Antidysrhythmic drug therapy for the termination of stable, monomorphic ventricular tachycardia: a systematic review

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ABSTRACT

Objective We performed a systematic review of the literature to compare the efficacy of different drug therapies for the termination of stable, monomorphic ventricular tachycardia (VT).

Methods We searched EMBASE, MEDLINE and Cochrane for trials from 1965 through July 2013 using a search strategy derived from the following clinical question in PICO format: *P*atients: Adults (≥18 years) with stable monomorphic VT; *I*ntervention: Intravenous antidysrhythmic drug; *C*omparator: Intravenous lidocaine or amiodarone; *O*utcome: Termination of VT. For all drug comparisons, we calculated relative risks (RR; 95% CI) and number needed to treat (NNT, 95% CI) between drugs. We also evaluated the methodological quality of the studies.

Results Our search yielded 219 articles by PubMed and 390 articles by EMBASE. 3 prospective studies (n=93 patients) and 2 retrospective studies (n=173 patients) met our inclusion and exclusion criteria. From the prospective studies, RR of VT termination of procainamide versus lidocaine was 3.7 (1.3–10.5); ajmaline versus lidocaine, RR=5.3 (1.4–20.5); and sotalol versus lidocaine, RR=3.9 (1.3–11.5). From the retrospective studies: procainamide versus lidocaine, RR=2.2 (1.2–4.0); and procainamide versus amiodarone RR=4.3 (0.8–23.6). All 5 reviewed studies had quality issues, including potential bias for randomisation and concealment.

Conclusions Based on limited available evidence from small heterogeneous human studies, for the treatment of stable, monomorphic VT, procainamide, ajmaline and sotalol were all superior to lidocaine; amiodarone was not more effective than procainamide.

INTRODUCTION

The pharmacologic treatment of stable, monomorphic ventricular tachycardia (VT) includes several options, and expert recommendations have changed over the past 15 years. In 2000, procainamide or sotalol (both IIa) were recommended over amiodarone or lidocaine (both IIb) for the treatment of stable VT in the presence of preserved ejection fraction. Amiodarone and lidocaine were equally recommended (both IIb) in the presence of impaired cardiac function.[1] During the years that followed, the ineffectiveness of lidocaine combined with the success of amiodarone in patients with *pulseless* ventricular dysrhythmias,[2–4] despite being indirect evidence, led to amiodarone's increased popularity for the treatment of stable VT. In guidelines published by the ACC/AHA/ESC in 2006, amiodarone was upgraded to a IIa recommendation in the setting of stable VT that was resistant to procainamide,[5] and it was the sole antidysrhythmic incorporated in the simplified AHA algorithm.[6] According to the most recent European Resuscitation Council guidelines, amiodarone remains the recommended antidysrhythmic agent for the treatment of stable, monomorphic VT.[7]

Recent evidence has suggested that amiodarone may not be as effective as once believed for the treatment of stable, monomorphic VT,[8 9] and as current AHA guidelines stand, procainamide is given a stronger recommendation (IIa) than amiodarone (IIb) and sotalol (IIb).[10] Despite all the changes and the differences between European and US guidelines, direct-current cardioversion remains the most effective therapy.[11 12] The most recent revision of AHA guidelines is based on few studies, some of which are retrospective in design.[8 9 13 14] We are not aware of any existing systematic review of the literature that examines the efficacy of different drugs for the treatment of stable VT. In order to determine which antidysrhythmic therapy is most effective, we reviewed all trials that compared such agents for the termination of stable, monomorphic VT.

METHODS

Study design

We conducted a systematic review of studies that examined the efficacy of antidysrhythmic therapies in terminating acute, sustained, monomorphic VT. We followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines.[15]

Search strategy

Two independent reviewers (ISd and JLM) screened the following databases from their inception to July 2013: EMBASE, MEDLINE and the Cochrane Controlled Trials Registry. Our medical librarian developed the Medical Subject Headings terms 'tachycardia, ventricular' and 'anti-arrhythmia agents' (see online appendix—web only file). Bibliographies of review articles and reference lists of original research articles were also reviewed.

