Adding remifentanil to propofol and etomidate in cardioversion anesthesia

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ABSTRACT

Objectives: To compare their effects on cardiorespiratoy and recovery parameters and side effects.

Methods: This study was performed in The Ministry of Health Ankara Numune Research and Training Hospital, Ankara, Turkey, from January to May 2005. The 40 American Society of Anesthesiology II/III patients were randomized into 2 groups. All patients received remifentanil 0.75 μg.kg^{-1}; and then received either etomidate 0.1mg.kg^{-1} (group E, n=20) or propofol 0.5mg.kg^{-1} (group P, n=20). Cardiorespiratory data, induction time, recovery parameters, pain scores, number of shocks (NS), total amount of energy used (TE), side effects, and patient/cardiologist satisfaction were recorded.

Results: Induction time and recovery parameters were shorter in group P. No differences were seen between the groups in NS and mean TE required. In group P, a statistically significant decrease in mean blood pressure occurred after induction and returned to its baseline levels in 6 minutes. After cardioversion over 2 minutes, the respiratory rates were decreased significantly more in group P when compared with group E. Two patients in group P became apneic and needed assisted ventilation. Pain scores, side effects and patient/cardiologist satisfaction were similar in both groups. No patients in either group had myoclonus.

Conclusion: We can induce hypnosis with propofol 0.5 mg.kg^{-1} or etomidate 0.1mg.kg^{-1} by adding remifentanil 0.75 μg.kg^{-1} in cardioversion anesthesia. Although recovery parameters were longer in group E, and cardiorespiratory parameters were less stable in group P, their usage with remifentanil was both acceptable for cardioversion anesthesia.

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External direct current cardioversion, after its first introduction in 1962,[1] is commonly used today for restoration of abnormal cardiac rhythm that is resistant to pharmacological therapy. Because of the unpleasant, stressful, frightening and often painful nature of this procedure, intravenous (IV) sedation is generally administered before cardioversion to blunt these undesired effects and to produce amnesia.[2] The procedure must be safe without cardiorespiratory depression; anesthesia must be effective with total amnesia of electrical discharge and should take a short time, and not require lengthy medical or nursing supervision. Different short acting drugs such as metohexitone,[3,4] diazepam,[5] midazolam,[3,6,7] etomidate,[6,8,9] sodium thiopentone,[6,10] and propofol,[2-4,6,9,10] have been used for this purpose. Propofol and etomidate were compared at different doses and different administering techniques for sedation in cardioversion.[6,8,11,12] In a few studies, fentanyl was used with propofol and etomidate.[6,9,13] And in a recent study, remifentanil usage was compared with fentanyl usage in cardioversion.[14] In this study, we combined the ultra-short acting opioid, remifentanil with reduced doses of propofol or etomidate, and compared their effects on cardiorespiratory and recovery parameters and side effects.

Methods. This study was performed in The Ministry of Health Ankara Numune Research and Training Hospital, Ankara, Turkey, from January to May 2005. The study was approved by the Hospital Ethics Committee and written informed consent was taken from all patients before the study. Forty unpremedicated patients, American Society of Anesthesiology (ASA) II/III, with atrial fibrillation, atrial flutter, and supraventricular tachycardia were enrolled in this study. Patients with serious heart and respiratory

