Comparative effects of thiopental and propofol on atrial vulnerability: electrophysiological study in a porcine model including acute alcoholic intoxication†

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**Background.** Atrial tachyarrhythmias (AT) frequently complicate the perioperative period. Alcohol intoxication is a recognized causative factor for dysrrhythmias. We studied the effects of propofol and thiopental on atrial electrophysiology and vulnerability to AT in a closed-chest porcine model in which AT are facilitated by ethanol.

**Methods.** Thirty-eight pigs were randomly assigned to thiopental (T-group, \(n = 19\)) or propofol (P-group \(n = 19\)). All animals were assigned to undergo a right atrial electrical stimulation protocol (RASP) at baseline. Thirty pigs were assigned to undergo additional RASP during ethanol infusion, while the remaining eight were assigned to undergo additional RASP during saline infusion (control group). We analysed effective refractory period (ERP), and intra-atrial conduction interval (ICI) (between atrial sites 4 cm apart), at several cycle lengths (CL).

**Results.** There were no significant differences at baseline. During ethanol infusion, propofol produced a greater rate-dependent decrease in excitability, manifested by a longer minimum paced CL with 1:1 atrial capture: 145 (11) vs 164 (27) ms in the T- and P-group, respectively \((P=0.01)\). Propofol was associated with a greater rate-related slowing in conduction: difference between ICI at CL of 300 ms and ICI at minimum CL: 30 ms in P-group and 22 ms in T-group \((P<0.03)\). In the P-group we observed a longer duration of induced arrhythmias (145 (131) vs 74 (91) s, \(P<0.03\)) and a higher proportion with atrial flutter (AFl) (76 vs 19%, \(P<0.001\)).

**Conclusions.** Propofol in this model was more arrhythmogenic than thiopental, as manifested by a longer duration of induced arrhythmias, particularly AFl.

**Keywords:** anaesthetics i.v., propofol; anaesthetics i.v., thiopental; heart, atrial refractoriness; heart, conduction velocity; heart, atrial tachyarrhythmias

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Atrial fibrillation (AFib), atrial flutter (AFl), or atrial tachycardia, frequently complicate the perioperative period, and are recognized as a major cause of morbidity, hospital stay, and cost of health care.1–3

Safe anaesthetic management of patients with atrial tachyarrhythmias (AT) depends on an understanding of the pathophysiology of AT and the effects of anaesthetic agents on cardiac electrophysiology and AT. However, information regarding the effects of i.v. anaesthetic agents, in particular thiopental and propofol, on atrial vulnerability is limited, but it suggests differences in their effects on electrophysiologic properties.4,5 Thus, we hypothesized that thiopental and propofol would behave differently in a model in which AT were facilitated.

The prevalence of alcoholism is increasing and the close association between drinking-related pathological disorders and acute trauma ensures that large numbers of alcoholic patients present for emergency procedures requiring anaesthesia or sedation.6–8 Moreover, there are several clinical reports relating alcohol consumption with AT and the term

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‘holiday heart syndrome’ is currently used to describe such an association. In this context it seems appropriate to: (i) use animal models to test anaesthetic agents before undergoing clinical trials; and (ii) include alcohol exposure as a part of the animal model.

The present study was designed to investigate the effects of propofol and thiopental on atrial electrophysiologic properties and on vulnerability to AT. The study was performed in an animal model in which it was shown previously that AT was facilitated by an infusion of ethanol.

**Materials and methods**

This study was performed in accordance with the guidelines of the Animal Research Committee of the Complutense University of Madrid, Spain.

**Experimental design (Fig. 1)**

Following pre-medication, anaesthetic agent infusion was started until the desired anaesthetic level was achieved. Then, the animal was instrumented, and a right atrial stimulation protocol (RASP) was performed (baseline RASP). Ethanol was subsequently infused intravenously and an identical RASP was performed (ethanol RASP). When an additional dose of ethanol was infused (second ethanol infusion, see below), a third identical RASP (ethanol RASP) was performed.

To analyse the effects of a potential animal deterioration as a result of manipulation and duration of the procedure, the same experiment was performed in a control group in which ethanol infusion was replaced by saline infusion.

**Animals**

The experimental model was attempted in 38 large white pigs (mean weight 34 kg) that were randomly assigned to receive thiopental (T-group, n=19) or propofol (P-group, n=19). Six were excluded: four in the T-group because of difficulties with femoral vein dissection (n=1), inadvertent induction of ventricular fibrillation by ventricular capture (n=1), severe respiratory depression (n=1), and extremely high ethanol concentration (n=1); two in the P-group because of an error in the stimulation protocol (9 ms instead of 1 ms pulse width) (n=1), severe respiratory depression (n=1). The remaining 32 animals formed the basis of this study.

