Catheter ablation using very high frequency current: effects on the atrioventricular junction and ventricular myocardium in sheep

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Background Radiofrequency ablation is currently used in the treatment of various cardiac arrhythmias. However, this technique is limited by impedance rise, leading to coagulum formation and desiccation of tissue. We developed a new generator, providing very high frequency (27 MHz) current, which is in the intermediate range between radiofrequency and microwave energy. The aim of this study was to evaluate the results for catheter ablation of the atrioventricular junction and characteristics of the lesions obtained at ventricular sites.

Methods and Results The generator was coupled to a specially designed 7-French coaxial catheter. The study included experiments performed on 10 sheep (Wt. 31–42 kg). In seven sheep, the catheter was introduced into the femoral vein and advanced across the tricuspid annulus to record the largest possible His electrogram. VHF current was applied for 25 s, with increasing energies. The energy needed to obtain complete atrioventricular (AV) block ranged from 60 to 100 Watts. Six animals were observed for 6 to 21 days. Complete AV block was found to be persistent. In those seven sheep in whom AV junction was ablated and in three additional sheep, the ablation catheter was positioned toward the right ventricular apex using the same approach and into the left ventricle via the femoral artery, and 20 to 90 Watts energy was delivered in order to assess the size of the induced lesions. Side effects included ventricular tachycardia degenerating into ventricular fibrillation in six cases, but the same effect was observed in this animal model with radiofrequency energy. No cardiac perforation was noted. No thrombus was observed at the catheter tip. The size of the lesion ranged from 3 to 45 mm in width and 1 to 15 mm in depth.

Conclusions Catheter ablation using VHF current is feasible and appears effective in producing stable AV block when applied at the AV junction and results in substantial myocardial lesions. Further studies are needed to define its clinical interest and side effects.

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Key Words: Catheter ablation, atrioventricular junctional ablation, atrioventricular block, radiofrequency, microwave.

Introduction

Radiofrequency (RF) energy, using 100 to 700 kHz current, is an established technique for catheter ablation[1,2]. It has proved to be very efficient in the treatment of supraventricular tachycardias[3,4]. However, some arrhythmias cannot successfully be ablated with RF energy, needing more extensive or linear lesions. Radiofrequency ablation is associated with a limited amount of tissue ablated, which is sufficient in most of supraventricular arrhythmias with a low risk of complications but may not be suitable in some cases of atrial or ventricular tachyarrhythmias. In other instances,
ablation may be achieved with radiofrequency energy, but requires a longer duration of the procedure to obtain a sufficient lesion size. Therefore, exposure of the patient and the physician to X-ray is increased.

We developed a new method of catheter ablation, based on delivery of very high frequency (VHF) current, using a frequency of 27 MHz, which is in the intermediate range between RF and microwave energy (30 to 3000 MHz). Very high frequency current was expected to obtain deeper lesions compared with regular RF ablation. Using this energy, the impedance variation during the energy delivery is much lower than with radiofrequency, reducing the role of tissue contact or thrombus formation. Moreover, experimental data showed that VHF current can be applied in the bipolar mode, with the ability to induce linear lesions in vitro. Our experimental experience in sheep with very high frequency current applied through a specially designed catheter at the AV junction and at ventricular sites is presented.

Methods

Technical data

VHF current was produced by a low power generator, delivering a 27·12 MHz sinusoidal waveform. The signal was amplified to supply power reaching 100 Watts. Special attention was given to power coming back from the catheter. This was obtained by a specially designed custom-made device, which allowed an automatic adaptation of the impedance[5]. Briefly, it consisted of a device supplying impedance adaptation in case of variation related to power reflected from the catheter. The amplified signal was conducted across a reflectometer, measuring transmitted and reflected wave amplitudes. An impedance matching software automatically adjusted the impedance. Our current system needs at least a 0·3-s pause in energy delivery to permit impedance adaptation. The experiments showed stable impedances with this equipment, ranging from 71 to 88 Ohms (unpublished data). Tissue temperature was found to increase to a maximal level of 76°C. Temperature and impedance were not systematically measured in the present study, but impedance monitoring was ensured by the software, without significant change.

