Atrial fibrillation in dialysis patients

Horst Zebe

Epidemiology and classification of atrial fibrillation

Atrial fibrillation is regarded as the most frequent supraventricular cardiac arrhythmia. Its incidence in the adult population is 0.5%. The probability of developing atrial fibrillation rises with increasing age. The Framingham study reports an incidence of 0.4% for persons under 30 years, whereas atrial fibrillation is observed in 2–4% of persons aged over 60 years.

Secondary forms resulting from cardiac and extra-cardiac diseases must be distinguished from the rarer primary (idiopathic) forms of atrial fibrillation without concomitant cardiac disease (lone atrial fibrillation) [1].

Without consideration of the aetiology and for reasons of practicability, atrial fibrillation is subdivided clinically into:

(i) Paroxysmal atrial fibrillation, which occurs episodically and converts spontaneously into sinus rhythm within 48 h at the most.
(ii) Persistent atrial fibrillation, which is sustained for longer than 48 h, but which continues to be convertible into sinus rhythm.
(iii) Permanent atrial fibrillation, which can no longer be converted into sinus rhythm with conventional treatment measures.

The classification is clinically relevant since paroxysmal atrial fibrillation can be converted by medication or by electrical means without prior anticoagulation, whereas an attempt at conservative treatment is no longer appropriate in patients with permanent atrial fibrillation. If clinical symptoms are present, invasive treatment should be considered. In persistent atrial fibrillation, effective anticoagulant treatment for at least 3 weeks is indicated before attempting conversion, in order to avoid thromboembolic complications.

Since atrial fibrillation tends to occur in cases with cardiac pathology, it is not surprising that intermittent atrial fibrillation occurs in dialysis patients (16%) significantly more often than in the general population [2].

In the Canadian Multicenter Study, pathological echocardiographical findings were seen in 75% of patients admitted for renal replacement therapy [3].

Atrial fibrillation is frequently observed during dialysis sessions. As a rule it stops spontaneously without therapeutic intervention 2–3 h after the dialysis session [2].

Clinical features

The clinical presentation of atrial fibrillation depends mainly on the rate of ventricular contraction. Whereas atrial fibrillation of normal frequency is mostly asymptomatic, ‘palpitations’ are typically reported at a high ventricular contraction rate. Apart from the high-ventricular contraction rate, the underlying cardiac condition is crucial for clinical presentation, i.e. angina pectoris, dyspnoea, pulmonary oedema. Vertigo or orthostatic dysregulation are frequent, and even syncope may occur.

Haemodynamics

Not only the atrial primer pump function (atrial ‘kick’), but also the powerful synchronous atrial contraction is lost when atrial fibrillation occurs. Consequently, development of atrial fibrillation causes relevant clinical and haemodynamic deterioration, especially in elderly people [4].

At present a major increase in volume of the right and left auricles is viewed by some authors [5] as a further potential factor predisposing to atrial fibrillation. This is particularly relevant for patients undergoing dialysis.

Haemodynamic impairment is in part explained by shortening of the diastole and impaired left ventricular filling. In part, however, it is also due to altered systolic contractility. The staircase phenomenon (Bowditch’s treppe) implies that cardiac contractility increases as heart rate goes up until a maximum is reached. This maximum differs from individual to individual, depending on the state of training and underlying cardiac disease. In patients with a high ventricular contraction rate the peak of Bowditch’s is reached at heart rates of no more than 80–90/min, so that any further increase of heart rate leads to a progressive decrease of cardiac contractility (‘tachycardia cardiomyopathy’).
Electrophysiology

The electrophysiology of atrial fibrillation is characterized by the presence of multiple small wavefronts and a very short excitable gap. During atrial fibrillation, the electrophysiological properties of the auricular myocardium change further: the atrial refractory phase shortens so that atrial fibrillation is perpetuated. Depending on the duration of pre-existing atrial fibrillation, this ‘electrophysiological remodelling’ can persist even after successful conversion into sinus rhythm. It is therefore ever more improbable that sustained conversion can be achieved, the longer atrial fibrillation had been present [6].

Prognosis

According to the results of many studies, it is questionable whether atrial fibrillation per se is associated with higher mortality. This is true even for patients who have suffered acute myocardial infarction with congestive heart failure or stroke. Nevertheless an in-hospital mortality from atrial fibrillation of about 8% has been reported [7].

