Original Research

Anaesthesia for Cardioversion: A Prospective Randomised Comparison of Propofol and Etomidate Combined with Fentanyl

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Introduction: External electrical cardioversion is mostly performed solely under sedatives or hypnotics, although the procedure is painful. The aim of this prospective randomised study was to compare two anaesthetic protocols that included analgesia.

Methods: Patients with persistent atrial fibrillation were randomised to receive intravenously either fentanyl 50 μg and propofol 0.5 mg/kg (group P) or fentanyl 50 μg and etomidate 0.1 mg/kg (group E), while breathing spontaneously 100% oxygen. In the case of inadequate anaesthesia, repeated doses of 20 mg propofol (group P) or 4 mg etomidate (group E) were given as often as necessary until loss of eyelid reflex. Cardioversion was achieved with an extracardiac biphasic electrical shock ranging from 200 to 300 J, performed three times at most.

Results: Forty-six patients (25 in group P, 21 in group E), aged 64 ± 9 years, were enrolled in the study. There were no differences between the study groups concerning left ventricular ejection fraction, the dimension of the left atrium, the number of shocks needed or the number of unsuccessful cardioversions. Patients in group E had a shorter time from injection of the induction agents until loss of consciousness (49 vs. 118 s, p=0.003) and until the first shock was given (61 vs. 135 s, p=0.004). Systolic blood pressure decreased significantly (repeated measurements ANOVA with Bonferroni adjustment) in group P when the baseline value was compared to that after anaesthesia induction (mean decrease 15.2 mmHg, 95% CI 5.6-24.8 mmHg, p=0.001) and to the value after recovery (mean decrease 15.2 mmHg, 95% CI 4.8-25.7 mmHg, p=0.002). Manual ventilation was required in 7 and 9 patients in groups P and E, respectively (p=0.360).

Conclusion: Both anaesthetic regimens provided excellent conditions for external electric cardioversion. In addition, etomidate in combination with fentanyl had a shorter induction time and ensured haemodynamic stability.

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External electrical cardioversion for atrial fibrillation (AF) resistant to pharmacological therapy is a minor procedure that requires sedation and analgesia, as it is painful and distressing.[1] In the majority of studies concerning external electrical cardioversion, anaesthetic agents without analgesics have been used. The most common complications reported were oxygen desaturation, airway obstruction, apnoea, bradycardia and hypotension, while unpleasant and painful memories have been described by the patients.[2-7]

The aim of this clinical, prospective, randomised study was to compare two anaesthetic agents, combined with the same analgesic, for external electrical cardioversion. The selected outcome parameters

were rapidity of induction of anaesthesia, time of patients' arousal, and adverse events such as haemodynamic instability, airway obstruction, apnoea, need for respiratory support, and recall of anything unpleasant or painful.

Methods

Patient selection

Patients with persistent AF were included in the study. The diagnosis of AF was made by means of the surface electrocardiogram (ECG), based on the following criteria: a) fluctuation of the baseline without regular P or F waves, and b) totally irregular RR intervals. The duration of AF was assessed at entry into the study, based on medical records and existing ECGs. Exclusion criteria were age more than 80 years, previous cardiac surgery, pacemaker or defibrillator implantation, a full stomach and haemodynamic instability. Thyroid dysfunction and abnormal electrolyte concentrations were ruled out in all subjects. Maximal left atrial diameter and left ventricular ejection fraction were assessed in all subjects according to the standard methods.

Signed written consent was obtained from all subjects before their participation in the study. The study was approved by the Ethics Committee of our institution. This investigation conforms with the principles outlined in the Declaration of Helsinki. The study period was six months.

Electrical cardioversion

Electrical conversion to sinus rhythm was attempted while patients with AF were on an acenocoumarol regimen that resulted in an international normalised ratio between 2.5 and 3.5 for at least one month. Cardioversion was performed in the electrophysiology laboratory with an extracardiac biphasic electrical shock ranging from 200 to 300 J (Zoll). The ECG was monitored continuously during the procedure until a stable sinus rhythm was established.

Anaesthetic protocol and study groups

Patients were monitored using a 3-lead electrocardiogram, pulse oximetry and non-invasive blood pressure. An 18 or 20 gauge peripheral intravenous (i.v.) catheter was inserted for injecting drugs. All patients were preoxygenated for 2-3 minutes while breathing spontaneously before induction of anaesthesia using 100% oxygen via a facemask and a Mapleson breathing system.

