# Anti-Dysrhythmic Drug Therapy for the Termination of Stable, Monomorphic Ventricular Tachycardia: A Systematic Review

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**Abbreviations:** None

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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).

**Method**s: 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: Patients: Adults (≥18 yrs.) with stable monomorphic VT. Intervention: Intravenous anti-dysrhythmic drug. Comparator: Intravenous lidocaine or amiodarone. Outcome: Termination of VT. For all drug comparisons, we calculated relative risks (RR; 95% confidence interval [CI]) and number needed to treat (NNT, 95% confidence interval [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, relative risk of VT termination of procainamide vs. lidocaine was 3.7 (1.3-10.5); ajmaline vs. lidocaine, RR = 5.3 (1.4 – 20.5); and sotalol vs. lidocaine, RR = 3.9 (1.3 – 11.5). From the retrospective studies: procainamide vs. lidocaine, RR = 2.2 (1.2 – 4.0); and procainamide vs. amiodarone RR = 4.3 (0.8-23.6). All 5 reviewed studies had quality issues, including potential bias for randomization 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 anti-dysrhythmic incorporated in the simplified AHA algorithm.[6] According to the most recent European Resuscitation Council guidelines, amiodarone remains the recommended anti-dysrhythmic 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 ventricular tachycardia,[8-9] And as current AHA guidelines stand, procainamide is given a stronger recommendation (IIa) than amiodarone (IIb) and sotalol (IIb).[10] Despite all of the changes and the differences between European and American 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 anti-dysrhythmic therapy is most effective, we reviewed all trials that compared such agents for the termination of stable, monomorphic ventricular tachycardia.

## METHODS

### Study Design

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

### Search Strategy

Two independent reviewers (I.S.d. and J.L.M.) 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 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 ventricular tachycardia 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 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 ventricular tachycardia episodes. Two reviewers (I.S.d. and J.L.M) 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 anti-dysrhythmic 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 ventricular tachycardia), (2) trial inclusion and exclusion criteria, (3) intervention type (type, dose, administration of anti-dysrhythmic 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 ventricular tachycardia; 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 anti-dysrhythmic drugs used in the crossover arms of prospective studies[13-14, 16] were excluded to minimize the risk of confounding from carryover drug effect. Similarly, from one

retrospective study,[17] we excluded data abstracted from observations when the drug in question was administered after another anti-dysrhythmic agent. Relative risk (RR) and number needed to treat (NNT) with 95% confidence intervals [CI] 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 randomization, 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 the Figure. 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 2 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, 5 were determined to meet inclusion criteria: 3 prospective studies with a total of 93 patients and 2 retrospective trials with a total of 173 patients (for all 5 studies, total n = 266).

A majority of these 27 studies were excluded because they evaluated the efficacy of intravenous drugs in suppressing the electrophysiologic induction of ventricular tachycardia. The primary outcome of these studies was determined to be different from our outcome measure of successful VT termination. Of the five selected trials, 4[13-14, 17, 19] were in English and 1[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 5 included studies, Ho et al,[13] Gorgels et al,[14] and Manz et al,[16] were randomized, prospective trials with cross-over 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 5 selected studies in Table 1.[13-14, 16-17, 19] Studies differed in their decision to exclude patients with ventricular tachycardia 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 studies but one[17] excluded subjects who had received intravenous anti-dysrhythmic therapy prior to administration of study drug.