Atrial fibrillation is of particular clinical importance mainly because of the increased rate of stroke: atrial fibrillation is an independent risk factor for stroke, increasing the risk by a factor of 3–5. At present it cannot be stated with certainty whether modern treatment of atrial fibrillation, including anticoagulation and normalization of the ventricular contraction frequency, alters the prognosis of atrial fibrillation. Nevertheless, the data of the Framingham study [8] indicate that whenever possible atrial fibrillation should be treated at an early stage to prevent development of permanent atrial fibrillation.

Conversion of atrial fibrillation into sinus rhythm as quickly as possible (or at least normalization of the ventricular contraction rate) is therefore the first goal of treatment, especially in patients with cardiac disease.

Criteria for therapy

Treatment of atrial fibrillation aims at controlling the ventricular contraction rate and improving compromised haemodynamics. Whenever possible, however, cardioversion should be tried in order to restore sinus rhythm.

(i) Non-drug treatment

In severely compromised patients with impaired consciousness, pharmacotherapy should not be tried. Transthoracic electroshock is the treatment of choice in such patients. A high-energy dose (400 J) should be applied immediately in synchronous discharge mode. Such a dramatic situation is rare in cases of atrial fibrillation. Pharmacotherapy is the primary form of treatment in most patients, especially those with paroxysmal atrial fibrillation.

(ii) Pharmacotherapy

It is beyond the scope of this editorial to discuss all antiarrhythmic agents in depth. We restrict the discussion to those agents that are likely to be used by the clinical nephrologist.

Antiarrhythmic class 1A and class 1C agents

On the basis of electrophysiological and clinical studies, class 1A and 1C drugs are recommended for rapid conversion of atrial fibrillation into sinus rhythm.

Class 1A

Quinidine

Quinidine is still given as the first-line medication for conversion of atrial fibrillation into sinus rhythm by 60–80% of doctors in the United States [9]. Quinidine is eliminated to some extent by renal excretion (15–40%) but mainly by the liver (60–85%). Therefore, in principle its use in dialysis patients is possible. It should be borne in mind, however, that the half-life of quinidine which is 9–19 h in normals [10,11] is substantially prolonged. It is not only this pharmacokinetic property that makes the administration of quinidine risky in dialysis patients, but also its substantial proarrhythmic effect. The latter is of considerable importance in patients with underlying cardiac disease or in patients with electrolyte disorders or in patients undergoing electrolyte shifts. The dreaded ‘torsade de points’ occurs with a frequency of 8% per patient year, a figure that is presumably even an underestimation [12,13].

Quinidine prophylaxis against paroxysmal atrial fibrillation may be harmful, since the mortality under quinidine therapy was reported to be 2.9%, significantly higher than in the control group (0.8%, P < 0.05) [14]. Theoretically the combination of quinidine and verapamil is rational. On the one hand the combination was shown to be effective in studies both on conversion of atrial fibrillation and on prophylaxis to prevent recurrence [15,16]. On the other hand, proarrhythmic effects could still be observed with combination treatment [17]. The SOPA study, currently in progress, is designed to test the effectiveness and safety of this combination in the treatment of paroxysmal atrial fibrillation [17].

Disopyramide

Disopyramide is effective to treat acute atrial fibrillation and to prevent recurrences. Unfortunately, it has a strong negative inotropic effect and increases peripheral vascular resistance. Its administration is no longer appropriate in patients with pre-existing cardiac damage. Moreover, clinically relevant stimulation of insulin secretion with subsequent hypoglycaemic shock.
was observed in dialysis patients when disopyramide was administered [18].

**Class 1C**

**Propafenone**

In recent years it has been pointed out repeatedly that propafenone can be used successfully not only in acute atrial fibrillation, but also as a prophylactic agent to prevent recurrences. Since propafenone is almost exclusively (99%) metabolized and excreted *via* the liver, its use in dialysis patients is not contraindicated in principle. Nevertheless, a disadvantage is the relatively long half-life: 12 h in patients with rapid metabolism and up to 32 h in patients with slow metabolism [19]. Such uncertainty with respect to the half-life is problematic, especially in dialysis patients.

**Other class 1C drugs**

The CAST (Cardiac Arrhythmia Suppression Trial) studies I and II investigated the antiarrhythmic activity of other class 1C drugs (flecainide, encainide, and moricizine). The results caused considerable concern since the number of sudden deaths in the study group tended to be higher compared to a control group treated with placebo (although the difference was not always significant). Today these drugs should be administered very cautiously, if at all, and this is particularly true for patients with myocardial disease [20].

