We report the case of a 67-yr-old man with intermittent Wolff–Parkinson–White (WPW) syndrome in whom neostigmine produced life-threatening tachyarrhythmias. The patient was scheduled for microsurgery for a laryngeal tumour. When he arrived in the operating room, the electrocardiogram showed normal sinus rhythm with a rate of 82 beat min\(^{-1}\) and a narrow QRS complex which remained normal throughout the operative period. On emergence from anaesthesia, the sinus rhythm (87 beat min\(^{-1}\)) changed to atrial fibrillation with a rate of 80–120 beat min\(^{-1}\) and a normal QRS complex. We did not treat the atrial fibrillation because the patient was haemodynamically stable. Neostigmine 1 mg without atropine was then administered to antagonize residual neuromuscular block produced by vecuronium. Two minutes later, the narrow QRS complexes changed to a wide QRS complex tachycardia with a rate of 110–180 beat min\(^{-1}\), which was diagnosed as rapid atrial fibrillation. As the patient was hypotensive, two synchronized DC cardioversions of 100 J and 200 J were given, which restored sinus rhythm. No electrophysiological studies of anticholinesterase drugs have been performed in patients with WPW syndrome. We discuss the use of these drugs in this condition.

Wolff–Parkinson–White (WPW) syndrome is characterized by pre-excitation in the ventricular myocardium from a cardiac impulse travelling along an accessory pathway that bypasses the atrioventricular (AV) node. It is manifest on the electrocardiogram (ECG) as a short PR interval, a wide QRS complex and a delta wave. One major problem associated with the anaesthetic management of patients with WPW syndrome is the risk of tachyarrhythmias as a result of the presence of the accessory pathway.\(^{1-4}\) Awareness of the electrophysiological effects of anaesthetic and antiarrhythmic drugs on normal AV and accessory pathway conduction is important to avoid tachyarrhythmias in these patients.\(^ {5,6}\) No electrophysiological studies of anticholinesterase drugs have been performed in patients with WPW syndrome.

Intermittent loss of the delta wave is observed in some patients with WPW syndrome; this is known as intermittent WPW syndrome. Klein and Gulamhusein demonstrated that patients with intermittent WPW syndrome have an accessory pathway with a longer refractory period and a benign clinical course.\(^ {7}\) We report a case of intermittent WPW syndrome in which administration of neostigmine during atrial fibrillation (AF) with a narrow QRS complex produced rapid AF with a wide QRS complex.

Case report

A 67-yr-old, 160-cm, 60-kg man with a laryngeal tumour was admitted to our hospital for laryngeal microsurgery. He had been diagnosed as having intermittent WPW syndrome 2 yr previously from a history of palpitations with ventricular pre-excitation on ECG. Disopyramide had been prescribed and he had been well since then. Preoperative 12-lead ECG showed normal sinus rhythm with a delta wave, at a rate...
Clinical examination, chest X-ray and routine laboratory investigations were normal. Disopyramide was continued until the time of operation. When he was connected to ECG lead II on arrival in the operating room, the ECG showed a normal sinus rhythm with a rate of 82 beat min⁻¹ and a narrow QRS complex. Arterial pressure was 130/82 mm Hg, ventilatory frequency 14 bpm and peripheral oxygen saturation in room air was 96%. General anaesthesia was induced with propofol 2 mg kg⁻¹, fentanyl 2 μg kg⁻¹ and vecuronium 0.1 mg kg⁻¹, and maintained with 1.5–2.5% sevoflurane and 60% nitrous oxide in oxygen. After an uneventful operation which lasted for 15 min, sevoflurane and nitrous oxide were discontinued. Three minutes later, the ECG showed conversion of the normal sinus rhythm with a rate of 87 beat min⁻¹ to AF with a rate of 80–120 beat min⁻¹. The width of the QRS complex remained normal (Fig. 1). Arterial pressure was 151/88 mm Hg.

As the patient was haemodynamically stable with normal AV conduction, we did not treat the AF. Residual neuromuscular block was antagonized with neostigmine 1 mg. Atropine was not used because of the increasing ventricular response through the normal AV pathway. Two minutes after administration of neostigmine, the ECG showed that the narrow QRS complex had converted to a wide QRS complex tachycardia with a rate of 110–180 beat min⁻¹ (Fig. 2). Systolic arterial pressure decreased to 76 mm Hg. At this time, arterial blood-gases and serum electrolyte concentrations were within normal limits. We diagnosed rapid AF with a wide ventricular complex because of the irregularity of the R-R interval (330–570 ms); a slow rising and slurring QRS complex; and the presence of a known accessory pathway. As the wide QRS complex tachycardia resulted in hypotension, a synchronized DC cardioversion of 100 J was given after administration of propofol 1 mg kg⁻¹. The first DC cardioversion was unsuccessful, but a second DC cardioversion of 200 J restored normal sinus rhythm. Disopyramide 60 mg was given to prevent recurrences. As the patient’s condition remained stable for 10 min after the rhythm returned to sinus, the trachea was extubated. The patient was transferred to the intensive care unit and observed overnight. He made an uneventful recovery and the ECG was normal the next day.

