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Esmolol in Cardiology, Emergency and Critical-Care Medicine
“Meet the Expert” Meeting – March 5th, 2012, Vienna

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Esmolol in Cardiology, Emergency and Critical-Care Medicine

“Meet the Expert” Meeting – March 5th, 2012, Vienna

Speakers: G. Krumpl, H. Domanovits, G. Stix, G. Heinz

Summarized by N. Hasenöhr

Beta blockers were introduced more than half a century ago. In 1958, the first beta blocker, dichloroisoproterenol, was synthesized, and the first clinically significant beta blockers – propranolol and pronethalol – were discovered in 1962. Beta blockers have revolutionized the medical management of heart disease and are considered by many to be one of the most important contributions to clinical medicine and pharmacology of the 20th century.

However, treatment with beta blockers even today is not trivial but still challenging, especially in critically ill patients.

The role of the very short-acting beta blocker esmolol in cardiology, emergency and critical-care medicine was the subject of an international Expert Meeting, held in Vienna in March 2012.

■ Clinical Pharmacokinetics of Beta Blockers

Ass.-Prof. Dr. Guenther Krumpl, Institute of Pharmacology, Medical University of Vienna

There are various important differences between beta blockers, beginning with the question of whether or not the compound exhibits partial agonistic activity (like e.g. pindolol), which is determined by its chemical structure. Another important distinction is between lipophilic and hydrophilic compounds. Lipophilic beta blockers usually have higher absorption rates, high first-pass effects, high rates of metabolism (90–100%) and short half-lives, whereas hydrophilic beta blockers have lower absorption rates, low first-pass effects, low rates of metabolism (0–10%) and long half-lives. Some beta blockers, like sotalol, labetalol, or propranolol, exhibit class-I/III antiarrhythmic effects and some, like carvedilol or labetalol, also have alpha-blocking activity. Some compounds, like atenolol

and sotalol, are mainly (> 90%) excreted in urine whereas others, like esmolol, hardly show any urinary excretion (0.7%).

Table 1 shows the pharmacokinetic differences of various beta blockers.

“Pharmacokinetics of beta blockers should be considered for their appropriate use”, said Krumpl. “While long- or medium-acting beta blockers are appropriate for chronic or subacute therapy, intravenous preparations should be used for acute treatment”, he added.

Esmolol is an intravenously administered beta blocker with very rapid onset of action – within 2 minutes – and a very short elimination half-life of only 9 minutes. Its intra- and inter-subject dose relation is linear [1]. It is the only intravenously administrable, short-acting beta blocker currently available. After administering appropriate bolus doses of usually 500 µg/kg within the first minute and continuous administration of 50–300 µg/kg/min thereafter, an esmolol steady state is reached within 5 minutes. Without a bolus dose it takes much longer to reach a steady state – about half an hour. About 55% of esmolol are bound to plasma proteins. Therefore, even if several drugs compete for plasma protein binding there will be no relevant change of esmolol plasma levels. Once the entire infusion has been administered, esmolol activity ceases within 10–20 minutes – complete recovery from beta blockade is achieved within 18–30 minutes [2, 3]. Esmolol is rapidly metabolized to an acid metabolite with very little beta-blocking activity (about 1000 times weaker than esmolol), and to methanol. Only 2% of the administered amount of esmolol are excreted unchanged in urine, about 73–88% are excreted in urine as free acid, the rest as methanol (< 2% of the threshold of toxicity).

Table 1. Pharmacokinetics of Beta Blockers. (Source: Data sheets of the various beta blockers)

Class*	Substance	Mode of administration	Onset**	Max. effect**	Half-life**	Duration of action**	Receptor
Ultrashort	Esmolol	i.v.	2	5–20	9	5–15	Beta 1
Medium	Metoprolol	i.v.	5–10	10	120–180	60–480	Beta 1
	Labetalol	i.v.	5–10	10	360	120–600	Alpha 1, not Beta 1-selective
	Propranolol	oral	60–90	90–120	240	60–360	Not selective
Medium-long	Metoprolol oral retarded formulation	oral	30–40 80–120	90–120 240–420	180–420 540–720	200–1200 400–1440	Beta 1
Long	Bisoprolol	oral	50–70	140	540–720	240–420	Beta 1
	Atenolol	oral	60–90	90–120	360–420	120–1200	Beta 1