In initial experiments conducted in our laboratory, we used currently available electrode catheters (USCI woven Dacron, 7-French size, Bard) connected to the generator. However, they appeared to transmit only part of the energy, because of excessive heating released into the catheter. We therefore designed a 7-French unipolar catheter with a 5 mm tip and a coaxial cable, allowing 100 Watts delivery and, thereby, reducing energy loss. This catheter was flexible, easy to build, with an ability to reach all intracardiac sites (bipolar recording was not necessary but it is possible to design a similar catheter with two electrodes). Very high frequency current was delivered between this electrode and a large posterior chest patch. Each application consisted of several pulses of 5 s duration each, with 5 s intervals in order to verify impedance adaptation.

Animal handling

Ten adult sheep, weighing from 31 to 42 kg, were studied. The procedure was conducted in accordance with National and Institutional Rules for invasive studies on animals. Animals were given an intravenous injection of sodium pentobarbital (10 to 30 mg/kg body weight) before being intubated. General anaesthesia was maintained with 1·0–1·5% halothane, ketamine chlorhydrate, and using an assisted ventilator. Blood samples were withdrawn on the day before and at the end of the procedure, in order to measure creatine kinase (MB), lactatedehydrogenase, blood cell count and standard biochemical levels. Standard ECG was monitored throughout all the study.

Procedure

The femoral vein and artery were exposed for catheter insertion. First, the venous catheter was advanced under fluoroscopic guidance into right atrium and ventricle. Intracardiac unipolar electrograms were filtered to pass 30 to 500 Hz then unfiltered in order to measure the magnitude of ST segment elevation. Tracings were displayed on a VR-16 E for M (Electronics for Medicine) oscilloscope and recorded on an Astro-Med strip chart recorder. In seven sheep, the catheter was slowly withdrawn from the right ventricle towards the right atrium in order to record the largest His deflection. VHF energy was delivered using increasing energies ranging from 10 to 100 Watts (five pulses of 5 s for each energy level, then increased by 10-Watt steps) until complete atrioventricular block was achieved. However, at the maximal energy level, longer times could be necessary to obtain complete AVB using different catheter positions. Then, VHF energy was delivered at the right ventricular apex. Immediately after right heart ablation, the catheter was inserted into the femoral artery and advanced into the left ventricle using a retrograde aortic approach. VHF current was delivered at the left ventricular apex. Sufficient contact with the myocardial wall was assessed by monitoring ST segment elevation aiming to achieve greater than 30% of the electrogram peak-to-peak amplitude. The energy was delivered using 5 pulses of 5 s; the power level was 60 and 90 Watts in the right and left ventricle, respectively, in the first three animals, then was decreased to 20 and 30 Watts in the remaining sheep, because of too extensive lesions. Energy was stopped in case of ventricular fibrillation needing external cardioversion. In one sheep, it was not possible to cross the aortic valve and the procedure was discontinued. Four sheep were sacrificed at the end of the

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procedure, to observe the acute pathologic changes induced. Six animals were followed up for 3 weeks. Electrocardiographic rhythm strips were recorded each week to evaluate AV conduction.

Pathological study

After death, the entire heart was fixed with 10% formaline and the lesions were stained with Masson’s trichrome. Pathological examination was performed in all cases; it included macroscopic quantitation of the lesion size by measuring diameter and maximal depth, and microscopic sections. The diameter given was the smallest one in case of an irregular shape.

Results

Atrioventricular junction

Characteristics, parameters and results of VHF application are summarized in Table 1. Ablation of the AV junction was attempted in seven sheep. Unipolar His bundle electrogram amplitude recorded from the coaxial catheter before VHF ablation ranged from 0·11 to 0·25 mV. Complete AV block was achieved in all seven sheep, using a maximum energy ranging from 60 to 100 Watts (Fig. 1). AV block was immediately third degree in five sheep, whereas in two cases, second degree AV block preceded complete AV block obtained at the next VHF application. No resumption of conduction was observed during or at the end of the procedure. The rate of the escape rhythm ranged from 52 to 92 beats. min \(^{-1}\). Standard ECG at day 6 showed persistent third degree AV block in all four animals who were not sacrificed at day 1; these sheep presented sudden death at day 6, 7, 7 and 11, respectively, presumably related to complete AV block or polymorphic VT secondary to the AV block, but without ECG monitoring at death (pacemakers not implanted because of the presence of an escape rhythm judged satisfactory). At pathological examination, haemorrhage and necrosis were observed, replaced by fibrosis 3 weeks later in those sheep who were sacrificed at the end of follow-up.