A pre-specified subset of four animals within each group (eight animals in total, control group) was assigned to receive comparable volumes of isotonic saline instead of ethanol during which a RASP was performed (saline RASP).

Our aim was to develop a closed-chest animal model with the least possible instrumentation. The animals were premedicated with ketamine at a dose of 20 mg kg\(^{-1}\) intramuscularly, and were supplemented with oxygen (at a flow of 4 litre min\(^{-1}\)) throughout the study. A superficial vein was cannulated to infuse the anaesthetic agent. The anaesthetic dose was intended to induce heavy sedation, maintaining spontaneous respiration, but without palpebral reflexes and purposeful movements either spontaneously or in relation to instrumentation/stimulation.

**Thiopental infusion**

As a result of the rapid distribution properties of thiopental, the dosing schemes involve the administration of several consecutive infusion rates, the first of which is a loading infusion designed to rapidly achieve therapeutic concentrations. The next infusion aims to replace drug lost from the circulation and hence maintain a constant plasma level. Our aim was to maintain a thiopental plasma concentration of 10–15 µg ml\(^{-1}\) to achieve sedation without losing spontaneous breathing and responses to hypercarbia and hypoxia.

We employed thiopental sodium at an initial dose of 4 mg kg\(^{-1}\), followed by a series of infusion steps of decremental rates from 0.3 to 0.09 mg kg\(^{-1}\) min\(^{-1}\). The rate of infusion was that which was found to produce an adequate clinical depth of anaesthesia. Some animals needed small additional doses of thiopental during the experiment. In these pigs, additional boluses of 25 mg were infused until clinical effects were achieved.

An attempt was made to maintain a stable level of anaesthesia (adequate respiratory rate, absence of purposeful movements) by altering the rate of hypnotic infusion in response to clinical signs of inadequate anaesthesia or excessive drug effect.

**Propofol infusion**

Propofol 1% at an initial bolus of 2 mg kg\(^{-1}\) was given, followed by a mean rate of infusion of 3–4.5 mg kg\(^{-1}\) h\(^{-1}\).
and when necessary modified to maintain an adequate level of clinical anaesthesia.

When ethanol infusion was started, the infusion of the anaesthetic agent was reduced to compensate for the depressant effects of ethanol in order to maintain the desired anaesthetic depth. This reduction was adjusted on an individual basis, but was usually significant. If the animal showed signs of inadequate ventilation, we stopped the anaesthetic infusion until respiration recovered. The animal was intubated if it was necessary.

**Monitoring**

The ECG was continuously monitored in all animals. In 18 consecutive animals arterial blood samples were obtained for gas analysis during ethanol infusion (during saline infusion in the control group); in 12 of those, arterial pressure was continuously monitored by means of an intra-arterial catheter (Arrow®, Monitor: Life Scope G. Nihon Kohhen®) and recorded (Fig. 1).

**Ethanol infusion protocol**

In 14 animals, an attempt was made to test the arrhythmogenic effects of two ethanol concentrations. After the observation of a tendency to a greater arrhythmogenicity of the higher concentration, in the remaining animals this concentration alone was tested. The first alcohol infusion intended to produce an ethanol blood level between 150 and 200 mg dl⁻¹. The second alcohol infusion aimed at a venous concentration between 250 and 350 mg dl⁻¹. Both alcohol infusions consisted of a loading dose followed by a maintenance infusion. Doses were calculated as described previously in detail.12 In summary, the initial loading dose was 1.24 mg kg⁻¹ infused as 40% ethanol, at a dose of 3 ml min⁻¹.

During each RASP, venous blood samples for ethanol concentration determination were obtained every 10 min, and whenever an arrhythmia was produced.

Ethanol concentrations were measured by Gas Chromatography (Series II 4890 Hewlett Packard Inc., Andover, MA, USA), incorporating a ‘headspace’ (Hewlett Packard 19395A) with an integrator (Hewlett Packard 3394). Ethanol concentration determinations were performed at an injection temperature of 250°C with a column HP 20 M-Carbowax at an oven temperature of 90°C with a flame detector (FID) at 250°C. Ethanol was eluted with a retention time of 2.45 min.