failure, neurological, hepatorenal dysfunction, and allergy to the study drugs were excluded. All the patients were fasting for at least 6 hours. After taking the patients to the cardioversion room, a brachial IV cannula was placed for administering of the study drugs. Standard monitoring including electrocardiogram, pulse oximetry, and non-invasive blood pressure performed by PETAS KMA-275 (Petas Corp, Ankara, TR) monitor. Measurements were recorded prior to induction, after giving the study drugs, one minute after cardioversion, 2 minutes intervals until 10 minutes, thereafter at the 15th and 30th minutes in recovery. All patients received supplemental oxygen via facemask (2 L/min). Anesthetic drugs were given by the same anesthetist; the cardiologist, patients and the nurse had no information on the drugs used. Patients were randomized via sealed envelope assignment into 2 groups. All patients in both groups first received remifentanil 0.75 $\mu g.kg^{-1}$ over 90 seconds. After that the patients in group etomidate (group E, n=20) received etomidate 0.1$mg.kg^{-1}$ over 15 seconds and the patients in group propofol (group P, n=20) received propofol 0.5 mg.kg-1 over 15 seconds. When the observer's assessment of alertness/sedation (OAA/S) scores[15] were obtained as 2, patients were synchronously defibrillated. Supplemental doses of propofol 10 mg in group P, and etomidate 2 mg in group E were given if sedation was not adequate to start cardioversion. Cardioversion was attempted by the same cardiologist using Nikon Kodhen Cardiolife (Nikon Corp, Japan) apparatus with paddles placed at the right upper sternal border and apex of the heart. The intensity of the shock was arranged depended on the type of the rhythm and the experiences of the cardiologist. If sinus rhythm were not restored, a second or third shock was delivered during the same session. Time from administering the drugs to obtain OAA/S score of 2 was noted as induction time. Awakening time (time from administering the drugs to eye opening), comprehension time (CT, time from administering the drugs to verbal contact) and time to reach Aldrete score[16] of 9-10 were also noted as recovery parameters. Pain at shock site was evaluated by visual analog score (VAS) with 0=none and 10=worst, immediately after verbal contact was obtained and one hour after the procedure. Number of shocks, total amount of energy used, side effects such as myoclonus, pain at injection site, apnea, nausea/vomiting, itching and recall were recorded. Patients and cardiologist satisfactions were evaluated by a 4 point scale with 1=poor, and 4=excellent.Power analysis to determine a minimum sample size, considering a α=0.05, 1-β=0.8, the mean recovery times are expected as 11.8±2.7 minutes for etomidate group and 9.4±1.8 min for propofol group,[11] revealed a minimum of 16 patients for comparing both groups. Data were analyzed using the Statistical Package for the Social Sciences. Between groups, comparisons for numerical data were performed with independent samples-t test and within group comparisons with paired samples-t test. Categorical variables were compared by Chi-Square test and Fisher's exact test. All data were reported as mean±standard deviation (SD) or the number of patients (%) unless otherwise noted. In all cases, p values of <0.05 were considered statistically significant.

Results. The 2 groups were comparable with respect to demographic data, ASA status, and indication for cardioversion (**Table 1**). Induction, awakening, comprehension times and time to reach Aldrete score of 9-10 were shorter in group P than in group E and this difference was statistically significant (**Table 2**). There were no differences between the groups in number of shocks (p=0.402) (**Table 3**), and the mean total amount of energy required for successful cardioversion (p=0.443). In group P, a statistically significant decrease in mean blood pressure occurred after induction when compared with group E (p<0.001), and returned to

Table 1 - Patient characteristics, American Society of Anesthesiology (ASA) status, and indications for cardioversion in the 2 groups.

Parameter	Group P (n=20)	Group E (n=20)
Gender: Male/Female	11/9	12/8
Age (years) mean±SD	63.9 ± 7.45	65.2 ± 5.85
Weight (kg) mean±SD	71.6 ± 7.38	69.8 ± 9.07
Height (cm) mean±SD	163.05 ± 6.85	162.6 ± 7.13
ASA status		
II	2	4
III	18	16
Indication		
Atrial fibrillation	15	13
Supraventricular tacychardia	3	4
Atrial flutter	2	3

Table 2 - Induction and recovery times in the 2 groups (mean+SD).

Time (minute)	Group P	Group E	*P* value
Induction time	2.93 ± 0.25	3.3 ± 0.22	<0.001
Awakening time	7.2 ± 0.5	8.4 ± 0.39	<0.001
Comprehension time	8.28 ± 0.69	9.8 ± 0.77	<0.001
Time to reach Aldrete score of 9-10	11.2 ± 0.74	13.4 ± 1.03	<0.001

Table 3 - Number of shocks required before restoration of sinus rhythm in groups.