*according to duration of action; **minutes

Table 2. Esmolol and Metoprolol: Pharmacokinetic key points. (Source: Prof. G. Kruppl, Medical University of Vienna)

	Esmolol	Metoprolol
Substantial genetic variability	–	+
Drug-drug interaction (induction, blockade)	–	+
Organ dependency of elimination	–	+
Kinetic influence of liver disease	–	+
Kinetic influence of kidney disease*	±	±
Relevant metabolites	–	+

*Metabolites of both esmolol and metoprolol accumulate in kidney failure, but because of the different beta-blocking potentials of those metabolites this is clinically much more relevant for metoprolol than for esmolol [9, 10].

This metabolic step is achieved by esterases in erythrocytes and in plasma, while there is no esmolol metabolism through the hepatic cytochrome P-450 (CYP) system [3]. Thus, contrary to other beta blockers, esmolol exhibits no drug-drug interactions through CYP enzymes. These erythrocyte esterases have hardly any relevant genetic variations and they cannot be saturated, therefore the esmolol metabolism will occur by all means.

In contrast, metoprolol has a half-life of 60–480 minutes, its elimination mainly depends on liver function [4] and since it is metabolized through the CYP 2D6 enzyme, it has a lot of relevant drug-drug interactions with inducers or inhibitors of CYP 2D6. It also has a metabolite, hydroxy-metoprolol, which adds about 5–10% of the beta-blocking activity and which is not beta-1-selective [5]. Metoprolol shows biphasic elimination and there is no linear dose relation between individuals [6]. The metoprolol metabolism exhibits massive and unpredictable genetic variability. In poor metoprolol metabolizers, the compound has a half-life of 480–840 minutes, in extensive metabolizers the half-life lasts for 180–360 minutes, and in ultra-rapid metabolizers the half-life amounts to only 60–120 minutes [7]. Also, above a certain plasma concentration, metoprolol loses its beta-1-specificity. This is not the case with esmolol, since esmolol concentrations theoretically necessary to achieve this effect do not occur in clinical practice.

Oral metoprolol has a rather unpredictable therapeutic window – after oral administration of 50 mg of the compound, the therapeutically necessary plasma concentration only lasts for 4.5 hours – even shorter in ultra-rapid metabolizers, but longer in poor metabolizers [8].

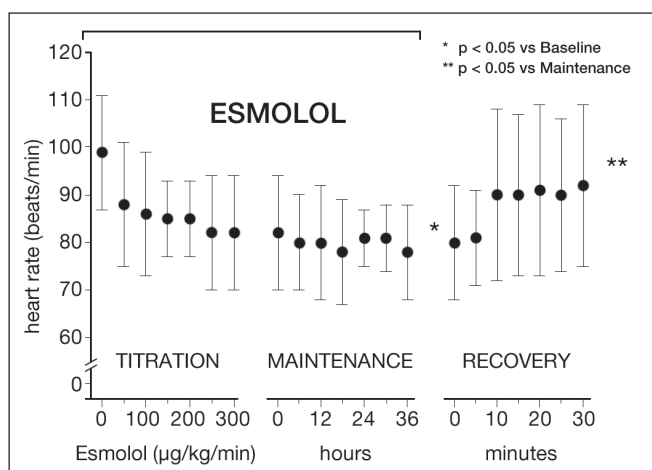
Table 2 summarizes key differences in pharmacokinetics between esmolol and metoprolol.