Inclusion and exclusion criteria

Studies comparing parenteral drug therapies in adults with stable, monomorphic VT were included. The time period of the search was from 1965 to March 2013, and the search was not limited to any language. Because our objective was to evaluate the efficacy of drug therapy on the termination of acute VT rather than the prevention of VT

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recurrence, we excluded studies that measured the suppressive effect of intravenous drugs on the electrophysiologic inducibility of VT. We also excluded those studies that measured the effect of oral drug therapies on the frequency of VT episodes. Two reviewers (ISd and JLM) performed eligibility assessment independently and in a blinded manner, and arbitration about article selection was not required. The intervention in the majority of the studies was any antidysrhythmic other than lidocaine. The comparator was lidocaine or its European derivative, lignocaine. An additional study compared procainamide with amiodarone.

Data collection and processing

Data elements extracted directly from included articles included: (1) patient characteristics (age, gender, method of diagnosis, underlying cause of VT), (2) trial inclusion and exclusion criteria, (3) intervention type (type, dose, administration of antidysrhythmic drug) and (4) efficacy of VT termination and adverse effects. We contacted the primary author of Marill *et al* in order to obtain data related to the adverse effects of amiodarone—specifically, the rate of hypotension observed in patients who received amiodarone as the initial agent.

Outcome measures and data analysis

Our primary outcome measure was the successful pharmacological termination of VT; more specifically, the restoration of baseline rhythm after intravenous drug administration. Two-by-two tables (termination vs non-termination of VT) were constructed with primary data extracted from each of the included studies. Data related to the efficacy of antidysrhythmic drugs used in the crossover arms of prospective studies[13 14 16] were excluded to minimise the risk of confounding from carry-over drug effect. Similarly, from one retrospective study,[17] we excluded data abstracted from observations when the drug in question was administered after another antidysrhythmic agent. Relative risk (RR) and number needed to treat (NNT) with 95% CIs were used to estimate treatment effect (RevMan5, Copenhagen). Our secondary outcome measure was the rate of adverse effects associated with each medication. We specifically looked for episodes of bradycardia, hypotension, acceleration of VT, neurologic symptoms and death. We did not perform a meta-analysis due to the significant heterogeneity across the included trials.

Quality assessment

Each prospective study was evaluated for its adequacy in randomisation, concealment of allocation and blinding. Retrospective studies were also appraised according to the Gilbert and Lowenstein criteria.[18] No studies were excluded based on risk of bias.

RESULTS

Search results

The flow diagram of our search is illustrated in figure 1. Our search of MEDLINE and EMBASE registries yielded a total of 574 unique studies. Search of the Cochrane Library did not return any studies, but we found an additional two from examination of references, which ultimately did not meet inclusion criteria. After review of titles and abstracts, 547 studies were rejected for relevance. Of the 27 studies reviewed in full-text format, five were determined to meet inclusion criteria: three prospective studies with a total of 93 patients and two retrospective trials with a total of 173 patients (for all 5 studies, total n=266).

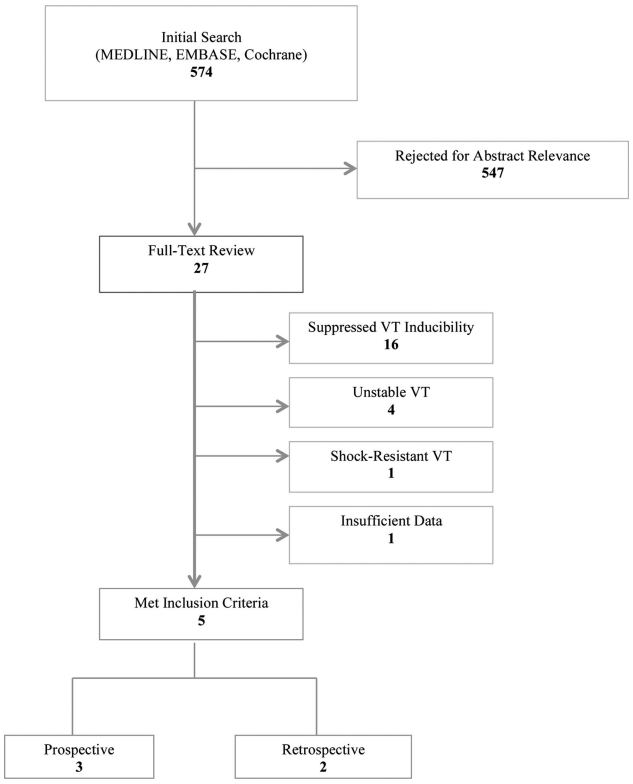

Figure 1 Selection process to obtain articles for review.