The patients were randomly allocated to two groups to receive either propofol (group P) or etomidate (group E). Anaesthesia was induced as follows. In all patients fentanyl 50 μg i.v. was given, and after 60 seconds one of the anaesthetic drugs, according to randomisation, was injected over 30 seconds. Group P received propofol 0.5 mg/kg i.v. and group E etomidate 0.1 mg/kg i.v. In the case of inadequate anaesthesia the patients received repeated doses of 20 mg propofol (group P) or 4 mg etomidate (group E) as often as necessary until loss of consciousness.

The depth of anaesthesia was considered adequate when the patients no longer responded to commands and had lost the eyelid reflex. Then the patients were synchronously defibrillated. If sinus rhythm was not restored, a second or third shock was delivered. In case of upper airway obstruction, a chin lift and jaw thrust manoeuvre was applied. If apnoea occurred during the procedure, patients were manually ventilated with 100% oxygen.

Data collection

In each patient, the following data were collected: age, height, weight, sex, American Society of Anesthesiologists Physical Status classification. Systolic blood pressure (SBP), heart rate and oxygen saturation were measured before drug administration, immediately after induction of anaesthesia, one minute after cardioversion and following recovery. The following time intervals were recorded: from the end of the injection of the induction agent until loss of consciousness (T1); until first shock (T2); until eyes opened (T3); and until ability to answer simple questions about age and name (T4). The occurrence of apnoea or upper airway obstruction and a need for opening the airway or manual ventilation, as well as any appearance of myoclonus, were noted. The number of shocks, or failure to restore sinus rhythm, was recorded. The ejection fraction of the heart and the dimension of the left atrium were obtained from the pre-procedural echocardiographic examination.

After full recovery, the patients were asked about unpleasant memories associated with the procedure or local pain during the injection of the induction agent.

Statistical analysis

Statistical analysis was performed using SPSS Statistics v. 17.0. Data were analysed using the independent samples t-test, chi-square test or Fisher's exact test,

where appropriate, to evaluate inter-group differences, and repeated measures ANOVA for intra-group changes. A p-value <0.05 was considered statistically significant. Values are expressed as mean ± standard deviation or percentages of patients, as appropriate.

Results

Forty-six patients (25 in group P and 21 in group E) with a mean (± SD) age of 64 (± 9) years were enrolled in the study. Patients' characteristics and vital signs before anaesthesia induction, clustered by the study groups, are shown in Table 1. Left ventricular ejection fraction was 54 ± 13%, while the dimension of the left atrium was 44 ± 4 mm. One, 2 or 3 cardioversions were needed in 33, 5, and 3 patients, respectively, while in 5 patients sinus rhythm was not restored. There were no differences between the study groups concerning these echocardiographic findings, the number of shocks needed to restore sinus rhythm, or the number of unsuccessful cardioversions (Table 2).

The time intervals needed for anaesthesia induction, first cardioversion and patient arousal are presented in Table 3. Patients in group E had a statistically significantly shorter time from injection of the induction agents until the loss of consciousness and until giving the first shock.

The time course of SBP in both groups is shown in Figure 1. SBP showed a statistically significant decrease in group P ($p=0.0002$), but an increase in group E ($p=0.013$). Bonferroni adjustment for mul-

Table 1. Characteristics of patients who underwent external electrical cardioversion and vital signs before induction of anaesthesia in the propofol (P) and etomidate (E) groups.

	Group P (n=25)	Group E (n=21)	p
Age (years)	67.0 ± 8.3	61.2 ± 9.2	0.029
Height (cm)	171 ± 8.9	171 ± 10.0	0.759
Weight (kg)	87.1 ± 13.4	87.5 ± 14.3	0.922
Sex (m/f)	18/7	12/9	0.360
ASA Physical Status (2/3/4)	18/7/0	9/10/2	0.061
Systolic blood pressure (mmHg)	145.0 ± 24.2	135.3 ± 18.6	0.140
Heart rate (min^{-1})	90.0 ± 20.5	87.2 ± 21.7	0.660
Oxygen saturation (%)	97.7 ± 1.7	97.9 ± 1.9	0.731

ASA – American Society of Anesthesiologists.

Table 2. Details of echocardiographic findings and external electrical cardioversion in the propofol (P) and etomidate (E) groups.

	Group P (n=25)	Group E (n=21)	p
Left ventricular ejection fraction (%)	53.6 ± 12.2	53.9 ± 14.6	0.950
Left atrial diameter (mm)	45.2 ± 4.1	42.9 ± 3.4	0.055
Number of shocks needed to restore sinus rhythm (n):			
1	19	14	0.846
2	2	3	
3	2	1	
Not cardioverted after three shocks (n)	2	3	0.648

Table 3. Actual doses of anaesthetic agents and time intervals needed for anaesthesia, cardioversion and arousal in the propofol (P) and etomidate (E) groups.

