Alcohol ablation of atrioventricular conduction

James F Sneddon, David E Ward, Iain A Simpson, Nicholas J Linker, Raymond J Wainwright, A John Camm

Abstract

Transcoronary ablation of atrioventricular conduction by dehydrated alcohol was attempted in 14 patients with refractory atrial arrhythmias. Alcohol (0.5 or 1.0 ml) was delivered after selective catheterisation of the atrioventricular nodal artery in the 10 patients in whom the artery could be identified by cineangiography. The other four patients underwent electrical ablation when the nodal artery could not be catheterised. Temporary atrioventricular block induced by dilute contrast and cold saline (0.9%) confirmed that the catheter was in the correct position before the alcohol was delivered. In all 10 patients complete atrioventricular block developed after alcohol ablation. The block persisted in all four patients given 1.0 ml alcohol but not in four of the six given 0.5 ml. The mean (SD) creatine kinase (MB fraction) at four to six hours after ablation was 76.5 (49.5) IU after 1.0 ml and 75.5 (43.1) IU after 0.5 ml alcohol (normal < 20 IU). The overall success rate of alcohol ablation in the whole group on an "intention to treat" basis was 43%. The procedure was a technical success in six of the 10 patients in whom the nodal artery was identified.

Transcoronary alcohol ablation of atrioventricular conduction should be considered in patients in whom electrical techniques have been unsuccessful.

Closed chest electrical ablation of atrioventricular conduction is now an accepted treatment for atrial arrhythmias that are refractory to drugs. Conventional high energy capacitor discharge, however, has several disadvantages. The success rate is only moderate and serious complications have been reported.¹ Because the shock is painful, the patient needs general anaesthesia and ablation often needs to be repeated.

These drawbacks have led to alternative techniques being developed. The initial results with radiofrequency energy and low energy direct current ablation were encouraging.^{2,3} A transcoronary approach has been used to treat ventricular tachycardia and atrial arrhythmias.^{4,5} We investigated the feasibility, safety, and clinical value of transcoronary alcohol ablation of atrioventricular conduction in patients who would otherwise have been considered for conventional electrical ablation.

Patients and methods

PATIENTS

We studied all 14 patients (mean age 64 (range 54-75); nine men) admitted for ablation of atrioventricular conduction between November 1989 and April 1990. Table 1 summarises the clinical characteristics of the study patients. Four patients had evidence of structural cardiac pathology: in two the mitral valve had been replaced because of rheumatic disease and two had haemodynamically insignificant mitral valve prolapse. The arrhythmia was atrial flutter or fibrillation in 12 patients, one patient had atrioventricular nodal re-entry tachycardia, and one had focal atrial tachycardia. Symptoms had been present for 1-60 years (median 3.5 years). These patients had been refractory to or intolerant of a mean (SD) of 4.4 (1.8) antiarrhythmic drugs, including amiodarone in 11. In three patients an earlier attempt at electrical ablation had been unsuccessful. The protocol was approved by the St George's Hospital ethics committee and all patients gave written consent for the procedure after the possible risks and benefits and its experimental nature had been explained.

EXPERIMENTAL PROTOCOL

For the initial coronary angiographic examination, we used the Judkins approach to identify the atrioventricular nodal artery. Multiple views of the dominant artery were taken to enhance the identification of the nodal artery before ablation. The ablation procedure was undertaken with the patients in a fasted, premedicated, and mildly sedated state. A 6F bipolar wire was placed in the right ventricular apex to serve as a temporary pacemaker and a 6F tripolar wire was positioned to record the largest bipolar His potential. A standard 8F or 9F angioplasty guiding catheter was positioned in the ostium of the coronary artery which gave rise to the atrioventricular nodal artery. 10 000 units of heparin and 250 µg of glyceryl trinitrate were administered prophylactically by intracoronary injection. The atrioventricular nodal artery was selectively cannulated with a 2.2F infusion catheter (Target Therapeutics Tracker-18 Hi-Flow), which was manipulated over a 0.013 inch steerable guide wire (Target Therapeutics Flex-Tip) (fig 1). The catheter was advanced as far as possible to wedge within the artery. Warm dilute contrast was then injected to exclude the presence of backflow into the main artery. If backflow occurred the catheter was remanipulated and the injection repeated. We confirmed that the catheter

Department of
Cardiological
Sciences, St George's
Hospital Medical
School, London

J F Sneddon
D E Ward
I A Simpson
N J Linker
A J Camm

The South East
Thames Regional
Cardiac Unit, The
Brook General
Hospital, London
R J Wainwright

Correspondence to
Dr James F Sneddon,
Department of Cardiological
Sciences, St George's
Hospital Medical School,
Cranmer Terrace, London
SW17 0RE.