A majority of these 27 studies were excluded because they evaluated the efficacy of intravenous drugs in suppressing the electrophysiologic induction of VT. The primary outcome of these studies was determined to be different from our outcome measure of successful VT termination. Of the five selected trials, four[13 14 17 19] were in English and one[16] was in German. The German study[16] was reviewed by an emergency medicine physician who is fluent in German (see acknowledgements).

Study characteristics

Three of the five included studies, Ho *et al*,[13] Gorgels *et al*[14] and Manz *et al*,[16] were randomised, prospective trials with crossover design. Studies by Marill *et al*[17] and Komura *et al*[19] were retrospective and observational in design. Sample sizes ranged from 29[14] to 90.[19]

Inclusion and exclusion criteria are described for the five selected studies in table 1.[13 14 16 17 19] Studies differed in their decision to exclude patients with VT in the setting of acute myocardial infarction (MI). Gorgels *et al*[14] and Komura *et al*[19] excluded patients with acute MI, whereas Ho *et al*,[13] Manz *et al*[16] and Marill *et al*[17] did not. All but one study[17] excluded persons who had received intravenous antidysrhythmic therapy prior to administration of study drug.

All but one study[16] limited their analyses to cases of spontaneous VT. Manz *et al*[16] included individuals with stimulus-induced VT; that is, the investigators electrophyiologically induced the dysrhythmia and then measured the response to antidysrhythmic agent. VT in 27 of this study's 31 individuals occurred by programmed stimulation rather than spontaneously. All studies[13 14 16 17 19] used ECG criteria to determine VT for inclusion in the trials. However, after enrolment, the diagnosis of VT was confirmed by electrophysiologic reproduction in variable percentages of patients (ranging from 39% to 100%) among the studies.[13 14 16 17 19]

Table 1 Baseline characteristics and study designs of the five selected studies

Study	Characteristics	Intervention	Comparison	Outcomes
Ho *et al*[13]	*Inclusion criteria*: ECG criteria *Exclusion criteria*: Previous enrolment, receipt of lignocaine or sotalol in previous 24 h, poor haemodynamic status requiring DCCV, torsade de pointes, or VT interrupted by sinus rhythm *Sample size*: n=33 *Gender*: male 79% *Age*: 68±6 years (sotalol); 61±18 years (lidocaine)	Sotalol 100 mg over 5 min	Lignocaine 100 mg over 5 min	VT termination in 15 min or haemodynamic deterioration
Gorgels *et al*[14]	Inclusion criteria: ECG criteria *Exclusion criteria*: severe CHF or hypotension during VT, polymorphic VT, acute MI, digitalis intoxication, extracardiac disorders *Sample size*: n=29 *Gender*: male 86% *Age*: 60±12 years (procainamide); 62±14 years (lidocaine)	Procainamide 10 mg/kg at 100 mg/min	Lidocaine 1.5 mg/kg over 2 min	VT termination in 15 min
Manz *et al*[16]	*Inclusion criteria*: ECG and EPS-confirmed *Exclusion criteria*: cardiogenic shock or previous treatment with amjalin or lidocaine *Sample size*: n=31 *Gender*: male 77% *Age*: 54±12 years (ajmalin); 58±10 years (lidocaine)	Ajmaline 50 mg over 3–5 min	Lidocaine 100 mg over 3–5 min	VT termination
Marill *et al*[17]	*Inclusion criteria*: ECG criteria, receipt of amiodarone or procainamide *Exclusion criteria*: VT during cardiac arrest, vasopressor requirement, EP-induced VT *Sample size*: n=83 *Gender*: male 70% *Age*: unknown	Procainamide 500 mg at minimum rate 15 mg/min	Amiodarone 150 mg at minimum rate 10 mg/min	VT termination in 20 min
Komura *et al*[19]	*Inclusion criteria*: ECG criteria, initial receipt of procainamide or lidocaine *Exclusion criteria*: altered consciousness, chest pain or ECG suggesting acute MI, previous DCCV or drug therapy *Sample size*: n=90 *Gender*: male 67% *Age*: 60±14 years	Procainamide 100 mg q1–2 min (maximum 800 mg)	Lidocaine 50 mg boluses (maximum 150 mg)	VT termination or haemodynamic deterioration

CHF, congestive heart failure; DCCV, direct current cardioversion; EP, electrophysiologic; EPS, electrophysiologic study; MI, myocardial infarction; VT, ventricular tachycardia.