Table 1. Baseline Characteristics and Study Designs of the 5 Selected Studies

| Study | Characteristics | Intervention | Comparison | Outcomes |
|---|---|---|---|---|
| Ho et al. 1994[13] | **Inclusion Criteria:** ECG criteria<br>**Exclusion Criteria:** Previous enrollment, receipt of lignocaine or sotalol in previous 24 hours, poor hemodynamic status requiring DCCV, torsade de pointes, or VT interrupted by sinus rhythm<br>**Sample Size:** N = 33<br>**Gender:** Male 79%<br>**Age:** 68 +/- 6 years (sotalol); 61 +/- 18 years (lidocaine) | Sotalol<br>100 mg over 5 min. | Lignocaine<br>100 mg over 5 min. | VT termination in 15 min. or hemodynamic deterioration |
| Gorgels et al. 1996[14] | **Inclusion Criteria:** ECG criteria<br>**Exclusion Criteria:** Severe CHF or hypotension during VT, polymorphic VT, acute MI, digitalis intoxication, extracardiac disorders<br>**Sample Size:** N = 29<br>**Gender:** Male 86%<br>**Age:** 60 +/- 12 years (procainamide); 62 +/- 14 years (lidocaine) | Procainamide<br>10 mg/kg at 100 mg/min. | Lidocaine<br>1.5 mg/kg over 2 min. | VT termination in 15 min. |
| Manz et al. 1988[16] | **Inclusion Criteria:** ECG and EPS-confirmed<br>**Exclusion Criteria:** Cardiogenic shock or previous treatment with amjalin or lidocaine<br>**Sample Size:** N = 31<br>**Gender:** Male 77%<br>**Age:** 54 +/- 12 years (ajmalin); 58 +/- 10 years (lidocaine) | Ajmaline<br>50 mg over 3-5 min. | Lidocaine<br>100 mg over 3-5 min. | VT termination |
| Marill et al. 2010[17] | **Inclusion Criteria:** ECG criteria, receipt of amiodarone or procainamide<br>**Exclusion Criteria:** VT during cardiac arrest, vasopressor requirement, EP-induced VT<br>**Sample Size:** N = 83<br>**Gender:** Male 70%<br>**Age:** Unknown | Procainamide<br>500 mg at minimum rate<br>15 mg/min. | Amiodarone 150 mg at minimum rate<br>10 mg/min. | VT termination in 20 min. |
| Komura et al. 2010[19] | **Inclusion Criteria:** ECG criteria, initial receipt of procainamide or lidocaine<br>**Exclusion Criteria:** Altered consciousness, chest pain or ECG suggesting acute MI, previous DCCV or drug therapy<br>**Sample Size:** N = 90<br>**Gender:** Male 67%<br>**Age:** 60 +/- 14 years | Procainamide<br>100 mg q1-2 min. (maximum 800 mg) | Lidocaine<br>50 mg boluses (maximum 150 mg) | VT termination or hemodynamic deterioration |

*ECG*, Electrocardiogram; *EPS,* electrophysiologic study; *CHF*, congestive heart failure; *VT*, ventricular tachycardia; *MI*, myocardial infarction; *DCCV*, direct current cardioversion; *EP*, electrophysiologic; *mg*, milligrams; *kg*, kilograms; *min*, minute.

All but one study[16] limited their analysis to cases of spontaneous ventricular tachycardia. Manz et al[16] included subjects with stimulus-induced VT; that is, the investigators electrophyiologically induced the dysrhythmia and then measured the response to anti-dysrhythmic agent. Ventricular tachycardia in 27 of this study's 31 subjects 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 enrollment, the diagnosis of VT was confirmed by electrophysiologic reproduction in variable percentages of patients (ranging from 39-100%) among the studies.[13-14, 16-17, 19]

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 minutes). 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 2 studies[14, 19] (10 mg/kg[14] and 800 mg[19]) that compared procainamide to lidocaine. In addition, Marill et al[17] included cases where procainamide was given as an infusion (average rate 21 mg/kg/minute), whereas Komura et al[19] allowed for upward titration of 100 mg bolus doses every 1-2 minutes. 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 ventricular tachycardia, although only 3 studies[13-14, 17] specified predetermined time periods (ranging from 15 to 20 minutes) 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 ventricular tachycardia 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 minutes of VT termination as failed termination. Thus, the definition of successful VT termination differed between these 2 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 summarized in Table 2. Subjects were reported as randomized in all three prospective studies;[13-14, 16] however, none of these studies described their specific randomization method. Only in Ho et al[13] did the investigators describe the method of allocation concealment and blinding in the study. None of

the 3 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 3 trials,[13-14, 16] the groups were analyzed with an intention-to-treat manner, and follow-up was complete.

