.8 (3-30)	45.8 ± 46.8 (15-180)*

*: Significant difference ($p<0.05$) between groups

Table II: Mean values of blood gas and hemodynamic changes during 6 hour sedation and analgesia

	B-I	B-II	1.h-I	1.h-II	3.h-I	3.h-II	6.h-I	6.h-II
PaO ₂ (mmHg)	94.1	90.8	113.9	106.7*	100.8	103.6	94.5	91.9
PaCO ₂ (mmHg)	37.1	39.7	39.4	41.8	38.7	46.5*	39.3	43.6
f (/min)	23.8	27.9	19.7	19.3*	19.6	19.4*	19.6	17.9**
HR (b/min)	97.1	99.7	86.9	95.4	82.9 *	90.9	84.4*	92.9
MAP (mmHg)	92.6	94.3	83.7	76.1*	80.1*	76.8*	82.9 *	83.5*
Asp. HR (b/min)	111.4	112.5	98.9	105.9	98.1	100.9	93.9 *	97.6*
Resp. MAP (mmHg)	112.4	119.0	99.6 *	95.8*	95.9 *	90.2*	100.1*	96.5*
Res.to Asp. (sec)	71.4	95.0	49.2	65.4	43.8 *	52.5*	46.3	47.7*

*: Significant difference ($p<0.05$) from baseline values of the same group Note: ±SEM values couldn't be shown on the table

*: Significant difference ($p<0.001$) from baseline values of the same group

Conclusion: The sedation and analgesia of the critically ill mechanically ventilated patients provided by low dose infusion following again a low dose bolus of midazolam and fentanyl maintained equally adequate, but more optimal levels of sedation and similar attenuation of hemodynamic response to aspiration when compared with propofol, but midazolam prolongs recovery and makes the patient prone to a mild CO₂ retention because of a slightly more pronounced reduction of respiratory rate.