	Group P	Group E	p
Number of patients requiring repeat doses of anaesthetic agents (n)	13	3	0.012
Total dose of anaesthetic agent (mg/kg)	0.70 ± 0.24	0.11 ± 0.01	n/a
Increase of actual anaesthetic dose in relation to predetermined (%)	40.7 ± 47.0	6.7 ± 14.3	0.002
Time from injection of induction agents until (s):			
Loss of consciousness	118 ± 95	49 ± 47	0.003
First shock	135 ± 104	61 ± 58	0.004
Opening of eyes	204 ± 117	195 ± 152	0.820
Answering simple questions	269 ± 112	251 ± 167	0.670

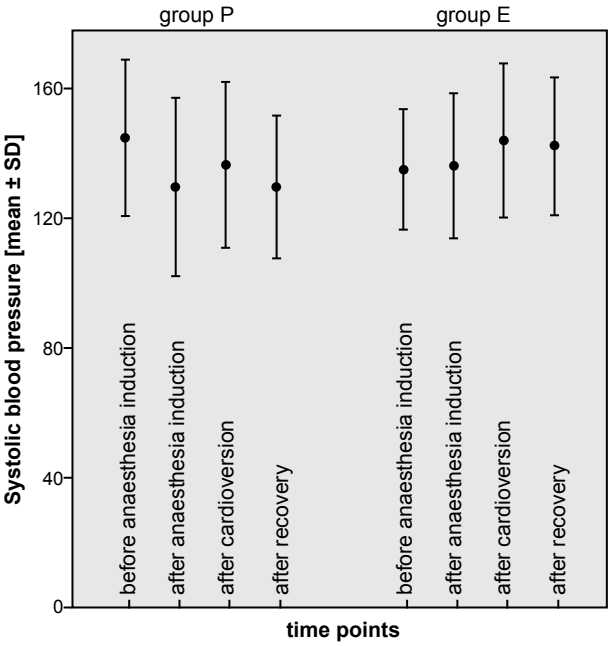

Figure 1. Time course of systolic blood pressure, clustered by study groups.

tiple comparisons revealed a statistically significant change only in group P when comparing the baseline SBP before drug administration to the value after anaesthesia induction (p=0.001, mean decrease 15.2 mmHg, 95% CI 5.6-24.8 mmHg) and to the value after recovery (p=0.002, mean decrease 15.2 mmHg, 95% CI 4.8-25.7 mmHg).

In Table 4, the two study groups are compared regarding the predefined complications. A decrease in SBP of more than 20% after anaesthesia induction was observed in 5 patients in group P, in contrast to none in group E. This difference did not reach statistical significance. Myoclonus appeared in half of the patients in group E, compared to none in group P. Only a few patients experienced pain during the i.v. injection or a recall of anything or anything painful during the cardioversion, without intergroup differences.

Discussion

As external electric cardioversion is a short, but painful procedure,[1] it is remarkable that in almost all studies solely sedative or hypnotic drugs have been used.[2-8] Despite the absence of analgesic agents, respiratory compromise has repeatedly been reported. Additionally, patients have complained about painful recall of the procedure. Thus, we decided to investigate two anaesthetic regimens that both included an analgesic agent.

Table 4. Complications in patients who received anaesthesia for external electrical cardioversion in the propofol (P) and etomidate (E) groups.

	Group P (n=25)	Group E (n=21)	p
Decrease of SBP ≥20%	5	0	0.054
Apnoea	7	10	0.225
Need for jaw thrust/chin lift	6	12	0.034
Need for manual ventilation	7	9	0.360
Myoclonus	0	11	0.0004
Painful i.v. injection	7	4	0.514
Recall of anything unpleasant	3	1	0.614
Recall of pain	3	1	0.614

SBP – systolic blood pressure; i.v. – intravenous.

In the present study, the time until loss of consciousness was significantly shorter for etomidate plus fentanyl in comparison to propofol plus fentanyl. This finding is consistent with pharmacokinetic studies of propofol and etomidate. The onset time after an anaesthetic induction dose of propofol and etomidate is 40 s and 15 to 30 s, respectively.[9] A possible explanation for the slight, albeit insignificant, differences in awakening times between the two drug combinations is the predetermined initial dose. The patients in the propofol group actually required more repeat doses than those in the etomidate group. Repeat bolus doses prolong the duration of sedation or hypnosis.[9]

The choice of the initial dose of propofol and etomidate in the present study was based on the pharmacology of each drug. As the recommended doses for induction of general anaesthesia in older (more than 60 years) and sicker patients are 1 mg/kg propofol and 0.2 mg/kg etomidate, we defined the initial dose for sedation at half these doses. However, the actual doses required exceeded the predetermined ones for propofol and etomidate by 40% and less than 10%, respectively. This difference is not related to a difference in the number of shocks required, which would necessitate differing length of sedation.