Table 2. Critical Appraisal of the 5 Selected Studies

| Study | Randomization | Concealment | Blinding | Intention to treat | Baseline Comparisons | Co-interventions | Complete Follow-up |
|---|---|---|---|---|---|---|---|
| Ho et al. 1994[13] | Randomized, cross-over | Yes | Yes | Yes | Yes | Concurrent oral anti-dysrhythmic therapy | Yes |
| Gorgels et al. 1996[14] | Randomized, unclear process; cross-over | No | No | Yes | Yes | Concurrent oral anti-dysrhythmic therapy | Yes |
| Manz et al. 1988[16] | Randomized, unclear process; cross-over | No | No | Yes | Yes | Concurrent oral anti-dysrhythmic therapy | Yes |
| Marill et al. 2010[17] | Retrospective cohort | No | No | No | Yes | Concurrent oral anti-dysrhythmic therapy; other anti-dysrhythmic given prior to study drug | Yes |
| Komura et al. 2010[19] | Retrospective cohort | No | No | Yes | Yes | None reported | Yes |

Although retrospective studies are typically excluded from systematic reviews of drug therapies, we included 2 such studies for the sake of completion. Due to inherent biases associated with retrospective design, we further evaluated the quality of the 2 retrospective studies[17, 19] using non-validated criteria proposed by Gilbert and Lowenstein.[18] The findings are summarized in Table 2a. Komura et al[19] only met criteria for case selection. Procainamide was the preferred drug to administer in this study (given to 70 patients, compared to 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 agent administered. The results from these observational studies serve to generate ideas towards future investigation; no substantial conclusions should be drawn from them.

Table 2a. Additional Appraisal of the 2 Retrospective Studies (Gilbert and Lowenstein criteria)

| Study | Abstractors | Case Selection | Abstraction Form | Variable Definition | Meetings | Monitoring | Inter-Rater Reliability |
|---|---|---|---|---|---|---|---|
| Marill et al. 2010[17] | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| Komura et al. 2010[19] | No | Yes | No | No | No | No | No |

**Primary Outcome Analysis**

The success rates of ventricular tachycardia termination are included in Table 3. In the 4 studies[13-14, 16, 19] that compared lidocaine with another anti-dysrhythmic medication, lidocaine successfully terminated VT less frequently than procainamide, sotalol, and ajmaline. In Ho et al,[13] the investigators report that 2 of the patients randomized to the lidocaine group had supraventricular tachycardia with aberrancy that was misdiagnosed as ventricular tachycardia. The dysrhythmia in these 2 patients was not successfully terminated, but even if removed from the data, the difference between sotalol (69%) and lidocaine (20%) remained significant.[13] The number needed to treat (NNT) of procainamide compared with lidocaine, based on data pooled from the two studies[14, 19] that compared these drugs was 2 (95% CI 1.5-3.6). In the retrospective trial[17] that compared amiodarone with procainamide, there was no significant difference in efficacy.

Table 3. 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. 1994[13] | 33 | 3/17 (18%) | -- | -- | -- | 11/16 (69%) | 3.9 (1.3-11.5) | 2.0 (1.2-4.5) |
| Gorgels et al. 1996[14] | 29 | 3/14 (21%) | 12/15 (80%) | -- | -- | -- | 3.7 (1.3-10.5) | 1.7 (1.1-3.4) |
| Manz et al. 1988[16] | 31 | 2/16 (13%) | -- | -- | 10/15 (67%) | -- | 5.3 (1.4-20.5) | 1.9 (1.2-3.9) |
| Marill et al. 2010[17] | 41 | -- | 4/7 (57%) | 8/34 (24%) | -- | -- | 4.3 (0.8-23.6) | 3.0 (-17.5-1.4)* |
| Komura et al. 2010[19] | 90 | 7/20 (35%) | 53/70 (76%) | -- | -- | -- | 2.2 (1.2-4.0) | 2.5 (1.6-5.7) |

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

## Secondary Outcome Analysis

The adverse effects reported in each study are summarized in Table 4. Death was reported in 4 subjects from the studies included in this review. One subject died in the setting of an acute large myocardial infarction 6 hours after successful termination of ventricular tachycardia by sotalol. A second death was attributed to the administration of lignocaine following the misdiagnosis of sinus tachycardia with QRS 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 ischemic cardiomyopathy died despite repeated ICD shocks and amiodarone bolus plus infusion over 15 hours.