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Table 1 Clinical characteristics of patients at entry

Patient	Age/sex	Arrhythmia	Duration (yr)	No of anti-arrhythmic drugs	Symptoms	Other cardiac diagnoses	Previous ablation
1	67/M	AFL	8	7	P, CP, D	MVP	No
2	67/M	PAF	5	4	P, D	None	No
3	62/M	PAF	3	6	P, D	MVP	No
4	54/M	AF	5	3	P, D	MVR	No
5	70/F	AVNRT	60	5	P, PS	None	No
6	75/M	AT	2	2	P, D	None	No
7	62/F	PAFL	2	4	P, D, PS	None	No
8	64/F	AF	3	3	P, D	MVR	Yes
9	63/M	AFL	4	1	P, S	? VT	No
10	60/M	PAF	3	4	P, D, PS	None	Yes
11	59/F	PAF	11	4	P, CP, D, PS	None	No
12	63/M	AFL	1	7	D, PS	None	No
13	59/M	AFL	2	6	P, D, PS	None	No
14	70/F	AF	10	6	P, D, PS	None	Yes

AF, persistent atrial fibrillation; AFL, persistent atrial flutter; AT, atrial tachycardia; AVNRT, atrioventricular nodal re-entry tachycardia; CP, chest pain; D, dyspnoea; MVP, mitral valve prolapse; MVR, mitral valve replacement; P, palpitation; PAF, paroxysmal atrial fibrillation; PAFL, paroxysmal atrial flutter; PS, presyncope; S, syncope; VT, ventricular tachycardia.

Figure 1 A right coronary angiogram in the left anterior oblique projection showing an 0.013 inch guide wire (arrow) manipulated deep into the atrioventricular nodal artery.

was correctly placed by injection of 2–10 ml cold saline (0.9%). If this caused a definite transient complete heart block we injected 0.5 or 1.0 ml of dehydrated alcohol over one second and then 1.0 ml of saline. Patients 2, 3, 4, and 14 were given 1.0 ml and patients 5 and 7–11 0.5 ml. The reasons why we changed the dose will be discussed later.

All patients were monitored on the cardiac ward for 24 hours after the procedure. If necessary a permanent pacemaker was inserted within 48 hours. All patients had cross sectional echocardiography with a Dasonics CFM 500 or a Hewlett Packard Sonos 1000S before and within three days of the procedure. Creatine kinase (MB fraction) activity was measured in blood samples taken four to six hours after injection of alcohol.

Results

IDENTIFICATION OF THE ATRIOVENTRICULAR NODAL ARTERY

In 10 patients the artery supplying the atrioventricular node was identified on the initial cineangiogram. In nine it originated from the right coronary artery (one of them had a dual arterial supply) (fig 2) and in one patient it arose from the left circumflex artery. The artery could not be identified in four patients, two of whom had a left dominant anatomy. In the four patients in whom the vessel could not be visualised during screening it was identified on the developed films.

CATHETERISATION OF THE ARTERY SUPPLYING THE ATRIOVENTRICULAR NODE

We successfully cannulated all 11 arteries (in 10 patients) that were visible on the angiograms and confirmed the position of the catheter by infusion of contrast and cold saline. The injection of dilute contrast led to varying degrees of atrioventricular block in all patients, but at that time we believed that it was necessary to inject cold saline to be certain that the correct vessel had been catheterised. Injection of cold saline into the nodal artery produced transient complete atrioventricular block in all patients. Incomplete block, notably slowing of the ventricular response in patients with atrial fibrillation or flutter, was seen when contrast or cold saline were injected into vessels which ran close to the nodal artery. Because the coronary artery went into spasm during three early procedures we reduced the volume of cold saline injected from 10 ml to 2 ml. Not surprisingly we could not catheterise the atrioventricular nodal artery in any of the four patients in whom the artery could not be identified on cineangiography, though it was probably entered with a guide wire in one case.