Lidocaine was the most commonly studied drug (in 4 of 5 studies).[13 14 16 19] Dosages of lidocaine were given as intravenous boluses and similar among these studies (1.5 mg/kg,[14] 100 mg,[13 16] 50–150 mg[19]). Two studies[14 19] compared procainamide with lidocaine and used comparable dosing regimens of procainamide (100 mg every 1–2 min). One study[17] retrospectively compared procainamide with amiodarone, and this trial reported a maximum dosage of procainamide of 500 mg. This procainamide dose was lower than that used in the other two studies[14 19] (10 mg/kg[14] and 800 mg[19]) that compared procainamide to lidocaine. Additionally, Marill *et al*[17] included cases where procainamide was given as an infusion (average rate 21 mg/kg/min), whereas Komura *et al*[19] allowed for upward titration of 100 mg bolus doses every 1–2 min. However, Komura *et al*[19] studied a more rapid rate of drug administration than that described in Marill *et al*[17]

In all studies,[13 14 16 17 19] group comparison data for baseline characteristics included underlying coronary artery disease, structural heart disease, and left ventricular ejection fraction. Potassium levels were reported in Ho *et al*,[13] Gorgels *et al*,[14] and Marill *et al*.[17]

All studies sought to evaluate the efficacy of intravenous drugs in terminating acute VT, although only three studies[13 14 17] specified predetermined time periods (ranging from 15 to 20 min) after which VT termination would be determined to be unsuccessful following drug administration. Komura *et al*[19] deemed termination of VT unsuccessful when VT was persistent after upward titration of drug reached threshold dosages (procainamide >400 mg, lidocaine 150 mg).

Recurrence of VT was handled differently by the two studies[13 17] that explicitly addressed this issue. Ho *et al*[13] classified subjects who had recurrence after termination of VT by study drug as successful responders to drug treatment. Marill *et al*[17] classified a recurrence of VT within 5 min of VT termination as failed termination. Thus, the definition of successful VT termination differed between these two studies.[13 17]

Trial quality

None of the prospective studies[13 14 16] were registered at clinicaltrials.gov or the EU Clinical Trials Register. The sources of bias in this review are summarised in table 2. Persons were reported as randomised in all three prospective studies[13 14 16]; however, none of these studies described their specific randomisation method. Only in Ho *et al*[13] did the investigators describe the method of allocation concealment and blinding in the study. None of the three prospective studies[13 14 16] reported a predetermined sample size estimate, and sample sizes ranged from 29[14] to 33.[13] All prospective studies[13 14 16] included a description of baseline characteristics of each group and reported both groups as similar. Also in these three trials,[13 14 16] the groups were analysed with an intention-to-treat manner, and follow-up was complete.

Although retrospective studies are typically excluded from systematic reviews of drug therapies, we included two such studies for the sake of completion. Due to inherent biases associated with retrospective design, we further evaluated the quality of the two retrospective studies[17 19] using non-validated criteria proposed by Gilbert and Lowenstein.[18] The findings are summarised in table 3. Komura *et al*[19] only met criteria for case selection. Procainamide was the preferred drug to administer in this study (given to 70 patients, as against the 20 who received lidocaine) and physicians may have been subject to selection bias in a way that exaggerates the difference in outcomes between drugs. The study by Marill *et al*[17] met all quality measures by Gilbert and Lowenstein, but the results are still subject to confounding; in some cases, the drug in question was not the first

Table 2 Critical appraisal of the five selected studies

Study	Randomisation	Concealment	Blinding	Intention to treat	Baseline comparisons	Cointerventions	Complete follow-up
Ho *et al*[13]	Randomised, crossover	Yes	Yes	Yes	Yes	Concurrent oral antidysrhythmic therapy	Yes
Gorgels *et al*[14]	Randomised, unclear process; crossover	No	No	Yes	Yes	Concurrent oral antidysrhythmic therapy	Yes
Manz *et al*[16]	Randomised, unclear process; crossover	No	No	Yes	Yes	Concurrent oral antidysrhythmic therapy	Yes
Marill *et al*[17]	Retrospective cohort	No	No	No	Yes	Concurrent oral antidysrhythmic therapy; other antidysrhythmic given prior to study drug	Yes
Komura *et al*[19]	Retrospective cohort	No	No	Yes	Yes	None reported	Yes

agent administered. The results from these observational studies serve to generate ideas towards future investigation; no substantial conclusions should be drawn from them.