Number of shocks	Group P n (%)	Group E n (%)
1	14 (70)	15 (75)
2	6 (30)	4 (20)
3	---	1 (5)

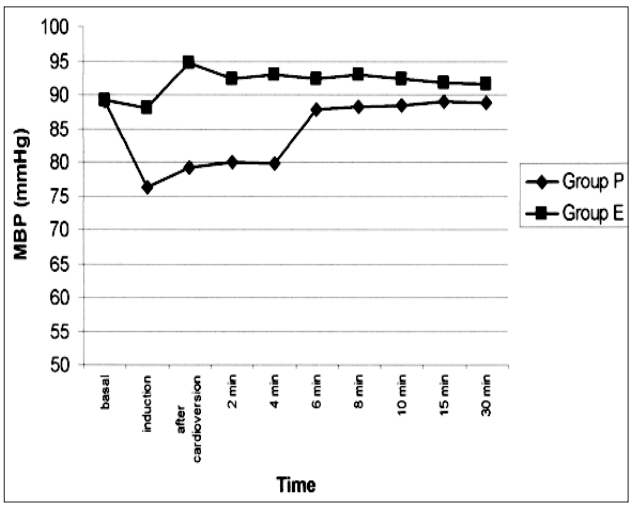

Figure 1 - Mean blood pressures (MBP) in the 2 groups.

Table 4 - Supplemental doses, side effects, and patient/cardiologist satisfactions in the 2 groups.

Parameters	Group P n (%)	Group E n (%)
Needed supplemental doses	1 (5)	2 (10)
Myoclonus	0 (0)	0 (0)
Apnea	2 (10)	0 (0)
Injection pain	3 (15)	0 (0)
Nausea/vomiting	2 (10)	3 (15)
Itching	0 (0)	0 (0)
Recall	1 (5)	0 (0)
Patient satisfaction		
Poor	0 (0)	0 (0)
Fair	0 (0)	0 (0)
Good	2 (10)	3 (15)
Excellent	18 (90)	17 (85)
Cardiologist satisfaction		
Poor	0 (0)	0 (0)
Fair	0 (0)	0 (0)
Good	3 (15)	2 (10)
Excellent	17 (85)	18 (90)

its baseline levels in 6 minutes. In group E, the mean blood pressure remained normal after induction, however, there was a slight increase after cardioversion. Mean blood pressures (MAP) were not different in other time intervals in group E (**Figure 1**). Hypotension (MAP<60 mm Hg) resolved without the use of vasoactive or inotropic drugs. After cardioversion over 2 minutes, the respiratory rate in group P decreased significantly when compared with group E (p=0.003). Two patients in group P became apneic (desaturation below 85% for 60 seconds) and needed assisted ventilation for 2 minutes. Pain scores at the shock site after cardioversion and at first hour were VAS ≤3 in both groups and were similar in groups (p=0.582). One patient in group P needed supplemental doses of propofol and 2 patients in group E needed etomidate. Side effects and patient/cardiologist satisfaction were similar in groups. No patient in either group had myoclonus (**Table 4**).

Discussion. The ideal anesthetic agent for cardioversion would provide amnesia, cardiorespiratory stability, a lack of motion, and a complete, rapid recovery for the patients with cardiac disease.[17] Many agents are used for this purpose, and all have some drawbacks.[6-8,10] The use of etomidate avoids hypotension, but the frequent occurrence of myoclonus often interferes with interpretation of electrocardiogram.[8] Because of excellent recovery profile, propofol was also preferred for cardioversion anesthesia, but undesired effects such as hypotension and apnea were reported frequently.[18,19] In some studies, fentanyl was also added to different induction agents for cardioversion anesthesia. Different doses of remifentanil were used as adjuncts to other induction agents for sedation in short procedures. In a very recent study by Maltepe F et al,[14] remifentanil usage was compared with fentanyl usage in cardioversion anesthesia. To reduce the doses of propofol and etomidate, we aimed at adding remifentanil and tried to decrease the side effects, such as myoclonus.