The key advantages of esmolol can be summarized as follows (Fig. 1):

- Organ-independent elimination
- Ultra-rapid elimination

therefore

- Possibility of effect-titrated treatment
- Possibility of rapid onset and termination of treatment

**Figure 1.** Esmolol: Ultra-short Action. Reprinted from [11], with permission from Elsevier.

■ The Role of Short-Acting Beta Blockers in Emergency Medicine

Univ.-Prof. Dr. Hans Domanovits, Department of Emergency Medicine, Medical University of Vienna

Case 1 – STEMI

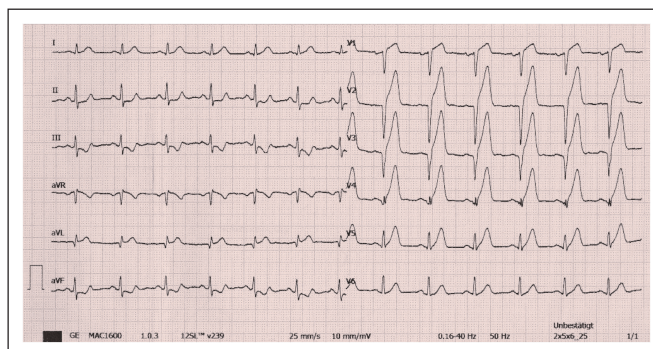
A 52-year-old male patient presents with chest pain that set on two hours before. He is 181 cm tall and weighs 112 kg. He is a smoker (40 cigarettes/day), and his father died of a myocardial infarction at the age of 52.

The ECG shows an extensive anterior myocardial infarction (STEMI; Fig. 2).

Treatment is initiated in the ambulance vehicle: ASS 250 mg i.v., morphine 5 mg i.v./s.c., unfractionated heparin (UFH) 4.000 IU i.v., prasugrel 60 mg orally, and oxygen 4 l/minute.

Upon arrival at the clinic, the patient is transported to the catheter lab immediately. Coronary angiography shows an occlusion of the proximal LAD (left anterior descending artery), a high-grade stenosis in the middle part of the LAD and a high-grade stenosis of the first diagonal branch.

Although the occlusion is reopened and stented, pain, tachycardia, tachypnea, rales, and vomiting persist. Oxygen saturation decreases to 81%.

**Figure 2.** STEMI in a 52-year-old man. (Source: Prof. Dr. H. Domanovits, Department of Emergency Medicine, Medical University of Vienna)

Therefore, the patient receives furosemide 40 mg i.v., morphine 5 mg i.v./s.c., metoclopramide 10 mg i.v., and oxygen is increased to 12 l/minute. The lactate level increases until reaching a plateau.

Blood pressure (BP): 150/85 mmHg, heart rate (HR): 130 beats per minute (bpm). It is decided to administer esmolol at a rate of 0.1 mg/kg/min. The BP decreases to 100/60 mmHg, and the HR to 100 bpm.

Outcome and Commentary

The patient recovered within eight hours. He required neither mechanical ventilation, nor intra-aortic balloon pump (IABP) or levosimendan. According to the current ESC guidelines, the benefit of long-term beta blockers after STEMI is well established, while the role of routine early i.v. administration is less firmly established. The early i.v. use of beta blockers is clearly contraindicated in patients with clinical signs of hypotension or congestive heart failure. In most patients, it is recommended to wait for the patient to stabilize before starting an oral beta blocker therapy [12].

“However, there are cases, like our patient here, who are hypertensive and tachycardic, and, in such situations, the treatment with esmolol is quite justified and allows us a titrated approach”, commented Domanovits.

Case 2 – HOCM (Hypertrophic obstructive cardiomyopathy)

A 55-year-old male (174 cm, 99 kg) experiencing chest pain for two hours smokes 40 cigarettes a day and is an alcohol abuser. He received 250 mg ASS and 4000 IU of UFH i.v. and 0.8 mg of nitroglycerin sublingually.

The ECG shows ST-elevations in V1, aVR, and ST-depressions in various other leads. Lactate is slightly elevated but pH and other blood gas parameters are not dramatically changed. BP is 180/110 mmHg, HR 114 bpm. There are persistent ECG changes. Esmolol is started with a 100 mg bolus over three minutes and then given by continuous infusion according to the lo-

cal protocol (Fig. 3). The ECG changes slightly improve, BP settles at 140/85 mmHg, HR 86 bpm. But at closer examination there is also a systolic murmur. A transthoracic echocardiography (TTE) then reveals a hypertrophic obstructive cardiomyopathy with a mean gradient of 60 mmHg.