RESULTS OF ALCOHOL INJECTION

Table 2 shows the initial results of the ablation procedure and table 3 shows the long term outcome. In all 10 patients complete atrioventricular block developed immediately after the injection of alcohol. All four patients in whom 1.0 ml alcohol was injected were still in complete heart block 4–7 months after the procedure. So too were patients 9 and 11 who were given 0.5 ml alcohol. Atrioventricular conduction returned in four patients who were given 0.5 ml of alcohol. One (patient 8) of them had two separate ablation procedures. Patient 5, who had atrioventricular nodal re-entry tachycardia, remained well with no clinical or inducible tachycardia. Patient 7, in whom conduction resumed 30 minutes after ablation, underwent a repeat procedure four days later. This was unsuccessful because the nodal artery was occluded. Two attempts at electrical ablation were also unsuccessful in this patient and she is awaiting surgical ablation. Patient 8, who had dual nodal arteries, had a further injection of 0.5 ml into the second artery after conduction recurred 24 hours after the initial attempt

Table 2 Results of alcohol ablation

Patient No	AVNA seen on angiogram	Presumed vessel of origin*	AVNA seen on screening	AVNA catheterised	Dose of alcohol (ml)	AV block with alcohol
1	No	R	No	No	None	—
2	Yes	R	Yes	Yes	1.0	Yes
3	Yes	R	Yes	Yes	1.0	Yes
4	Yes	R	Yes	Yes	1.0	Yes
5	Yes	R	No	Yes	0.5	Yes
6	No	L Cx	No	No	None	—
7	Yes	L Cx	Yes	Yes	0.5	Yes
8†	Yes	R	Yes	Yes	0.5 + 0.5	Yes + yes
9	Yes	R	Yes	Yes	0.5	Yes
10	Yes	R	No	Yes	0.5	Yes
11	Yes	R	No	Yes	0.5	Yes
12	No	L Cx	No	No	None	—
13	No	R	No	No	None	—
14	Yes	R	No	Yes	1.0	Yes

*When the atrioventricular nodal artery could not be seen on the developed films, it was assumed to originate from the vessel supplying the posterior descending artery.

†This patient underwent two alcohol ablation procedures.

AV, atrioventricular; AVNA, atrioventricular nodal artery; L Cx, left circumflex artery; R, right coronary artery.

Table 3 Follow up results of all patients

Patient No	Peak CK MB (IU/l)*	Repeat procedures	Current state	Follow up (mnth)	Current antiarrhythmic medication
1	—	EA	AV block	7	None
2	48	None	AV block	7	None
3	35	None	AV block	7	None
4	146	None	AV block	6	None
5	131	None	CR, NT	6	None
6	—	FEA	AT	6	Amiodarone
7	102	FAA, FEA	SR, PAFL	5	Flecainide
8†	62 and 15	FAA, FEA	AF	4	None
9	100	None	AV block	5	None
10	†	None	CR	5	Digoxin
11	43	None	AV block	5	None
12	—	EA	AV block	4	None
13	—	FEA	SR, PAFL	4	Sotalol
14	77	None	AV block	4	None

*Normal < 20 IU/l.

†This patient underwent two alcohol ablation procedures.

‡The creatine kinase results for patient 10 are not available owing to a laboratory mishap.

AF, atrial fibrillation; AT, atrial tachycardia; AV, atrioventricular; CR, conduction returned; CK MB, creatine kinase MB fraction; EA, electrical ablation; FAA, failed alcohol ablation; FEA, failed electrical ablation; NT, no tachycardia; PAFL, paroxysmal atrial flutter; SR, sinus rhythm.

(fig 2). Unfortunately, this attempt also failed because conduction resumed after 48 hours. A further attempt was thwarted by both vessels being occluded. Atrioventricular conduction returned after nine days in patient 10 who is now awaiting a further attempt at electrical ablation. The chances that an ablation procedure would produce long term heart block were significantly improved ($p < 0.05$) when 1.0 ml of alcohol was given (Fisher's exact test).

The injection of alcohol was well tolerated by all patients though most reported minor transient chest discomfort immediately after the injection. All patients were monitored for 24 hours after the procedure; none showed any new arrhythmias. The echocardiographic ejection fraction did not change in patients given alcohol and there were no new segmental wall motion abnormalities. The mean (SD) creatine kinase (MB fraction) concentrations measured four to six hours after each alcohol injection were 76.5 (49.5) IU for patients given 1.0 ml alcohol and 75.5 (43.1) IU for those given 0.5 ml (normal range < 20 IU). The mean serum concentration of creatine kinase MB in patients in whom long term complete heart block occurred after alcohol was 74.8 (42.5) IU and in those in whom conduction recovered it was 77.0 (50.0) IU. Unfortunately the enzyme results of patient 10 are unavailable owing to a laboratory mishap.