**Electrical stimulation and recordings**

Electrical stimulation was bipolar, consisting of square pulses of 1-ms duration at five times diastolic threshold, delivered by a programmable stimulator (Medtronic 5325 (Medtronic Inc., Minneapolis, MN, USA)). Each RASP included single, double, and triple extra stimuli at a variety of coupling intervals, as well as trains of rapid atrial pacing at different rates. The endpoint of each stimulation protocol was the initiation of a sustained AT. All RASP were performed in a stable cardiorespiratory condition.

Recordings were made by means of a Mingograph 4 (Siemens-Elema, Solna, Sweden) at a paper speed of 25–100 mm s⁻¹. A custom-made decapolar catheter (Bard®) was used for stimulation and intracardiac recordings (filtered between 70 and 500 Hz). This catheter was inserted into the right femoral vein (usually percutaneously, and under local anaesthesia with mepivacaine 1%), and advanced under fluoroscopic guidance to the right atrium, usually to its lateral wall.

**Definitions**

AT: an atrial rhythm at a rate more than 200 beats min⁻¹ lasting for more than 1 s. This was considered sustained when it lasted for more than 1 min.

AFl: if the atrial rhythm was irregular and at a rate more than 300 beats min⁻¹.

AFl: if the atrial rhythm was regular at a rate more than 250 beats min⁻¹.

Arrhythmia duration: this was studied in three ways: the duration of the arrhythmic episode in seconds; if this was sustained or not; if duration was longer than 5 min (designated as a ‘long-lasting arrhythmia’).

Arrhythmia cycle length (CL): interval (in ms) between two consecutive atrial ECG. It was analysed by the mean CL every 6 s. The longest arrhythmia observed during each RASP was considered ‘the arrhythmia’ induced during that protocol.

Atrial effective refractory period (AERP): the longest S1–S2 interval that failed to result in atrial depolarization.

Intra-atrial conduction interval (ICI): the conduction time between dipole 1–2, and the dipole 5–6 and 7–8 (32 and 48 mm away from the stimulation electrode, respectively) of the decapolar catheter that was used for stimulation and recording. For statistical purposes, the mean of the values obtained at pairs of electrodes 5–6 and 7–8 for each individual experiment was used.

Minimum paced CL: is the shortest paced CL with 1:1 atrial capture.

P wave duration: we measured the P wave duration always at 300 ms CL.

**Statistical analysis**

Comparisons of baseline and of ethanol RASP were only performed between thiopental and propofol. In contrast, in saline RASP, as its purpose (as a control group) was to evaluate a potential biological deterioration, saline RASP was compared with baseline RASP. During ethanol infusion, statistical analysis was performed including all the electrophysiologic evaluations, as some animals underwent two electrophysiologic studies with different ethanol concentrations. Three types of RASP were compared: (i) baseline RASP (one RASP per animal); (ii) ethanol RASP: as five
animals in the T-group and eight animals in the P-group underwent only two ethanol infusions there were finally 16 RASP in the T-group to compare with 21 RASP in the P-group; (iii) saline RASP: two saline RASP per animal were attempted in the eight animals assigned to the control group, and seven animals completed the second saline RASP, to a total of 15 saline RASP.

All measurements are reported as mean (SD). Continuous variables were compared using independent Student’s t-test. To compare the difference between conduction interval at 300 ms and minimum CL we used an ANCOVA type analysis to study the influence of the anaesthetic and a cofactor: the minimum CL with 1:1 atrial capture. Categorical variables were compared using the $\chi^2$ or Fisher’s exact test, as appropriate. Statistical analysis was performed using commercially available computer software SPSS version 9.

Results

The electrophysiological findings of individual RASP in thiopental and propofol groups are displayed in Tables 1 and 2. There were no differences between the T- and P-groups in general characteristics: animal weight, study duration, first and second venous ethanol concentration, blood gas analysis, and haemodynamic parameters (Tables 3 and 4).

One major issue in this study was the provision of stable, long-lasting anaesthesia with minimal depression on the circulatory or respiratory systems. However, it was necessary to intubate some animals in both study groups, especially during alcohol infusion (eight in the T-group vs five in the P-group, $p$=n.s.). This is reflected in higher $\text{Po}_2$ values in the T- and P-groups compared with the control group (Table 3).

Baseline protocols (Table 5)

No statistical differences were found in electrophysiologic parameters. A tendency was noted towards a longer ICI in the propofol group, but this did not reach statistical significance. There were no differences in induced arrhythmias between the groups.