Outcome and Commentary

After continuing the esmolol infusion and giving some volume to this hypovolemic patient, another TTE shows that the gradient fell to 18 mmHg. According to the ACCF/AHA guideline for the diagnosis and treatment of hypertrophic cardiomyopathy, beta blockers are recommended for the treatment of symptoms (angina or dyspnea) in adult patients with obstructive or nonobstructive HCM, but should be used with caution in patients with sinus bradycardia or severe conduction disease (Class IB recommendation) [13].

“In such cases, we have to make cautious case-by-case decisions about the use of beta blockers”, Domanovits said.

Case 3 – Atrial Fibrillation

A female 66-year-old patient (166 cm, 73 kg) has had an infection of the upper airway for three days. She now complains about palpitations, tachycardia, and nausea. She also has a history of arterial hypertension.

Laboratory values: TSH 3.87 μ U/ml (normal range 0.44–3.77), NTproBNP 195.6 pg/ml (0–125), cholesterol 232 mg/dl (< 160 for secondary prevention), CRP 5.53 mg/dl (< 1 mg/dl), fibrinogen 654 mg/dl (180–390), troponin T 0.025 ng/ml (< 0.03 ng/ml).

The ECG shows a tachycardic atrial fibrillation (AF) which explains the feeling of palpitations and tachycardia. The TTE shows left ventricular hypertrophy and a mildly dilated left atrium.

The patient receives low-molecular weight heparin s.c. and 5 mg of verapamil i.v., without achieving satisfactory improvement, so the verapamil dose is repeated, but still no

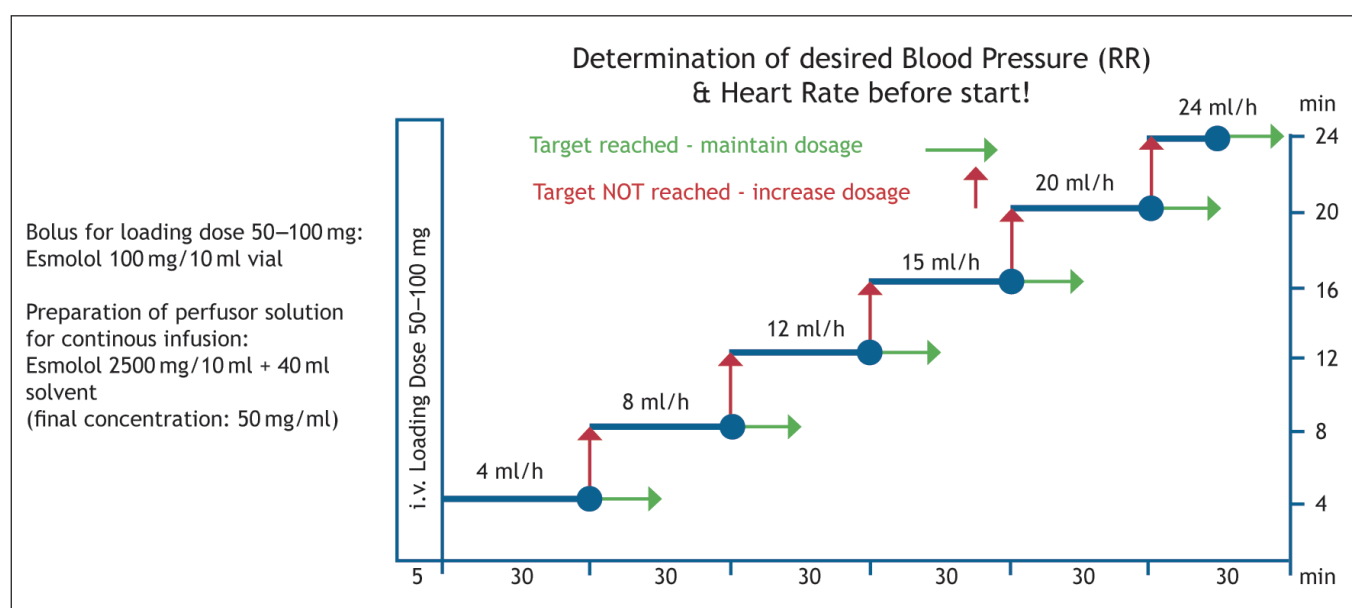


Figure 3. Esmolol Titration scheme for Perfusor. (Source: Prof. Dr. H. Domanovits, Prof. Dr. W. Schreiber, Department of Emergency Medicine, Medical University of Vienna)

satisfactory improvement. Esmolol is started (100 mg bolus, then continuous infusion according to the local protocol [Fig. 3]).

