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CAT – Chemical Cardioversion of New Onset Atrial Fibrillation

P: In otherwise healthy ED patients presenting with new onset a-fib

I: Which agents for chemical cardioversion

C: Compared to standard rate control/non-cardioversion

O: Are associated with higher rates of cardioversion and lowest side effect/complication profile

Scenario 1:

A 77 yo female with well controlled HTN presents with complaint of palpitations and mild dyspnea of abrupt onset six hours ago. She states that she can tell with some certainty that she began to feel poorly just after lunch. She has never experienced this before and tells you when asked that she's never heard the words atrial fibrillation or irregular heart rate before. She sees only her primary physician, who manages her HTN with monotherapy. ECG at bedside shows atrial fibrillation with RVR of 140s. She has BP 138/80, SpO2 99% on RA, and temp 98.6. She appears well, and speaks to you with no discernable discomfort. She does continue to complain of palpitations.

Should you offer this patient chemical cardioversion? If so, what agent should you use?

Scenario 2:

A 46 yo male with no known medical problems presents with sensation of palpitations and rapid heartbeat starting while running 5 miles, which he does 4-5 days a week. He does not smoke and he has no family history of heart disease. He complains that he felt his heart start beating faster and harder halfway through his run, which was 3 hours ago. He stopped running, but the symptoms

continued. He denies chest pain, dyspnea, nausea. ECG at bedside shows atrial fibrillation with RVR of 140s. He has BP 138/80, SpO2 99% on RA, and temp 98.6. He appears well, and speaks to you with no discernable discomfort

Should you offer this patient chemical cardioversion? If so, what agent should you use?

Guidelines:

Canadian Cardiovascular Society Atrial Fibrillation Guidelines 2010: Management of Recent-Onset Atrial Fibrillation and Flutter in the Emergency Department

Ian G. Stiell, MD, MSc, Laurent Macle, MD, FRCPC, and the CCS Atrial Fibrillation Guidelines Committee. Canadian Journal of Cardiology 27 (2011) 38–46

“We recommend that in stable patients with recent-onset AF/AFL, a strategy of rate control or rhythm control could be selected (Strong Recommendation, High-Quality Evidence).”

“In hemodynamically stable patients with AF/AFL of known duration <48 hours in whom a strategy of rhythm control has been selected: We recommend that rate-slowng agents alone are acceptable while awaiting spontaneous conversion (Strong Recommendation, Moderate-Quality Evidence). We recommend that synchronized electrical cardioversion or pharmacologic cardioversion may be used when a decision is made to cardiovert patients in the emergency department”

2011 ACCF/AHA/HRS Focused Updates Incorporated Into the ACC/AHA/ESC 2006 Guidelines for the Management of Patients With Atrial Fibrillation

A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2011;123:e269–e367

“Administration of flecainide, dofetilide, propafenone, or ibutilide is recommended for pharmacological cardioversion of AF.”

“One may conclude from these studies that rate control is a reasonable strategy in elderly patients with minimal symptoms related to AF.”

Guidelines for the management of atrial fibrillation

The Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC) European Heart Journal (2010) 31, 2369–2429

“The acute management of patients with AF is driven by acute protection against thrombo-embolic events and acute improvement of cardiac function. The severity of AF-related symptoms should drive the decision for acute restoration of sinus rhythm (in severely compromised patients) or acute management of the ventricular rate (in most other patients).”

Drug	Dose	Follow-up dose	Risks
Amiodarone	5 mg/kg i.v. over 1 h	50 mg/h	Phlebitis, hypotension. Will slow the ventricular rate. Delayed AF conversion to sinus rhythm.
Flecainide	2 mg/kg i.v. over 10 min, or 200–300 mg p.o.	N/A	Not suitable for patients with marked structural heart disease; may prolong QRS duration, and hence the QT interval; and may inadvertently increase the ventricular rate due to conversion to atrial flutter and 1:1 conduction to the ventricles.
Ibutilide	1 mg i.v. over 10 min	1 mg i.v. over 10 min after waiting for 10 min	Can cause prolongation of the QT interval and torsades de pointes; watch for abnormal T-U waves or QT prolongation. Will slow the ventricular rate.
Propafenone	2 mg/kg i.v. over 10 min, or 450–600 mg p.o.		Not suitable for patients with marked structural heart disease; may prolong QRS duration; will slightly slow the ventricular rate, but may inadvertently increase the ventricular rate due to conversion to atrial flutter and 1:1 conduction to the ventricles.
Vernakalant	3 mg/kg i.v. over 10 min	Second infusion of 2 mg/kg i.v. over 10 min after 15 min rest	So far only evaluated in clinical trials; recently approved. ^{68-70a}