ESCAPE RHYTHMS

Four to six weeks after the procedure all patients in whom alcohol ablation had been successful showed stable escape rhythms—RR interval 1272 (160) ms and QRS duration 97 (25) ms.

COMPLICATIONS

In two patients ventricular fibrillation developed when contrast was injected into the right coronary artery before the infusion catheter was introduced. Prompt defibrillation restored sinus rhythm immediately and the procedure was successfully completed in both patients. Coronary artery spasm developed in three patients after injection of cold saline. Two of these had been given intracoronary glyceryl trinitrate. The ensuing hypotension and ST elevation resolved rapidly with further nitrate. The two patients in whom spasm developed and who did not go on to receive alcohol showed no increase in cardiac enzymes. One patient had evidence of a small dissection of the right coronary artery seen on the final injection of contrast. This was not associated with any short or long term adverse effects.

Discussion

We showed that alcohol ablation of atrio-

Figure 2 A right coronary arteriogram taken in the left anterior oblique projection in a patient (case 8) who had dual nodal arteries. The proximal artery (white arrow) was cannulated at the first ablation attempt and was occluded at a later study. The distal artery (black arrow) was entered and alcohol injected but atrioventricular conduction returned. A third attempt was made but both main nodal vessels were occluded and injection of cold saline into the third artery (small arrow) had no effect on conduction.

ventricular conduction is a safe and practical procedure in most patients

SUCCESS OF ALCOHOL ABLATION

The atrioventricular nodal artery must be identified on the initial coronary angiogram before it can be cannulated. We do not recommend speculative attempts unless a suitable candidate vessel has been seen. Inability to see the nodal artery during screening, however, did not reduce the likelihood of successful cannulation if the vessel was identified on the original developed films. In all patients in whom the nodal artery was cannulated complete heart block developed when alcohol was injected, but in three atrioventricular conduction returned and their symptoms continued. The ablation procedure in the patient with nodal re-entry was technically unsuccessful but the clinical outcome was satisfactory. The procedure was significantly more successful when 1.0 ml rather than 0.5 ml alcohol was used. The initial choice of a dose of 1.0 ml was based on the reports of Brugada *et al.*⁵ In an attempt to minimise myocardial damage we reduced the dose but this led to reduced success with no change in enzyme release and so we returned to 1.0 ml for the last patient in the series. Enzyme release was not related to the amount of alcohol injected or the technical success of the procedure.

MECHANISM OF ACTION OF ALCOHOL ABLATION

Studies of patients with inferior myocardial infarction and experimental work in dogs showed that simple occlusion of the nodal artery does not result in major long term structural or electrophysiological abnormalities in the node.⁶⁻⁸ This accords with our observation that the nodal vessels were occluded proximally in the two patients restudied

after conduction had recurred. Because the atrioventricular node, in common with other areas of the conducting system, is more resistant than the myocardium to ischaemia it must have an adequate collateral blood supply from atrial and septal vessels.^{9,10} The instantaneous block produced by alcohol suggests a direct toxic effect upon nodal tissue. The fact that the release of creatine kinase is independent of the dose of alcohol suggests that the normal myocardial tissue supplied by the nodal artery is fully infarcted by the toxic effects of even the lower dose of alcohol. The specialised conducting tissue also seems to be more resistant than the myocardium to the effects of alcohol. Slow infusion of alcohol into renal arteries caused ischaemic damage secondary to vascular sludging by denatured red cells but our rate of alcohol delivery was rapid enough to subject all areas supplied by the nodal artery to very high concentrations of alcohol.¹¹ One possible explanation for the failures with the lower dose was that the alcohol was not long enough in contact with the node before it was flushed out either actively or by resumption of flow after removal of the catheter. It might be better to leave the catheter wedged in the artery for longer and increase the time that the nodal tissue is bathed in alcohol. This would probably cause a little extra myocardial damage because much of the muscle supplied by the vessel is likely to be jeopardised by the initial toxic effects. The ideal dose, concentration, and flow rate of alcohol for maximum efficacy and safety have yet to be determined.