Outcome and Commentary

The diagnosis was bronchopneumonia hypertension and AF. The esmolol infusion was continued overnight and in the morning, sinus rhythm was established.

“We cannot say if the recovery of sinus rhythm was due to the beta blocker alone or to the combination of beta blocker and calcium antagonist, but certainly using esmolol in this case was a good decision”, was Domanovits’ comment.

According to the ESC, esmolol is one of the options for acute rate control in atrial fibrillation (Class IC) [14].

Case 4 – Aortic Dissection and Hypertension

A 53-year-old male patient experienced a sudden onset of pain in the neck during work in the morning. His medical history is unremarkable.

The ECG shows no pathologic changes, but the BP is 180/85 mmHg, HR 113 bpm. Troponin T is negative, D-dimer elevated. A CT scan shows an aortic dissection Stanford-type B. The patient is started on urapidil with a bolus of 25 mg, then two more similar bolus injections, then he receives a continuous urapidil infusion. Since the patient’s BP remains high, in this high-risk situation he also receives esmolol (bolus dose and continuous infusion according to the local protocol [Fig. 3]) and also clonidine and nitroglycerin, both as continuous infusions. This combination finally allowed to control his blood pressure after 24 hours. Later on, a conservative approach with oral beta blockade in combination with ACE-inhibition was successfully established.

Commentary

According to ESC guidelines, in patients with suspected aortic dissection, reduction of systolic blood pressure with beta blockers (i.v. metoprolol, esmolol, or labetalol) is a class-I recommendation [15].

Generally, in hypertensive patients, beta blockers are indicated in coronary artery disease (CAD), after myocardial infarction (MI), in congestive heart failure (CHF), in pregnancy, and in tachyarrhythmia. Contraindications include bronchial asthma, COPD, and AV block IIb and III [16].

■ Beta Blockers as Antiarrhythmic Drugs with Focus on Acute Settings

Ass.-Prof. Dr. Guenter Stix, Department of Cardiology, Medical University of Vienna

There is a number of arrhythmias which can be treated with beta blockers. Table 3 lists the most important ones.

Electrophysiology

“The antiarrhythmic actions of beta blockers are not completely understood yet”, said Stix. “Most of the antiarrhythmic actions of beta blockers are indirect ones, by reducing and

blocking the effect of beta-agonists on the heart. The most pronounced direct antiarrhythmic mechanism concerns the reduction of automaticity, especially of the sinus node and the AV node. Beta blockers suppress the phase-IV depolarization and elevate the depolarization threshold and thus reduce heart rate”, Stix added.

All other antiarrhythmic actions of beta blockers are indirect and affect various ion channels and phases of the action potential.

Inappropriate Sinus Tachycardia

This kind of sinus tachycardia often occurs with moderate physical activity or even without any particular reason, but can be very distressing for the patient. Heart rates approaching 160 bpm and even higher are seen. In this scenario, lowering the HR with beta blockers can be extremely helpful.

A group of patients prone to inappropriate sinus tachycardia are those with mitral valve prolapse syndrome. The reasons are not entirely understood, but there seems to be some dys-autonomia with elevated adrenergic activity and reduced vagal input.

Sinus node reentry tachycardia is another rare form of sinus tachycardia which is difficult to diagnose, but which responds very well to beta blockers, including i.v. compounds if indicated.