Article	Population	Study Type and Outcome	Key Results	Conclusions	Limitations
<p>A Comparison of Rate Control And Rhythm Control in Patients with Atrial Fibrillation (AFFIRM)</p> <p>N Engl J Med, Vol. 347, No. 23</p>	<p>4060 patients at least 65 years of age with atrial fibrillation</p> <p>(35% enrolled at first detection of afib)</p>	<p>Randomized multi-center comparison</p> <p>Mortality at 5 years.</p>	<p>More deaths occurred in the rhythm-control group than in the rate-control group, but the difference in mortality between the two groups was not statistically significant (P=0.08; hazard ratio, 1.15 [95 percent confidence interval, 0.99 to 1.34]; both adjusted for interim monitoring but not for base-line covariates). The rates of the composite end point of death, disabling stroke, disabling anoxic encephalopathy, major bleeding, or cardiac arrest were also similar in the two groups (P=0.33).</p>	<p>the strategy of restoring and maintaining sinus rhythm had no clear advantage over the strategy of controlling the ventricular rate and allowing atrial fibrillation to persist. There was a trend toward increased mortality in association with the rhythm-control strategy (P=0.08).</p>	<p>Older patients only, does not address acute management directly.</p>
<p>Rhythm or rate control in atrial fibrillation— Pharmacological Intervention in Atrial Fibrillation (PIAF): a randomised trial</p> <p>Lancet 2000; 356: 1789–94</p>	<p>252 pts with symptomatic afib of 7-360 days' duration</p>	<p>Open, randomized pilot study.</p> <p>Amiodarone vs diltiazem orally.</p> <p>Symptoms at one year, performance of 6 minute walk</p>	<p>Cardioversion group had more admissions, all but 23% had at least one electrical cardioversion, performed better on 6 minute walk starting at 12 weeks out.</p>	<p>neither of the two therapeutic strategies is superior in terms of improvement in atrial fibrillation-related symptoms.</p> <p>Rhythm control may be associated with greater side effects and more hospitalizations</p>	<p>Amiodarone was only antiarrhythmic agent used. DC cardioversion left to discretion of physician, with some pts receiving up to 3x.</p> <p>Did not address new onset.</p>

<p>Rate-control vs. rhythm-control in patients with atrial fibrillation: a meta-analysis</p> <p>European Heart Journal (2005) 26, 2000–2006</p>	<p>5239 pts</p> <p>From RACE, AFFIRM, PIAF, STAF, HOT CAFE</p>	<p>Meta—analysis of all cause mortality, embolic CVA, intracranial bleed, systemic embolism</p>	<p>A rate-control strategy compared with a rhythm-control approach was associated with a significantly lower risk of the CEP [OR 0.85 (0.73,0.98), P ¼ 0.03]. There was a non-significant trend towards a reduced risk of the single endpoint of death [OR 0.87 (0.74, 1.02), P ¼ 0.09] and thromboembolic stroke [OR 0.8 (0.6, 1.07), P ¼ 0.14]. Rate-control vs. rhythm-control yielded a favourable risk difference for the CEP of 20.02 [(20.04, 20.01), P ¼ 0.006], resulting in an NNT of 50</p>	<p>NNT to avoid one death was 50 and to avoid one thromboembolic stroke 100. These findings imply that allocation of 1000 patients to a rate-control approach vs. a rhythm-control strategy, would avoid 20 deaths and 10 thromboembolic strokes per year</p>	<p>Most patients (4060) from a single trial (AFFIRM) which showed a nonsignificant trend towards rate control.</p>
<p>Pharmacological cardioversion for atrial fibrillation and flutter</p> <p>Cochrane review</p>	<p>PIAF and AFFIRM</p>	<p>Cochrane review meta-analysis</p> <p>Death, hospitalization rate, discontinuation of therapy</p>	<p>Mortality- pooling the data of the two studies reveals a non-significant relative risk of 1.14 (95% confidence interval 1.00 to 1.31; P=0.06) in favour of rate control. Both studies show a significantly higher hospitalisation rate in the rhythm control group of</p>	<p>The pooled data does not favour one treatment approach over another though there is a trend in favour of rate control.</p>	<p>Only two studies, AFFIRM with many more patients. Limitation: as above with individual studies.</p>

			patients. overall relative risk of 1.16		
<p>Conversion efficacy of intravenous ibutilide compared with intravenous amiodarone in patients with recent-onset atrial fibrillation and atrial flutter</p> <p>International Journal of Cardiology 118 (2007) 321–325</p>	<p>152 (103 men and 49 women) consecutive patients with AF or Af of 3–48 h duration</p>	<p>Prospective, randomized, single blind.</p> <p>Conversion to SR within 4 hours.</p> <p>Ibutilide 10 mg over 10 min, repeat q 10 min x 1 prn vs 5 mg/kg amio + 1200 mg over 24 hrs</p>	<p>conversion rate of group A (ibutilide) was significantly higher than the conversion rate of group B (amiodarone) (80% vs. 57%, p=0.0054)</p> <p>The mean time to arrhythmia termination was significantly shorter with ibutilide than with amiodarone for AF (53.4±25.8 vs. 492±186 min, p=0.000) and for Af (28.4±16.3 vs. 762± 318 min, p=0.000).</p>	<p>ibutilide acts faster than amiodarone in conversion AF or Af to SR. On the other hand, amiodarone certainly appeared to be safer, yet ibutilide induced ventricular arrhythmias caused no deaths, meaning that the administration of this drug needs hospital environment and close monitoring.</p>	<p>Not double blind. No follow up after 24 hours.</p>
<p>Ibutilide for treatment of atrial fibrillation in the emergency department</p> <p>Emerg Med J 2006;23:133–134</p>	<p>46 patients with new onset afib of duration less than 7 days</p>	<p>Retrospective cohort analysis (all patients who received ibutilide through ED protocol over 3 years)</p> <p>Conversion to SR within 4 hours after ibutilide infusion vs physicians choice rate control</p>	<p>64% of ibutilide pts converted in one hour of infusion.</p> <p>29% of rate control pts converted within 12 hours.</p>	<p>The main results of our study suggest that ibutilide is more successful than rate control drugs in early restoration of sinus rhythm in recent onset AF. Ibutilide appears to be a safe drug to use in the ED setting.</p>	<p>The data collection was done retrospectively and therefore the patients were not randomised. The groups are thus not identical and the patients in the rate control group were older than those in the ibutilide group. Consequently, patients in the rate control group may conceivably have had more comorbidities.</p>