Ethanol protocols (Table 5)

No differences in conduction or refractoriness were observed at usual pacing rates (400 and 300 ms, equivalent to 150 and 200 beats min$^{-1}$). There were no differences in P wave duration and ICI at paced CL of 400 and 300 ms. However,

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different electrophysiological effects were observed at high pacing rates. The minimum CL with 1:1 atrial capture was shorter in the T-group than in the P-group. At very high pacing rates a rate-related increase in ICI was observed.

Table 2 Description of electrophysiologic findings in propofol group. Baseline/ethanol: study performed in the baseline or during ethanol infusion. SHR: sinus heart rate; beats min⁻¹. Arr.: arrhythmia induced. AFib: atrial fibrillation, AFl: atrial flutter. A.Durat.: arrhythmia duration (in seconds). When an arrhythmia lasted more than 300 s it was terminated by overdrive atrial pacing, and it was classified as a ‘longer duration arrhythmia’. PWD: P wave duration. ERP 400, 300: effective refractory period at a paced CL of 400, 300 ms. ICI 400, 300, min: intra-atrial conduction interval measured at a CL of 400, 300 and min CL. Min CL: shortest CL with 1:1 atrial capture.

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<td>40</td>
<td>40</td>
<td>125</td>
<td>55</td>
<td></td>
</tr>
<tr>
<td>7 B</td>
<td>122</td>
<td>AFI &gt;300</td>
<td>105</td>
<td>130</td>
<td>130</td>
<td>48</td>
<td>48</td>
<td>160</td>
<td>95</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 B</td>
<td>146</td>
<td>AFI &gt;300</td>
<td>120</td>
<td>130</td>
<td>130</td>
<td>60</td>
<td>63</td>
<td>155</td>
<td>73</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14 B</td>
<td>115</td>
<td>AFI</td>
<td>10</td>
<td>105</td>
<td>170</td>
<td>165</td>
<td>60</td>
<td>58</td>
<td>180</td>
<td>83</td>
<td></td>
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<tr>
<td>17 B</td>
<td>92</td>
<td>AFib</td>
<td>15</td>
<td>130</td>
<td>135</td>
<td>150</td>
<td>63</td>
<td>68</td>
<td>130</td>
<td>93</td>
<td></td>
</tr>
<tr>
<td>21 B</td>
<td>87</td>
<td>AFI</td>
<td>9</td>
<td>–</td>
<td>146</td>
<td>138</td>
<td>68</td>
<td>68</td>
<td>150</td>
<td>88</td>
<td></td>
</tr>
</tbody>
</table>

Table 3 General experimental characteristics. Blood gas analysis was performed during ethanol infusion (saline infusion in the control group). Values are mean (SD). Numbers in square parentheses represent number of experiments. P refers to a statistical comparison between thiopental and propofol.

<table>
<thead>
<tr>
<th>Control</th>
<th>Thiopental</th>
<th>Propofol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>34 (5)</td>
<td>33 (4)</td>
</tr>
<tr>
<td>Duration of study (min)</td>
<td>168 (22)</td>
<td>170 (34)</td>
</tr>
<tr>
<td>Ethanol venous concentration (g litre⁻¹)</td>
<td>1st infusion</td>
<td>7.0 (0.67)</td>
</tr>
<tr>
<td>Blood gas analysis</td>
<td>pH</td>
<td>7.4 (0.04)</td>
</tr>
</tbody>
</table>

Table 4 Haemodynamic parameters. Values are mean (SD). SBP: systolic arterial pressure; DBP: diastolic arterial pressure; HR: heart rate; Δ HR B-E: baseline-ethanol. There were no statistical differences between thiopental and propofol groups in any of the data.

<table>
<thead>
<tr>
<th>Control</th>
<th>Thiopental</th>
<th>Propofol</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP (mm Hg)</td>
<td>111 (12)</td>
<td>116 (15)</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td>68 (9)</td>
<td>64 (7)</td>
</tr>
<tr>
<td>HR (beats min⁻¹)</td>
<td>104 (17)</td>
<td>113 (29)</td>
</tr>
<tr>
<td>Δ HR B-E</td>
<td>47 (16)</td>
<td>45 (25)</td>
</tr>
</tbody>
</table>

different electrophysiological effects were observed at high pacing rates. The minimum CL with 1:1 atrial capture was shorter in the T-group than in the P-group. At very high pacing rates a rate-related increase in ICI was observed.
in all experiments. The amount of this increase was significantly greater in the P-group, as the difference between ICI at the minimum pacing CL and ICI at pacing CL of 300 ms was significantly greater in the P-group (Table 5). This was observed despite a longer minimum pacing CL in the P-group.