Primary outcome analysis

The success rates of VT termination are included in table 4. In the four studies[13 14 16 19] that compared lidocaine with another antidysrhythmic medication, lidocaine successfully terminated VT less frequently than procainamide, sotalol, and ajmaline. In Ho *et al*,[13] the investigators report that two of the patients randomised to the lidocaine group had supra-VT with aberrancy that was misdiagnosed as VT. The dysrhythmia in these two patients was not successfully terminated, but even if removed from the data, the difference between sotalol (69%) and lidocaine (20%) remained significant.[13] The NNT of procainamide compared with lidocaine, based on data pooled from the two studies[14 19] that compared these drugs was two (95% CI 1.5 to 3.6). In the retrospective trial[17] that compared amiodarone with procainamide, there was no significant difference in efficacy.

Secondary outcome analysis

The adverse effects reported in each study are summarised in table 5. Death was reported in four patients from the studies included in this review. One died in the setting of an acute large MI 6 h after successful termination of VT by sotalol. A second death was attributed to the administration of lignocaine following the misdiagnosis of sinus tachycardia with QRS complex widening secondary to severe hyperkalemia. A third patient died after receiving lignocaine followed by a dose of sotalol. Clinical history suggests this patient may have died in the setting of digoxin toxicity. One patient with ischaemic cardiomyopathy died despite repeated implantable cardiovascular defibrillator (ICD) shocks and amiodarone bolus plus infusion over 15 h.

When data is pooled by drug, hypotension occurred at a rate of 5% with lidocaine/lignocaine, 6% with sotalol, 3% with procainamide, and 7% with amiodarone. The rate of hypotension due to procainamide may be underestimated, as a large proportion of cases are from Komura *et al*[19] whose investigators reported no adverse effects associated with either lidocaine or procainamide. This under-reporting may actually be due to missing data, a bias typically associated with retrospective study design. Neurologic symptoms (dizziness, transient speech problems, visual problems, paresthesias) were associated with lidocaine administration in Manz *et al*.[16] Other neurologic symptoms (tinnitus, transient hearing impairment) were reported after lignocaine in Ho *et al*.[13] When data was pooled from those two studies,[13 16] neurologic symptoms occurred after lidocaine/lignocaine at a rate of 16%.

DISCUSSION

Our systematic review of the pharmacological termination of stable, monomorphic VT dissuades us from recommending lidocaine as the optimal treatment choice. The current literature is limited to few prospective trials with small sample sizes, and retrospective observational studies with the latter group inherently subject to selection bias and confounded results.[20] However, the available evidence based on prospective studies supports the use of procainamide, sotalol, or ajmaline as initial drug treatment for terminating stable, monomorphic VT.

The two studies[13 19] that compared lidocaine and procainamide excluded patients with acute MI. Lidocaine is thought to block sodium channels more effectively in ischaemic myocardium; it may be a more effective therapy in suppressing automaticity, which is believed to be the typical mechanism of dysrhythmia induction in VT in the setting of acute MI.[21] Therefore, the difference in treatment effect between lidocaine and procainamide might have been less significant had these studies included patients with acute MI. By contrast, Ho *et al*[13] and Manz *et al*[16] did not exclude patients with acute MI; therefore, the difference in treatment effect between lidocaine and sotalol/ajmaline may be considered more clinically relevant. The variation in exclusion of patients with MI from the reviewed studies precludes us from making recommendations to all comers presenting to an emergency department with stable, monomorphic VT.