Table 4. Adverse Effects Reported During the Treatment of Ventricular Tachycardia

| Study | Bradycardia | Hypotension | VT Acceleration | Neurologic Symptoms | Death |
|---|---|---|---|---|---|
| Ho et al. 1994[13] | Lignocaine<br>0<br><br>Sotalol<br>2 (13%) | Lignocaine<br>1 (6%)<br><br>Sotalol<br>1 (6%) | Not reported | Lignocaine<br>2 (12%)<br><br>Sotalol<br>0 | Lignocaine<br>1 (6%)<br><br>Sotalol<br>1 (6%)<br><br>Lignocaine, Sotalol*<br>1 (7%) |
| Gorgels et al. 1996[14] | Not reported | Lidocaine<br>2 (14%)<br><br>Procainamide<br>1 (7%) | Lidocaine<br>0<br><br>Procainamide<br>1 (7%) | Not reported | 0 |
| Manz et al. 1988[16] | Not reported | 0 | 0 | Lidocaine<br>9 (56%)<br><br>Ajmaline<br>0 | 0 |
| Marill et al. 2010[17] | Not reported | Amiodarone<br>3 (9%)<br><br>Procainamide<br>2 (25%) | Not reported | Not reported | Amiodarone<br>1 (3%) |
| Komura et al. 2010[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."

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 2 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 ventricular tachycardia 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 myocardial infarction (MI). Lidocaine is thought to block sodium channels more effectively in ischemic myocardium; it may be a more effective therapy in suppressing automaticity, which is believed to be the typical mechanism of dysrhythmia induction in ventricular tachycardia 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. In 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 ventricular tachycardia.

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 received lidocaine and 15 received ajmaline. It is unclear why these patient enrollment 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 randomized trials[14, 16] included in this review did not describe how randomization was conducted or state which mechanisms, if any, there were to conceal the randomized allocation sequence. Trials with inadequate allocation concealment may overestimate treatment effect[22] and undermine the goal of minimizing selection bias by randomization. Selection bias may affect study outcomes more significantly when sample sizes are small. The same two trials[14, 16] administered anti-dysrhythmic drugs in an un-blinded

fashion. Ascertainment bias from lack of blinding, however, was unlikely to have played a role in the subjects' electrophysiologic response to drug administration and the provider's determination of successful ventricular tachycardia termination.

The European Council Guidelines for Resuscitation currently recommend amiodarone 300mg over 20-60 minutes for the treatment of stable, monomorphic ventricular tachycardia.[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 (300mg) 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 United States, intravenous sotalol and nifekalant are unavailable, and procainamide is rarely used as the initial drug treatment for termination of stable, monomorphic ventricular tachycardia. Marill et al[17] reported the use of procainamide as the initial agent in only 8 cases in 4 centers over an average of 7.2 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 minutes. Current guidelines[10] recommend an infusion rate of 20-50 mg/min, so that maximum infusion rate would require a minimum of 27 minutes. Even this shorter required time for drug administration may be considered unacceptably long for the clinician to remain at the bedside to monitor the patient and wait for drug effect. It must also be recognized 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 anti-dysrhythmics, 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 ventricular tachycardia may be due to their common electrophysiologic effect of lengthening the refractory period and thus prolonging repolarization in cardiac myocytes.[23] In 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 repolarization; its anti-dysrhthmic efficacy is largely time-dependent and due to accumulation of its active metabolite.[24-25]

We decided to exclude studies where the efficacy of anti-dysrhythmics in suppression of ventricular tachycardia 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] 7 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 anti-dysrhythmic 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 multicenter, double-blind, randomized 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 anti-dysrhythmic agent is preferred for the suppression of inducible VT.

While this review focuses on anti-dysrhythmic therapies, it remains clear that direct current cardioversion is the most effective treatment for monomorphic ventricular tachycardia, stable or otherwise.[9, 11-12] If anti-dysrhythmics are to be administered to treat stable VT, the clinician should be vigilant for subsequent hypotension and prepared to perform 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 anti-dysrhythmic treatment for stable, monomorphic ventricular tachycardia is extremely limited. The few prospective, randomized 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, randomized, 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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