**Class II**

Besides the classical antiarrhythmic agents, beta blockers have now regained a position of prominence in the treatment of tachycardic arrhythmias, especially in view of the CAST studies. Nevertheless, when using beta blockers one should be aware of the appreciable differences in the pharmacodynamic profile, and especially the major substance-specific differences with regard to plasma half-lives. We would like to point out, however, that half-lives do not correspond to the duration of action at the receptor level.

**Propranolol and metoprolol**

At present, more than 50 different beta blockers are on the market in the Federal Republic of Germany. Apart from propranolol, metoprolol is particularly suitable for use in dialysis patients. It is lipophilic and β1-selective, and of proven efficacy.

**Esmolol**

Esmolol is a highly cardioselective beta blocker that can be injected intravenously. It differs from all other beta blockers by its very short half-life of only 10 min. Esmolol proved to be very effective in treating atrial fibrillation with tachyarrhythmia. In a comparison with verapamil, the rate of conversion after administration of an esmolol bolus of 10 or 20 mg was significantly greater (four times greater) than after 5 or 10 mg verapamil i.v. In every case, the heart rate could be effectively reduced, giving rise to a corresponding improvement of haemodynamics. Moreover, a decrease in blood pressure was only rarely observed, and if present it was of short duration. The baseline blood pressure was restored within 4–10 min after administration [21,22].

Esmolol is metabolized by erythrocyte esterase, so that there are no pharmacokinetic restrictions to administer a single dose of this compound in patients with end-stage renal failure [8]. Nevertheless, its metabolites accumulate, and esmolol should not be administered more than once in a 4 h interval. Adaptation of the dose is not necessary [22].

If sinus rhythm is not restored, because of the short half-life of esmolol, it is possible to switch to other agents without delay. Overlapping administration of other beta blockers (e.g. metoprolol) has been shown to cause no problems.

**Class III**

**Sotalol**

In patients without renal disease, sotalol is used successfully both for treating acute atrial fibrillation and for preventing its recurrence. Since sotalol is mainly excreted *via* the kidneys, its use in dialysis patients cannot be recommended, especially in view of its critically relevant proarrhythmic effect, particularly the risk of torsade de pointes even at normal plasma levels. Torsade de pointes is a form of polymorphic ventricular arrhythmia. It is characterized by the fact that the electrical axis rotates around the isoelectric line. The heart rate is in the range of 150–300/min with varying RR intervals. Torsade de pointes occurs on a background of a prolonged QT interval, reflecting prolonged cardiac repolarization [23]. Therefore drugs that prolong the duration of the action potential predispose to this life-threatening arrhythmia. Extreme caution in the indication and use of sotalol in dialysis patients is warranted, especially in women who are more prone to torsade de pointes than men. Because it occurs most frequently during the first days of therapy, a daily dose of 40 mg should not be exceeded during the titration phase. The QT interval has to be monitored by daily ECG controls. The medication should be stopped immediately if excessive QT prolongation occurs [24].

**Amiodarone**

In patients with frequent paroxysmal atrial fibrillation, low doses of amiodarone can be recommended as prophylaxis against recurrence. However, the drug is associated with a high rate of side-effects (hypothyroidism, hyperthyroidism, photosensitization of the skin, lens opacity) [25,26].

**Class IV drugs**

**Verapamil**

For many physicians, verapamil is still the standard first-line treatment for absolute tachyarrhythmia, especially because of the rapid onset of the bradycardic
effet [27]. Verapamil treatment occasionally causes severe hypotension and excessive bradycardia, and this may occur up to 4–6 h after a single i.v. bolus [28].

Class V drugs

Digitalis

Digitalis is occasionally used, either alone or in combination, as first-line treatment in paroxysmal atrial fibrillation, but it is not effective. Only minor reduction in frequency of attacks can be achieved. In controlled double-blind studies, the rate of conversion did not differ from that of placebo [29].

All therapeutic measures for rapid restoration of the sinus rhythm may entail more risk than benefit. Nevertheless it appears justified to lower the ventricular contraction rate when episodes of tachyarrhythmia are triggered by dialysis sessions, especially in view of the pronounced spontaneous remission rate of episodes of atrial fibrillation during dialysis.

Other measures

AV node ablation with subsequent implantation of a pacemaker must be considered primarily when the sinus rhythm cannot be stabilized and an adequate ventricular contraction rate cannot be attained with beta blockers.

References