Paroxysmal Supraventricular Reentry-Tachycardia

Of all the forms of supraventricular tachycardias, the paroxysmal supraventricular reentry-tachycardias and the AV-nodal reentry- and AV-reentry tachycardias are the ones that respond best to beta blockers. These tachycardias require fast conduction through the AV node to be sustained, so a critical decrease of conduction velocity in the AV node by beta blockers will effectively terminate these tachycardias.

Acute intravenous application of beta blockers or adenosine is indicated. Especially in case of incessant AV-nodal reentry tachycardia, i.v. administration of beta blockers like esmolol is a highly successful option.

For long-term treatment, radiofrequency (RF) ablation has to be considered.

Ectopic Atrial Tachycardia

Some kinds of ectopic atrial tachycardias respond to beta blockers. Among them, unifocal ectopic atrial tachycardias tend to respond better to beta blockers than multifocal ones.

Table 3. Arrhythmias treatable with Beta Blockers. (Source: Prof. G. Stix, Medical University of Vienna)

- Inappropriate sinus tachycardia
- Paroxysmal supraventricular reentry-tachycardia
- Ectopic atrial tachycardia
- Atrial fibrillation, atrial flutter
- Ventricular tachyarrhythmias, electrical storm
- Long QT syndrome

Unifocal ectopic atrial tachycardias can be paroxysmal or persistent, and frequently they are driven adrenergically. Usually, this condition cannot be cured by means of beta blockers, but there is a good response in terms of decreasing the number of episodes and the HR, thereby alleviating symptoms. RF ablation is an option for long-term treatment.

Multifocal ectopic atrial tachycardias are much more difficult to treat. They often accompany progressive parenchymatous pulmonary diseases and usually do not respond well to beta blockers; sometimes a response to calcium antagonists is seen.

Case 5 – Atrial Flutter/Fibrillation

A 52-year-old male patient (178 cm, 89 kg) felt palpitations for half an hour the day before the present visit, during work in his office. He “could not move anymore”, felt thoracic pressure, a very fast HR, and fear. In general, he feels quite healthy, but in retrospect, he had two episodes of palpitations two years and nine months ago, respectively. He has no history of cardiac disease and smokes ten cigarettes per day.

His BP is 130/95 mmHg, the HR 72 bpm, his physical status is inconspicuous. The present ECG shows normal sinus rhythm.

Several days later, he incurs another episode of palpitations: the emergency ECG shows narrow complex tachycardia with a HR of about 150–160 bpm, BP 140/80 mmHg. The patient is treated with enoxaparin s.c. and esmolol i.v. (Fig. 3), the HR decreases and the patient is stabilized. By reducing the heart rate, atrial flutter is unmasked.

“While the official titration dosage scheme for esmolol recommends a bolus each time before the perfusor dose is increased, we have developed a different scheme which seems more practical”, said Stix. This titration dosage scheme is shown in Figure 3.

For definitive treatment of the arrhythmia the patient was referred to RF ablation. Several months later he came back with another episode of severe palpitations, this time caused by atrial fibrillation with a mean heart rate of 180 bpm.

Outcome and Commentary

The patient was again treated with s.c. heparin and i.v. esmolol according to the titration scheme shown in Figure 3. The heart rate decreased to approximately 90 bpm and converted to sinus rhythm several hours later.

In the ESC guidelines on tachycardic AF, i.v. beta blockers are primary therapeutic options, esmolol being one of three drugs mentioned (the other ones being metoprolol and propranolol) [17]. The guidelines state that “short-acting beta blockers (i.e. esmolol) are particularly useful, when hemodynamic instability is a concern” [17].

Control of ventricular rate in patients with rapid AF or flutter is especially important in patients with structural heart disease like CAD (coronary artery disease), hypertension, or hypertrophic cardiomyopathy. Furthermore, the rate control

achieved by beta blockers supports the efficiency of other drugs given, e.g. antiarrhythmic drugs [18].

Ventricular Tachyarrhythmias

Patients with CAD, especially those after MI, show frequent premature ventricular beats and have an increased risk of ventricular tachycardias (VT) and sudden cardiac death (SCD). If these patients are treated with class-I antiarrhythmics, their SCD risk increases further. Beta blockers reduce this risk of VT and SCD significantly, both as an acute intravenous treatment as well as a continuous p.o. treatment.