<p>Comparison of intravenous ibutilide vs. propafenone for rapid termination of recent onset atrial fibrillation</p> <p>Int J Clin Pract, December 2005, 59, 12, 1395-1400</p>	<p>Eighty-two consecutive patients with AF (onset in 2 h to 90 days)</p>	<p>Single blinded randomized, controlled clinical trial.</p> <p>Conversion to SR within 90 minutes of infusion of 1 mg ibutilide over 10 mins or 70 mg propafenone over 10 mins with repeat if no effect in 10 mins</p>	<p>In the ibutilide group, 29 (70.73%) patients converted to sinus rhythm, and in the propafenone group, 20 (48.78%) patients did. The conversion rate of ibutilide was significantly higher than that of propafenone (p ¼ 0.043).</p>	<p>In overall patients and each agent group, patients with AF duration no more than 24 h or left atrium diameter no more than 4.0 cm had statistically higher conversion rates than those with AF duration more than 24 h or left atrium diameter more than 4.0 cm, respectively</p>	<p>Single blinded, single dose instead of weight based, no follow up after d/c.</p>
<p>A Randomized Active-Controlled Study Comparing the Efficacy and Safety of Vernakalant to Amiodarone in Recent-Onset Atrial Fibrillation</p> <p>JACC Vol. 57, No. 3, 2011</p>	<p>254 adult patients with symptomatic afib between 3 and 48h duration</p>	<p>multicenter, randomized, double-blind, double-dummy, active-controlled study</p> <p>Conversion to SR within 90 mins. 3 mg/kg vernakalant over 10 min rpt q 10 min x 1 prn vs 5 mg/kg amio over 60 mins + 50 mg</p>	<p>Sixty of 116 (51.7%) vernakalant patients met the primary end point, compared with 6 of 116 (5.2%) amiodarone patients (p 0.0001); relative risk 10.0 (95% confidence interval: 4.5 to 22.2).</p>	<p>This study shows that vernakalant provides a safe and effective alternative to amiodarone for the acute conversion of recent-onset AF. Conversion with vernakalant was rapid and significantly more effective than amiodarone (52% vs. 5% within 90 min). Patients treated with</p>	<p>There was a higher incidence of AFL in vernakalant patients (8.6%) compared with amiodarone patients (0.9%) within 4 h post-dose. Of the 10 vernakalant patients who developed AFL, 5 spontaneously converted and 4 were electrically cardioverted to SR within 4 h, and 1 patient spontaneously converted to SR</p>

		over 60 mins		vernakalant had significantly greater symptom relief at 90 min and a greater perceived feeling of well-being at 2 h.	within 24 h. Short follow up, non-ideal administration of amio.
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Clinical bottom line: Current evidence suggest that cardioversion may not be the most appropriate treatment for the elderly, those with paroxysmal atrial fibrillation or chronic atrial fibrillation. However, in the new onset atrial fib patient, conversion with ibutilide appears to be safe and effective in the short term.

Further discussion & local expert recommendations:

Patients with new onset atrial fibrillation should be risk stratified for thromboembolic CVA with a validated prediction tool such as the CHADS₂ score or the CHA₂DS₂-VASc score. Those with a score of 0-1 may be offered chemical cardioversion in the ED with several (4-6) hours of observation (Scenario 2).

Patients with a CHADS score of 2-3 may be considered for chemical cardioversion if short term anti-thrombotic therapy and same day stress echo can be arranged, due to the risk of thromboembolism during the conversion period and previously unrecognized coronary artery disease. This seems appropriate for an ED observation protocol, in which the patient with CHADS₂ score 2 or CHA₂DS₂-VASc score 4 (as in Scenario 1 above), with new onset atrial fibrillation and negative initial cardiac enzymes may be offered a single dose of enoxaparin and chemical cardioversion, with serial enzymes and a stress echo in the morning before discharge with cardiology follow up. (Significant assistance from Dr. Mark East- interventional cardiologist, in developing this idea)

Patients with higher thromboembolic disease scores should be rate controlled and admitted for TEE and anticoagulation prior to any attempt to D/C cardiovert. Up to 20% of these will convert spontaneously within 24 hours.