Herregods et al[11] used propofol 1 $mg.kg^{-1}$ and etomidate 0.2 $mg.kg^{-1}$ for cardioversion and provided stable hemodynamic conditions in unpremedicated patients. Their recovery scores, and psychomotor tests showed a faster recovery in the propofol group. They also reported that, manually assisted ventilation was needed in 7 patients in the etomidate group and 5 patients in the propofol group. In this study, myoclonus was reported in 6 patients after etomidate administration. Hullander et al[8] used propofol and etomidate infusions in cardioversion anesthesia. The induction doses of propofol was 1.4±0.3 $mg.kg^{-1}$ and of etomidate was 0.22±0.006 $mg.kg^{-1}$. They reported similar recovery times in both groups. Apnea was reported in 2 patients in

the propofol group and in one patient in the etomidate group. Myoclonus was high (45%) in the etomidate group. They also reported that, the hypotensive effect of propofol was attenuated by the infusion technique method to clinically insignificant levels.

Kick et al[12] used etomidate 0.25 mg.kg^{-1} and propofol 1.5 mg.kg^{-1} for cardioversion anesthesia and reported a significant decrease in the blood pressure, heart rate, and respiratory rate in the propofol group. Myoclonus was reported only in etomidate group. They found similar recovery characteristics, and therefore concluded that the choice of drug can be carried out by evaluating the side effects.

Jan et al[13] added fentanyl 2 μg.kg^{-1} to propofol 1.0 mg.kg^{-1} and sodium thiopentone 1.5 mg.kg^{-1}, they reported that both drugs were suitable for cardioversion anesthesia but the high incidence of apnea in this study was attributed to the additive effect of fentanyl. Canessa et al[6] added fentanyl 1.5 μg.kg^{-1} to propofol 1.5 mg.kg^{-1}, etomidate 0.15 mg.kg^{-1} sodium thiopentone 3 mg.kg^{-1} and midazolam 0.15 mg.kg^{-1} and they reported a high incidence of hypotension and apnea in the propofol group. Etomidate was reported as the only agent that did not decrease blood pressure, however, the only agent that caused myoclonus. Hagemeijer et al[9] also added fentanyl 0.9 mg to etomidate 14.5 mg, and except slight respiratory depression, the concurrent use of these drugs was reported as safe for cardioversion.

By adding remifentanil, we could reduced the doses of propofol and etomidate, and myoclonus, which was usually seen with the use of etomidate was not seen in our study. While performing this study, remifentanil usage in the cardioversion anesthesia had not been reported, therefore, we decided to arrange the dose of remifentanil according to the use of it in sedation of other short procedures. We had performed a pre-study using the remifentanil 1 μg.kg^{-1} with propofol 0.5 mg.kg^{-1} and etomidate 0.1 mg.kg^{-1} in our clinic.[20] In this pre-study, significant hypotension and apnea were seen in propofol used patients. Also, the recovery times of this study, which cause prolongation of stay in cardioversion room, were significantly longer than the recovery times that reported in some studies.[8,12] By these experiences, we decided to use a lower dose of remifentanil. As given, we could have induced unconsciousness by using the remifentanil 0.75 μg.kg^{-1} with propofol 0.5 mg.kg^{-1} and etomidate 0.1 mg.kg^{-1}. These doses of propofol and etomidate are the lowest doses reported in cardioversion anesthesia. Maltepe et al,[14] used 0.25 μg.kg^{-1} remifentanil in the cardioversion, and the mean propofol dose was found 0.9±0.43 mg.kg^{-1}, which is approximately more than 2 fold compared to our study. When compared with this study, we used propofol and etomidate in lower doses, so hypotension and apnea were seen less in our study. As mentioned before, myoclonus was also not seen in our study. As expected, recovery parameters were shorter in group P and cardiorespiratory stability was better in group E. Also patient and cardiologist satisfactions were similar in both groups. Nausea and vomiting were seen 10% in group P and 15% in group E and this was attributed to remifentanil usage.

We concluded that, we can induce hypnosis with propofol 0.5 mg.kg^{-1} or etomidate 0.1 mg.kg^{-1} by adding remifentanil 0.75 μg.kg^{-1} in cardioversion anesthesia. Although the recovery parameters were longer in group E, and the cardiorespiratory parameters were less stable in group P, these were clinically insignificant and their usage with remifentanil was both acceptable for cardioversion anesthesia.

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