The lesions produced by intracoronary alcohol have mainly been studied after injection into left ventricular branches in animals. Inoue *et al* reported the results of infusion of 100% alcohol using occlusive cannulation into a diagonal branch of the left anterior descending artery in eight dogs.¹² This produced predominantly focal discrete transmural infarction but in two dogs patchy or diffuse lesions developed. In the absence of histological information it is not possible to predict the exact morphology of the lesions produced in our patients. The possibility that alcohol infusion induces irregular lesions raises concern about new ventricular arrhythmias developing, especially as the nodal artery may supply a small area of the upper interventricular septum.

The escape rhythms in the patients who had alcohol ablation of the ventricular node were predominantly narrow complex but one patient showed a left bundle branch block configuration and another showed incomplete right bundle branch block. This is consistent with previous studies that showed that blood was supplied to the His bundle and its branches by a continuation of the nodal artery.¹³

COMPARISON WITH OTHER TECHNIQUES OF ABLATION

In this prospective study, alcohol ablation was a technical success, on the basis of an "intention to treat", in six (43%) out of 14 patients. In patients in whom the nodal artery could be identified alcohol ablation was technically suc-

cessful in 60% and a clinical success in 70%. There is good reason to believe that the results will improve with further development of the technique. Certainly the procedure is limited to patients with identifiable arteries and no important coronary artery disease of the dominant vessel. de Swart *et al* who used similar doses in most of their patients reported complete success in five of 10 patients, modification of conduction in two, and in three coronary artery disease or failure of visualisation of the nodal artery precluded alcohol ablation.¹⁴ The technique avoids the need for general anaesthesia and the risks of barotrauma associated with conventional high energy ablation.

Success rates with other techniques, however, are higher. When long term complete heart block was regarded as the end point, conventional ablation was successful in 65% of 354 patients.¹ Successful low energy direct current ablation was reported in 79–100% and radiofrequency energy was successful in 56–71% of patients.^{3 15 16}

The release of cardiac enzymes after alcohol ablation is appreciably higher than has been reported for other methods of ablation. Brugada *et al* reported a mean aspartate aminotransferase of 89 U (normal < 40) in six of their patients; one patient who sustained an inferior wall infarction was excluded from this analysis.⁵ Direct comparison of peak creatine kinase MB concentrations after conventional ablation (22–40 IU) and alcohol ablation (76 IU) is hampered because different assay methods were used.^{2 17} Enzyme release was negligible after low energy and radiofrequency ablation. The large release of enzymes after alcohol ablation is disturbing; however, the nodal artery supplies only a small area of muscle and echocardiographic study did not show any new abnormalities. We are currently studying whether there is a more rapid or complete release of enzymes after an alcohol injury than after other insults.

The occlusion of the nodal artery after alcohol unfortunately precludes repeated attempts at ablation except when, unusually, there are dual arteries. With other techniques subsequent procedures are possible if conduction returns.

COMPLICATIONS

The two cases of ventricular fibrillation occurred before the infusion catheter was introduced and were simply secondary to injection of contrast material. Coronary artery spasm followed injection of cold saline in three patients and was associated with significant haemodynamic disturbance. This complication can be minimised by an initial injection of warm dilute contrast into the selected candidate vessel. This will usually cause block if the catheter is correctly positioned and if any backflow into the main artery is seen the catheter can be repositioned. Atrioventricular block can be achieved with a much smaller dose of cold saline than has been previously reported; 1–2 ml is sufficient if the catheter is properly wedged within the artery.⁵ We have more recently abandoned the use of cold saline if dilute contrast produces convincing evidence that the correct vessel has been catheterised. A

combination of these precautions and prophylactic intracoronary nitrates should minimise the risk of spasm. Backflow of alcohol if the infusion catheter is not completely wedged can be disastrous. Brugada *et al* reported the dangers of attempted repeat ablation when, though the main vessel seems to be patent, occlusion of the distal segments causes backflow.⁵

Conclusions

This prospective study of the use of alcohol ablation showed the feasibility of the technique. The modest success rate, concern about the release of cardiac enzymes, and the potential for serious complications suggest that this technique should probably be reserved for patients in whom other ablative treatments have failed. Alcohol ablation, which began as a treatment of last resort for ventricular tachycardia, should now be seriously considered before the more radical approach of surgical interruption of atrioventricular conduction. Further study to determine the optimal dose, concentration, and contact time between the node and alcohol is likely to improve the results. If backflow of alcohol or cold saline is scrupulously avoided, perhaps by use of a balloon occlusion catheter, the risks of significant complications may be reduced.

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