One major methodological concern raised in our review of the included prospective trials was a lack of a priori sample size determination. Gorgels *et al*[14] ended their study after 14 patients had received lidocaine and 15 received procainamide as initial study drugs. Manz *et al*[16] terminated their study after 16 patients

Table 3 Additional appraisal of the two retrospective studies (Gilbert and Lowenstein criteria)

Study	Abstractors	Case selection	Abstraction form	Variable definition	Meetings	Monitoring	Inter-rater reliability
Marill *et al*[17]	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Komura *et al*[19]	No	Yes	No	No	No	No	No

Table 4 Rates of successful termination of acute ventricular tachycardia

Study	Sample size	Lidocaine/lignocaine (%)	Procainamide (%)	Amiodarone (%)	Ajmaline (%)	Sotalol (%)	Relative risk (95% CI)	NNT (95% CI)
Ho *et al*[13]	33	3/17 (18)	–	–	–	11/16 (69)	3.9 (1.3 to 11.5)	2.0 (1.2 to 4.5)
Gorgels *et al*[14]	29	3/14 (21)	12/15 (80)	–	–	–	3.7 (1.3 to 10.5)	1.7 (1.1 to 3.4)
Manz *et al*[16]	31	2/16 (13)	–	–	10/15 (67)	–	5.3 (1.4 to 20.5)	1.9 (1.2 to 3.9)
Marill *et al*[17]	41	–	4/7 (57)	8/34 (24)	–	–	4.3 (0.8 to 23.6)	3.0 (–17.5 to 1.4)*
Komura *et al*[19]	90	7/20 (35)	53/70 (76)	–	–	–	2.2 (1.2 to 4.0)	2.5 (1.6 to 5.7)

*The CI for NNT includes negative numbers and zero. An alternative way to express the CI here is (NNH=17.5 to ∞ to NNT=1.37 to ∞) where ∞ represents 1/ARR, absolute risk reduction of 1/0.
NNH, number needed to harm; NNT, number needed to treat.

received lidocaine and 15 received ajmaline. It is unclear why these patient enrolment endpoints were chosen. The risk of failing to predetermine sample size is the selective termination of a study when a difference in treatment effect becomes statistically or clinically significant. Ho *et al*[13] described a goal of enrolling 24–40 patients, although an explanation for this number range is not provided. An interim analysis was performed after accrual of 33 patients; at this point, the efficacy of sotalol was determined to be superior to that of lidocaine, and the study was terminated. It is unclear if this interim analysis was planned or was performed after multiple statistical examinations of data as it was accumulated. The latter approach increases the risk of a statistically significant result occurring by chance.

Two of the randomised trials[14 16] included in this review did not describe how randomisation was conducted or state which mechanisms, if any, there were to conceal the randomised allocation sequence. Trials with inadequate allocation concealment may overestimate treatment effect[22] and undermine the goal of minimising selection bias by randomisation. In addition selection bias may affect study outcomes more significantly when sample sizes are small. The same two trials[14 16] administered antidysrhythmic drugs in an unblinded fashion. Ascertainment bias from lack of blinding, however, was unlikely to have played a role in the patients' electrophysiologic response to drug administration and the provider's determination of successful VT termination.

The European Council Guidelines for Resuscitation currently recommend amiodarone 300 mg over 20–60 min for the treatment of stable, monomorphic VT.[7] This suggested dose is double the dose that was demonstrated by Marill *et al*[8 17] to be of limited effectiveness. However, Tomlinson *et al*[9] examined patients who were given the larger bolus dose of amiodarone (300 mg) for stable VT and also reported a similarly low termination rate. The European Council Guidelines also state that specialist consultation should be sought prior to considering alternatives, such as procainamide, sotalol and nifekalant.[7]

In the USA, intravenous sotalol and nifekalant are unavailable, and procainamide is rarely used as the initial drug treatment for termination of stable, monomorphic VT. Marill *et al*[17] reported the use of procainamide as the initial agent in only eight cases in four centres over an average of 10.8 years. The investigators suggested that the then recommended rate of infusion of 20 mg/min to a total dose of 17 mg/kg[6] made for a prohibitively long infusion time of 68 min. Current guidelines[10] recommend an infusion rate of 20–50 mg/min, so that maximum infusion rate would require a minimum of 27 min. Even this shorter time required for drug administration may be considered unacceptably long for the clinician to remain at the bedside to monitor