A special group of patients are those with an implantable cardioverter/defibrillator (ICD); especially in case of electrical storm, the intravenous beta blocker esmolol ($\pm$ class-III antiarrhythmics) appears to be absolutely lifesaving. And even on the basis of a class-III treatment, the addition of increasing doses of i.v. beta blockers proves to significantly augment the antiarrhythmic action of the class-III drug in the acute setting.

■ Clinical Applications of Short-Acting Beta Blockers in the ICU and Postoperative Setting

Univ.-Prof. Dr. Gottfried Heinz, Director ICU, Department of Cardiology, Medical University of Vienna

Case 6 – Critically Ill Patient with New Onset AF

A 57-year-old patient had CAD, three-vessel disease with a chronic total occlusion of the LAD. An attempt to open up the LAD via PCI (percutaneous coronary intervention) failed and the patient suffered a LAD perforation and a cardiac tamponade. Therefore, emergency pericardiocentesis and open heart surgery (aorto-coronary bypass graft) had to be done. After some difficulties going off bypass the patient had to be put on intra-aortic balloon pump (IABP) and extracorporeal membrane oxygenation (ECMO). Two days later, he developed tachycardic AF with a HR of approximately 180 bpm (maximum 250 bpm).

The first step in such a case is direct current (DC) cardioversion according to the ESC guidelines [17] – however, the primary success rate may be as low as 35%, and as few as 13.5% of patients may remain in sinus rhythm after 48 hours [19]. In this particular patient, four attempts at DC cardioversion were made, all unsuccessfully. A bolus dose of amiodarone, followed by continuous amiodarone infusion, followed by a fifth attempt at DC cardioversion was unsuccessful as well. The patient then received digitoxin 0.1 mg i.v. and esmolol at a rate of 200 mg/h. Several hours later, sinus rhythm was re-established.

Commentary

In unstable AF patients, the conjoint ACC/AHA/ESC-guidelines on AF (2006) as well as the current ESC guidelines (2010) recommend immediate DC cardioversion. In hemodynamically stable postoperative patients, however, the guidelines favor rate control [17, 20, 21]. In AF outpatients, rate control is not inferior to cardioversion in terms of mortality [22] and in terms of symptomatic improvement [23].

In the ACC/AHA/ESC and ESC guidelines for the management of patients with AF, there is a class-I indication for an AV-nodal blocking agent if a patient develops postoperative AF [17, 20]. Esmolol is given a class-I indication [17, 20]. The ACCP guidelines recommend beta blockers as first choice for patients who develop AF after cardiac surgery, calcium antagonists are second choice, antiarrhythmics are not recommended [24]. As already mentioned, the 2010 ESC guidelines also recommend esmolol for AF, especially in hemodynamically unstable patients [17].

“In our ICU we use esmolol without giving a bolus dose”, said Heinz. “This works well if you do not need to achieve rate control very quickly”, he added.

One should be aware that the onset of the esmolol effect on the blood pressure is somewhat slower than the effect on the HR [25]. A trial including 45 patients who suffered from AF or atrial flutter (some with new onset, some with longer duration) compared rate control with verapamil and esmolol and found that 50% of patients converted under esmolol, but only 12% under verapamil ($p < 0.03$) [26].

Case 7 – Incessant VT

A 68-year-old patient with CAD developed ischemic cardiomyopathy after a series of MIs. He came to the hospital with tachycardia and hypotension. The patient was in pre-shock, BP was 90/60 mmHg, and the ECG showed a wide-QRS tachycardia with a HR of 170 bpm. There were indications of AV dissociation, thus tachycardia was most likely of ventricular origin, and adenosine was given for differential diagnosis of wide-QRS-complex tachycardia in the emergency department.

Neither adenosine nor DC cardioversion proved successful in this patient. The patient was started on amiodarone and underwent further DC cardioversion attempts which were all ineffective. The patient was transferred first to a normal ward, then – since VT continued incessantly except for short bouts of sinus rhythm with ongoing amiodarone – was admitted to the ICU. His HR then was 190 bpm, BP 100/70 mmHg, left ventricular ejection fraction 25%.