Arrhythmia duration was longer in the P-group (145 (131)s) than in the T-group (74 (91)s, P=0.03). As shown in Table 6, a higher tendency to sustainability of AT was found in the P-group: arrhythmias lasted longer, were sustained more often, and were significantly more long lasting. These effects were observed in the presence of a greater atrial CL and expressed more often as AFI.

**Saline protocols**

Table 7 shows electrophysiologic parameters in the control group. There were no differences in duration and type of induced arrhythmias between baseline and saline protocols. The animals in which AFib was induced at baseline also presented AFib on saline, the same was observed with AFI.

**Discussion**

The main finding of this study is that, in this animal model, when studied under the arrhythogenic effects of ethanol, propofol anaesthesia was more arrhythogenic than thiopental anaesthesia, as manifested by a higher proportion of animals having sustained AT, and a longer duration of induced arrhythmias. Some differences found in the electrophysiologic behaviour at high pacing rates between animals assigned to each agent could relate to this finding.

**Electrophysiological parameters**

Several studies have provided evidence that thiopental increases effective refractory period (ERP) and/or action potential duration, whereas propofol produces a decrease or no change in these parameters. However, the majority of these experiments were performed in ventricular myocytes. We failed to show a difference between groups in atrial refractoriness.

Previous studies evaluated the effects of both anaesthetics on conduction properties. Azuma, Matsumura and Kemmotsu in the isolated guinea pig papillary muscle showed no effect on Vmax at any propofol concentration (0.2–0.6 μM); in contrast in rat papillary muscle, propofol caused a decrease in Vmax to 85.9% of control at 0.6 μM concentration and 0.5 Hz stimulation. In the same study Azuma, Matsumura and Kemmotsu

| Table 5 | Electrophysiologic findings. Values are mean (SD). PWD: P wave duration. HR: heart rate; beats min⁻¹; ST: stimulation threshold. ERP 400, 300: effective refractory period at paced CL of 400 and 300 ms (equivalent to 150 and 200 beats min⁻¹). ICI 400, 300: min: intra-atrial conduction interval (CI) measured between two atrial sites 4 cm apart, at a CL of 400, 300 and min CL. Min CL: shortest CL with 1:1 atrial capture. D.CL (in milliseconds): rate-related slowing in conduction represented by difference in CI between the shortest CL and CL of 300 ms. Thiopental vs propofol. In square parentheses number of RASP performed
| Table 6 | Arrhythmias induced as a result of RASP performed during ethanol infusion. Values are mean (sd), or number [proportion]

**Table 7** Electrophysiologic parameters in the control group. Values are mean (SD). PWD: P wave duration. HR: heart rate; beats min⁻¹. ST: stimulation threshold. ERP 400, 300: effective refractory period at paced CL of 400 and 300 ms. ICI 400, 300, min: intra-atrial conduction interval measured between two atrial sites 4 cm apart, at a CL of 400, 300 and min CL. Min CL: shortest CL with 1:1 atrial capture. D.CL (in milliseconds): rate-related slowing in conduction represented by difference in CI between the shortest CL and CL of 300 ms

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showed that thiamylal (thiobarbiturate similar to thiopental) decreased $V_{\text{max}}$ in papillary muscles of both pigs and rats to 47 and 46% of control, respectively.

Napolitano and colleagues\textsuperscript{4} compared conduction velocity modulation by thiopental and propofol at a paced CL of 300 ms in a porcine model, and found no differences.

Wu, Su and Sun\textsuperscript{20} studied the effects of propofol on atrial and ventricular conduction in the rabbit under autonomic block. Sodium current was decreased dose dependently by propofol, and this suppression was frequency-dependent. That is, a greater inhibitory effect was observed at more rapid stimulation rates.

In rat ventricular myocytes Saint\textsuperscript{21} showed an intense depressant effect of propofol at Na channels at clinically used doses. In agreement with these experimental studies, we observed a rate-related increase in intra-atrial conduction time, expressed as a decrease in conduction velocity, at very high pacing rates. This phenomenon was more intense in the propofol group than in the thiopental group.

Stowe, Bosnjak and Kampine\textsuperscript{22} showed that on a molar basis, propofol was more potent than thiopental for depressing cardiac excitability. In our study the stimulation threshold was not different between both groups, that is, the excitability was similar at slow stimulation rates. In contrast, the shortest CL with 1:1 atrial capture during ethanol infusion was shorter in the thiopental than in the propofol group (145 vs 164 ms). This could reflect a more profound decrease in excitability in the propofol group.