Table 5 Adverse effects reported during the treatment of ventricular tachycardia

Study	Bradycardia (%)	Hypotension (%)	VT acceleration (%)	Neurologic symptoms (%)	Death (%)
Ho *et al*[13]	Lignocaine 0 Sotalol 2 (13)	Lignocaine 1 (6) Sotalol 1 (6)	Not reported	Lignocaine 2 (12) Sotalol 0	Lignocaine 1 (6) Sotalol 1 (6) Lignocaine, Sotalol* 1 (7)
Gorgels *et al*[14]	Not reported	Lidocaine 2 (14) Procainamide 1 (7)	Lidocaine 0 Procainamide 1 (7)	Not reported	0
Manz *et al*[16]	Not reported	0	0	Lidocaine 9 (56) Ajmaline 0	0
Marill *et al*[17]	Not reported	Amiodarone 3 (9) Procainamide 2 (25)	Not reported	Not reported	Amiodarone 1 (3)
Komura *et al*[19]†	Not reported	Not reported	Not reported	Not reported	0

*Patient received sotalol after unsuccessful VT termination by lignocaine, developed hypotension and died.
†Komura *et al*[19] reported 'no major side effects were observed in any patient'.
VT, ventricular tachycardia.

the patient and wait for drug effect. It must also be recognised that the relatively high success rates reported by Gorgels *et al*[14] and Komura *et al*[19] involved repeated bolus doses which corresponded to a rate of 50–100 mg/min; rates that are higher than what is recommended by AHA guidelines.[10]

Both ajmaline and procainamide are Vaughan–Williams class IA antidysrhythmics, while lidocaine is class IB, and amiodarone and sotalol are class III. Although they span different classes, the relatively greater success of ajmaline, procainamide and sotalol in terminating re-entrant VT may be due to their common electrophysiologic effect of lengthening the refractory period, and thus, prolonging repolarisation in cardiac myocytes.[23] By contrast, lidocaine and amiodarone may be less effective because lidocaine predominantly affects automaticity,[23] and amiodarone, when given intravenously, has no significant acute effect on ventricular refractoriness and repolarisation; its antidysrhthmic efficacy is largely time-dependent and due to accumulation of its active metabolite.[24 25]

We decided to exclude studies where the efficacy of antidysrhythmics in suppression of VT induction was examined, because these patients may be different than those who present to the ED with spontaneous VT. In the Electrophysiologic Study Versus Electrocardiographic Monitoring (ESVEM) trial,[26] seven agents were examined for efficacy in preventing death or recurrent dysrhythmia. The investigators reported that sotalol was more effective and safer than a number of antidysrhythmic drugs, including procainamide.[26] However, evaluating drug efficacy was not the primary purpose of the study, and efficacy compared with placebo was not measured. A multicentre, double-blind, randomised study[27] later evaluated intravenous sotalol and procainamide with regards to their ability to suppress inducible ventricular dysrhythmias. Following sotalol infusion, 15/50 patients (30%) no longer had inducible, sustained VT, whereas after procainamide, the rate was 10/50 (20%). This difference was not statistically significant. Therefore, further studies are needed to determine which antidysrhythmic agent is preferred for the suppression of inducible VT.

While this review focuses on antidysrhythmic therapies, it remains clear that direct current cardioversion is the most effective treatment for monomorphic VT, stable or otherwise.[9 11 12] If antidysrhythmics are to be administered to treat stable VT, the clinician should be vigilant for subsequent hypotension and be prepared to perform direct current (DC) cardioversion. If the drug is unsuccessful after infusion, procedural sedation and urgent DC cardioversion should be performed.

Limitations

Our systematic review has demonstrated that the available evidence comparing antidysrhythmic treatment for stable, monomorphic VT is extremely limited. The few prospective, randomised studies that address this clinical question involved small sample sizes, suboptimal methodology and significant bias. We included retrospective observational studies in order to give a more complete review of published data, but these trials are subject to additional biases related to selection, confounding and missing data. This review is also limited by the heterogeneity of drugs chosen for direct comparison; formal meta-analysis of our primary outcome could not be performed. Publication bias may have led to overstated drug efficacy, and we did not perform a review of abstracts, unpublished trials and conference proceedings. Future studies should be prospective, randomised, methodologically sound trials that use larger, predetermined sample sizes. An example of such a trial would be one that compared amiodarone and procainamide, giving particular consideration to procainamide's rate of infusion with efficacy, safety and practicality of use in mind.

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