Ventricular sites (Table 2)

Acute lesions (Fig. 2) ranged from 3 to 45 mm in diameter (mean ± SD=10·3 ± 10) and from 1 to 15 mm in depth (6·7 ± 3·9). Gross inspection of the lesions revealed coagulation necrosis and haemorrhage. Endocardial thrombus was not observed at the site of ablation. Chronic lesions appeared to be smaller, in depth (1–4 mm) as in diameter (7–20 mm). They included neutrophil infiltration and fibrosis, well

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**Table 1** Biophysical parameters and results of VHF energy in the sheep undergoing AV junctional ablation

<table>
<thead>
<tr>
<th>Animal no.</th>
<th>Maximum VHF power (Watts)</th>
<th>Duration (s)</th>
<th>His amplitude (mV)</th>
<th>Escape rate (beats · min (^{-1}))</th>
<th>Side effects</th>
<th>Outcome</th>
<th>Lesion diameter × depth (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>100</td>
<td>140</td>
<td>0·15</td>
<td>72</td>
<td>VF</td>
<td>Sacrificed</td>
<td>3 × 3 (acute)</td>
</tr>
<tr>
<td>2</td>
<td>100</td>
<td>167</td>
<td>0·20</td>
<td>73</td>
<td>None</td>
<td>Sacrificed</td>
<td>9 × 10 (acute)</td>
</tr>
<tr>
<td>3</td>
<td>100</td>
<td>30</td>
<td>0·11</td>
<td>90</td>
<td>NS-VT</td>
<td>Sacrificed</td>
<td>8 × 1 (acute)</td>
</tr>
<tr>
<td>4</td>
<td>100</td>
<td>10</td>
<td>0·12</td>
<td>90</td>
<td>NS-VT</td>
<td>SD day 11</td>
<td>10 × 2 (chronic)</td>
</tr>
<tr>
<td>5</td>
<td>100</td>
<td>25</td>
<td>0·18</td>
<td>52</td>
<td>NS-VT</td>
<td>SD day 7</td>
<td>15 × 2 (chronic)</td>
</tr>
<tr>
<td>6</td>
<td>60</td>
<td>25</td>
<td>0·25</td>
<td>92</td>
<td>NS-VT</td>
<td>SD day 6</td>
<td>20 × 3 (chronic)</td>
</tr>
<tr>
<td>7</td>
<td>100</td>
<td>110</td>
<td>0·19</td>
<td>68</td>
<td>VF</td>
<td>SD day 7</td>
<td>No lesion found</td>
</tr>
</tbody>
</table>

VF=ventricular fibrillation (successfully resuscitated in all cases); NS-VT=non-sustained ventricular tachycardia; SD=sudden death.
demarcated from the neighbouring myocardium. Transmural lesions were observed in six animals.  

**Side effects**

During VHF ablation at ventricular sites, ventricular arrhythmias including ventricular premature beats, monomorphic and polymorphic non-sustained ventricular tachycardia were observed (Fig. 3). In six cases, VT led to ventricular fibrillation, requiring DC cardioversion. Creatine kinase levels increased in some animals, probably related to DC cardioversion. These arrhythmias were transient, occurring during or immediately following the energy application and lasting up to 3 min. The same effect was observed in this animal model with 25-Watt radiofrequency applications in the ventricle (Fig. 4). Sudden death occurred in four animals which may have been related to ventricular proarrhythmic effects. However, sudden death was observed only in the sheep that underwent AV ablation, which is considered more likely to have been responsible for the lethal arrhythmias. Pathological examination performed in two animals who experienced sudden death at day 6 and 7 (presumably related to AV block), revealed slight pericardial inflammation, without effusion. Complete examination showed a renal infarction in one of these sheep.

**Catheter tip**

No thrombus was detected at the catheter tip following VHF ablation. However, adherence to right ventricular wall was observed following a 20-Watt pulse. Withdrawal and visual examination of the catheter did not reveal any thrombus.

**Discussion**

This study suggests that extensive lesions may be induced by VHF energy, using a 7-French coaxial catheter connected to a specially designed generator. This new type of energy produced coagulation necrosis of the endomyocardium similar to the lesions obtained with radiofrequency energy, allowing deep heating in the ventricular muscle. Chronic lesions appeared to be well
demarcated from the neighbouring myocardium without perforation despite the use of high power levels.