Outcome and Commentary

The patient was started on esmolol 200 mg/h, increased to 300 mg/h; a higher dosage was not possible because of low systolic pressure. Amiodarone was still administered continuously, and on this combination sinus rhythm was achieved.

The ACC/AHA/ESC guidelines for the management of patients with ventricular arrhythmias give a class-I indication for revascularization and beta blockade for patients with incessant VT. When ineffective or no ischemic substrate is present, rapid saturation with intravenous amiodarone (up to 2 g/24h) is indicated (Class IIa). In particular, combination of beta blockers and amiodarone may be effective in resistant cases (IIb) [27]. Sedation or procainamide are further alternatives. If unsuccessful, VT ablation should be attempted (class IIa) [27].

Complementary Cases and Reviews

Electrical Storm

Electrical storm is defined as repeated bouts of VT, it often occurs after MI, and many patients already have ICDs. One trial of 49 patients with electrical storm showed that sympathetic blockade (stellate ganglion blockade, esmolol, or propranolol) is significantly superior to antiarrhythmic drugs in this indication (overall mortality 67% under antiarrhythmics vs. 5% under sympathetic blockade; $p < 0.0001$) [28].

Postoperative Patients and Autonomous Nervous System

The autonomous nervous system is an important trigger for arrhythmias with potentially fatal outcomes. That is especially true for the postoperative phase. A meta-analysis of 20 randomized trials with a total of 778 patients who underwent cardiac surgery showed that the use of esmolol (given before or at some time point during surgery) was associated with a significant decrease in episodes of myocardial ischemia (OR 0.42; $p = 0.007$ – although only one paper provides detailed information on how myocardial ischemia was monitored) and a decrease of arrhythmia episodes after cardiopulmonary bypass of borderline significance (OR 0.42; $p = 0.05$). There was also a significant increase in episodes of bradycardia [29]. A similar meta-analysis was done in patients after noncardiac surgery. Here, the authors found a significant decrease of myocardial ischemia in the esmolol group (OR 0.16; $p = 0.003$) and no difference in the incidence of MIs, arrhythmias, bradycardia, and hypotension [30].

For hypertension after cardiac surgery, which is often quite brief, esmolol can be used; it was compared to sodium nitroprusside in one small study. Esmolol was safe, effective, and fast and caused less unwanted decreases in diastolic blood pressure and oxygen saturation compared to sodium nitroprusside. However, esmolol caused more decreases in heart rate and cardiac index than sodium nitroprusside [31].



Summary

- Intravenous esmolol
 - has a very fast onset of action and is eliminated rapidly, independent of liver and kidney function,
 - allows flexible, targeted response through individualized dose titration,
 - allows good control of activity due to short duration of action,
 - allows rapid termination of adverse effects.
- Esmolol is helpful in treating life-threatening conditions such as
 - STEMI with hypertension and high HR
 - Hypertrophic obstructive cardiomyopathy
 - Blood pressure control in aortic dissection (class I indication to keep systolic BP at 100–120 mmHg, level of evidence C; class-I indication for using beta blockers and esmolol)
- Esmolol can be used in a wide range of supraventricular and ventricular tachycardias, like inappropriate sinus tachycardias, supraventricular reentry-tachycardias, unifocal ectopic atrial tachycardias, atrial flutter, or fibrillation and VT (especially in patients with CAD, after MI or with an ICD).
- AF in critically ill patients is often resistant to DC cardioversion, and rate control in stable postoperative patients with AF can be achieved with beta blockers. There is a class-I recommendation for esmolol in AF. There is also a higher rate of conversion to sinus rhythm with esmolol than with verapamil.
- In incessant VT, beta blockers are also recommended and esmolol can be used in combination with amiodarone.
- There are firm data on the safe and beneficial use of esmolol postoperatively, after cardiac as well as noncardiac surgery.
- Esmolol is also safe to be used in postoperative hypertension.

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Correspondence:

Dr. med. Norbert Hasenöhr

E-Mail: info@medizinjournalist.at