The differences in total doses and recovery times might be explained by the addition of fentanyl to both hypnotics. While the addition of small doses of fentanyl to etomidate for short surgical procedures reduces the required dose of etomidate and allows earlier awakening, the effect of fentanyl administration on propofol pharmacokinetics is controversial.[9] Experimental studies have shown conflicting

effects on propofol pharmacokinetics, depending on whether propofol is administered immediately after fentanyl or three minutes later.[10] As the hypnotic drug in the present study was administered one minute after fentanyl injection, it is difficult to determine whether propofol clearance was reduced or increased in comparison to propofol administration without fentanyl.

In two other studies that compared propofol to etomidate for cardioversion, a faster recovery time was noted in the propofol group.[2,11] This is contrary to the findings of the present study, although it can be explained by the different anaesthetic regimens. In these studies, a higher induction dose of both hypnotic agents was administered, compared with the present study, with no repeat doses, and furthermore, neither fentanyl nor any other analgesic agent was used.[2,11] In another study comparing propofol and etomidate, where incremental doses were given but no analgesic agent, no difference in recovery times was observed.[12] Thus, it seems that the time sparing effect of propofol only exists if one single dose without repetition and without analgesic drug is administered.

We observed a decrease in SBP in group P, as was expected from the pharmacodynamics of propofol. A usual anaesthesia induction dose of 2 mg/kg propofol produces a decrease in arterial blood pressure by as much as 40%, mainly due to vasodilatation and potentially enhanced by a direct myocardial depressant effect.[9] It is known that older and sicker patients in particular develop more profound hypotension, especially when propofol is combined with an opiate. We avoided a more pronounced hypotension by a slow injection and a careful titration of the required dose. Still, one fifth of the patients in group P showed a decrease in SBP by 20% to 35% after anaesthesia induction. In contrast, SBP in group E remained stable, as etomidate neither inhibits sympathetic tone nor impairs myocardial function, even in patients with valvular or ischaemic heart disease.[13] Neither did the addition of fentanyl to etomidate lead to hypotension. We would suggest that, especially in older patients with concomitant heart disease and/or borderline hypotension, etomidate with fentanyl should be preferred over propofol with fentanyl.

In twice as many patients in group E as in group P, an obstruction of the upper airway appeared that required a jaw thrust and chin lift manoeuvre. This is a simple and routinely performed movement which releases the obstructed airway. Apnoea with the need for manual assisted ventilation occurred in about one third of all patients, without any differences between the study groups. None of the patients exhibited a desaturation. Either of the studied drug combinations may impair the patency of the upper airway or the spontaneous respiration. Therefore, the presence of an experienced anaesthesiologist is a basic requirement for performing external electrical cardioversion under deep sedation.

Myoclonus occurred in half of the patients in the etomidate group. Myoclonic movements, a known side effect of etomidate, result from activity either in the brainstem or in deep cerebral structures;[9] however, they are not associated with seizure-like electroencephalogram activity.[14] The incidence of myoclonus is reported to be 60-80% in unpremedicated patients after etomidate injection and has been found to be reduced after pre-administration of fentanyl in a dose-dependent manner.[13,15,16] The proportion of patients who exhibited myoclonus in the present study lies well within the range expected from the literature. In none of these patients did the myoclonic movements disturb the ECG reading or interfere with or delay the electrical cardioversion.

Regarding recall of the procedure, we could not verify the superiority of propofol in comparison to etomidate that was found by Mitterschiffthaler and colleagues.[11] In that study, none of the 28 patients treated with propofol, compared to 4 of the 20 patients treated with etomidate, complained of recall of the cardioversion. However, almost double the dose of the hypnotic agents, compared to the present study, was used, and besides, there was no analgesic. These differences may account for the conflicting findings concerning recall. Our findings are in agreement with those of another recent study investigating recall of brief procedures, including cardioversion, in an emergency department.[17] In that study, too, a similarly low incidence of recall was observed, regardless of the combination of anaesthetic drugs used.[17]

In conclusion, the present study showed that both of the anaesthetic regimens used were adequate for external electrical cardioversion. Both pharmacological combinations provided rapid anaesthesia induction and excellent conditions for cardioversion, as well as a good safety profile and a quick recovery. We suggest that in older or sicker patients etomidate with fentanyl should be preferred over propofol with fentanyl to maintain haemodynamic stability. The presence of an anaesthesiologist is a precondition, to recognise and manage potential upper airway obstruction or apnoea.

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