**Comparison with radiofrequency energy**

Catheter ablation with radiofrequency energy currently uses frequencies ranging between 300 kHz and 3 MHz. The major advantage of this method is the very limited amount of injured tissue, reducing the risk of serious complications, as confirmed by wide clinical experience. Moreover, the size of the lesion clearly related to the duration and the power of the applications, and sufficient in most of clinical instances. However, high radiofrequency energies may lead to arcing, gas bubble release, impedance rise, coagulum formation and proximal delivery of the energy. Despite research aimed at decreasing proximal heating, it appears still difficult to obtain heating beyond 8 mm. VHF energy seems to produce larger lesions by allowing higher levels of energy with limited impedance rise. Since experimental data showed the ability to obtain linear lesions in vitro using VHF energy with a bipolar catheter, it could be interesting to treat some atrial arrhythmias with this method. However, in vivo experiments are needed. Obviously, our study did not attempt to answer questions about tissue temperature, relation between power and lesion size and the use of unipolar catheter versus bipolar.

**Other techniques**

Alternatives to current methods of catheter ablation are desirable, for the reasons above mentioned. Two different ways have so far been explored: modification of regular RF ablation and the use of different energies. Modification of RF may be achieved using saline infusion flushing at the catheter tip, in order to produce cooling and to limit excessive heating. An experimental study showing deep lesions obtained using this technique was performed on a thigh muscle model. Interesting results were obtained in some clinical instances.

Other methods include DC ablation, cryothermia, laser, microwave and ultrasound. Direct current ablation was the first clinically available method and was successful in some cases refractory to radiofrequency ablation. However, the risk of complications and the need for general anaesthesia have dramatically limited the clinical use of DC ablation to the failures of radiofrequency energy. Trials using cryothermia aimed at obtaining reversible injury as well as ablation.
of muscular tissue. The catheter size first used was 10 to 12 French which may cause difficulties in the clinical setting, especially in reaching some endocardial sites; recently the catheters have been improved [13]. Extravasation of blood into the pericardium and coronary artery lesions have been reported with this technique. There is also a potential risk of gas release in case of catheter disruption. Laser ablation has been used but seems limited by the risk of complete destruction and perforation of the myocardial wall when vaporizing all tissues [14]. Microwave ablation has emerged as a promising technique. Using 2450 MHz frequency, it would be able to propagate without the same decrease in current density noted with RF energy. However, the same limitation may appear because conductivity increases, leading to poor dielectric properties. The use of a helical antenna has improved the results, producing large lesions in vitro [15,16] and in vivo [17]. However, microwave ablation currently needs a long catheter tip, and it may be difficult to obtain the desired orientation. Ablation using ultrasound energy has been reported, and showed interesting properties. The lesions induced were well circumscribed reaching 8 mm in depth [18]. The catheters presently available seem inadequate for the use by the percutaneous approach.

**Side effects**

One renal infarction, presumably related to remote embolism, has been observed in this study. This is a well-known complication of RF energy, requiring prophylactic anticoagulation specially when ablation involves left-sided catheterization. Such preventive therapy was not used in this study. Sudden death was only observed in the sheep undergoing AV junctional ablation. The occurrence of polymorphic ventricular tachycardias and sudden death has been reported following AV junctional ablation in humans. Of more concern is the occurrence of ventricular arrhythmias. VHF energy showed particular propensity to induce dangerous non-sustained ventricular arrhythmias, leading to ventricular fibrillation in six cases. This high level of VF occurrence may be a major limitation for the clinical use of this technique, but also suggests the good propagation of VHF waves. On the other hand, it is likely that the animal model used in this study carries a particular risk of ventricular arrhythmias. With radio-frequency energy delivered to ventricular myocardium in six sheep, we observed the same ventricular arrhythmias (unpublished data, Fig. 4). Ventricular fibrillation was also been reported with RF and microwave energy in other animals [19-20]. Moreover, non-sustained or sustained ventricular arrhythmias may occur with any currently available method of ablation applied to the ventricles.

**Conclusions**

This experimental study in sheep suggests that percutaneous ablation is feasible using VHF energy. The ability to induce large myocardial lesions using a flexible catheter similar to those used in the clinical setting with radiofrequency energy may be valuable in ablation of ventricular tachycardias associated with organic disease or to obtain long linear lesions. The technique may present a risk of ventricular proarrhythmic effects, but the same life-threatening arrhythmias were observed using radiofrequency ablation applied to the ventricle in sheep and microwave ablation in dogs. Additional trials in other animal models are needed to establish the precise relation between delivered energy, tissue temperature and lesion size and to assess the risk of side effects. Bipolar energy delivery must also be studied in order to appreciate its potential value in producing linear lesions.

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