**Induced arrhythmias**

To our knowledge, there are no clinical and or experimental comparative studies evaluating the effects of thiopental and propofol on AT. Some case reports have associated the clinical use of propofol with bradyarrhythmias,\textsuperscript{23} atrioventricular conduction block,\textsuperscript{24} asystole\textsuperscript{25} and conversion of supraventricular tachycardia to normal sinus rhythm.\textsuperscript{26}

Sympathovagal interaction may play a more important role in the pathogenesis of atrial arrhythmias.\textsuperscript{27} Vagal stimulation and acetylcholine administration, by causing a heterogeneous shortening of refractoriness, can facilitate AT. Propofol is known to affect the autonomic nervous system in a different way to thiopental. Propofol possesses sympatholytic and vagolytic properties, but a greater reduction in sympathetic than parasympathetic tone compared with thiopental.\textsuperscript{28}

Conduction abnormalities favour AT by reducing the wavelength for re-entry and are usually considered to be secondary to underlying atrial disease. Buxton and co-workers\textsuperscript{29} evaluated intra-atrial conduction in patients with and without spontaneous AT, and showed that a delay in conduction of early premature atrial stimuli was a marker of patients with AT. Cosio and colleagues\textsuperscript{30} showed that patients with AT had a higher tendency than controls to develop slow intra-atrial conduction of premature impulses. In a chronic dog model Gaspo and colleagues\textsuperscript{31} demonstrated that rapid atrial activation caused time-dependent decreases in conduction velocity which, along with other factors, provided the substrate for development of AT. Thus, it is conceivable that the greater slowing in conduction noted in the P-group at high rates could have contributed to the increase in arrhythmia duration.

Our results could indicate either an arrhythmogenic effect of propofol or, alternatively, an antiarrhythmic effect of thiopental. Both the abovementioned differences in sympathovagal interactions and the observed differences in electrophysiologic properties would favour the former.

**Limitations**

Development of the model as described (i.e. with maintenance of spontaneous ventilation throughout the experiment) was sometimes difficult, and some animals eventually required intubation. In order to prevent further depression during the infusion of ethanol, the anaesthetic doses had to be reduced individually, this was usually significant. This is a limitation of our model. We accept that the decision to develop the model in this way as opposed to intubating the animals from the beginning, can be controversial, but it was made for two reasons: (i) previous models that had failed to demonstrate that alcohol-facilitated arrhythmias were performed under full general anaesthesia;\textsuperscript{32} (ii) as the depressant effects of alcohol were expected to appear (at least haemodynamically) and to indicate a need for a decrease in the anaesthetic rate, the concentration of the anaesthetic could never have been constant, even with the alternative intubated model. We feel that the model, as used, could be closer to the clinical situation in which the anaesthetic dose needs to be carefully adjusted during the procedure any time the effect of a depressant agent is added or has been present previously.

**Clinical implications**

Some recent case reports suggest that propofol may have antiarrhythmic properties.\textsuperscript{33,34} These findings could be considered at variance with our observations. However, two of these reports dealt with arrhythmias of different origin (ventricular tachycardia or junctional tachycardia) and suggested sympathetic block and effects on the AV node to explain these antiarrhythmic observations.\textsuperscript{26} A third study reported on the case of a young man with hyperthyroidism and AFib that reverted to sinus rhythm after the infusion of propofol before electrical cardioversion.\textsuperscript{35} It is well known that in a minority of cases sympathetic activation usually precedes and/or facilitates AFib and in such cases it is conceivable that induced sedation can terminate atrial fibrillation. This is unlikely to relate to the observations in our model in which already sedated animals developed AT. In anaesthetic practice it is not infrequent to find patients with a background of spontaneous AT, and/or patients that need a procedure or anaesthetic and are under the effects of alcohol. Although the exact percentage of patients presenting for anaesthesia whilst exposed to alcohol is not...
clearly established, recent reports highlighting the importance of alcohol exposure during surgical procedures\textsuperscript{36} suggest a relatively high prevalence. A recent report found that 31–45\%\textsuperscript{7,37} of patients admitted for major traumatic injury had significant blood ethanol levels. Our data suggest that different anaesthetic agents could behave in different ways in terms of a tendency towards atrial arrhythmias, at least in relation to alcohol. This would deserve consideration in terms of future study designs to improve selection of anaesthetic agents in specific clinical situations.

**Acknowledgement**

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**References**

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