Discussion

Patients with WPW syndrome have an accessory AV pathway that bypasses the AV node. The existence of an accessory pathway without the physiological delay of the cardiac impulse in the AV node causes arrhythmias. The most frequent arrhythmias associated with WPW syndrome are paroxysmal supraventricular tachycardia caused by atrioventricular re-entry, and AF with a rapid ventricular response. The electrophysiological properties of the accessory pathway affect the prognosis if these tachyarrhythmias occur. Patients with intermittent WPW syndrome, defined as intermittent loss of the delta wave, have precarious conduction through the accessory pathway but a benign prognosis.
Anaesthetic management is aimed at avoiding these tachyarrhythmias in patients with WPW or intermittent WPW syndrome. Thus adequate suppression of the sympathetic response to surgical stimulation and appropriate choice of anaesthetic drugs that do not enhance accessory pathway conduction are essential. Although the electrophysiological effect of anaesthetic drugs on accessory pathway conduction has been investigated in patients with WPW syndrome, there are no studies of the use of anticholinesterase drugs in this condition. Little information is available on the use of neostigmine for pharmacological antagonism of non-depolarizing neuromuscular blocking agents in these patients. We have demonstrated the occurrence of a life-threatening tachyarrhythmia after administration of neostigmine in a patient with intermittent WPW syndrome. We believe that neostigmine was the causative agent for the following reasons: first, no agents other than neostigmine had been given when the tachyarrhythmia occurred during emergence from anaesthesia; and second, the tachyarrhythmia occurred 2 min after i.v. administration of neostigmine, which correlates with its peak pharmacological effect when given i.v.

With regard to the use of anticholinesterase drugs to antagonize non-depolarizing neuromuscular blocking agents in patients with WPW syndrome, Stoelting and Dierdorf suggested that these drugs did not increase the risk of arrhythmia. In contrast, in patients with intermittent WPW syndrome, several reports demonstrated that an increase in vagal tone or administration of an anticholinesterase produced accessory pathway conduction as a result of lengthening of the refractory period in the normal AV pathway. In our patient, administration of neostigmine converted narrow QRS complexes to wide ventricular complexes and accelerated the ventricular response during AF. The cause of a widening QRS complex can be explained by an inhibitory effect of neostigmine on the normal AV conduction pathway. If neostigmine affects only the normal AV conduction system, ventricular rate during AF should decrease after administration. As the ventricular rate during AF in patients with WPW syndrome is determined by the duration of the refractory period of the accessory pathway, as with digitalis and verapamil, neostigmine may enhance accessory pathway conduction. Therefore, there is a risk that administration of neostigmine during AF in patients with WPW syndrome may lead to rapid ventricular rates that may result in ventricular fibrillation. The use of neostigmine should be avoided during AF associated with WPW syndrome.

As atropine theoretically increases the risk of tachyarrhythmias because of a relative increase in sympathetic nervous system activity secondary to its vagolytic effect, it was not used for antagonism of vecuronium in this patient. However, a previous study demonstrated that atropine produced normal AV conduction with disappearance of the delta wave in these patients. Thus, the decision to use atropine in WPW syndrome must be made according to the individual patient.

Recurrence paroxysmal AF has been reported in approximately 32% of patients with WPW syndrome. In our patient, normal sinus rhythm converted suddenly to AF with normal AV conduction during emergence from anaesthesia. Sharma and colleagues demonstrated that the accessory pathway properties and atrial vulnerability predispose to AF in patients with WPW syndrome. Increased sympathetic activity can induce AF by affecting both factors. One possible explanation for the conversion to AF in this patient is an increase in sympathetic nervous system activity during emergence from anaesthesia. We did not treat AF to restore sinus rhythm because of the stable haemodynamic conditions and a normal width QRS complex. However, failure to treat AF may have allowed progression to wide QRS complex tachycardia after administration of neostigmine. Wells and colleagues demonstrated that the ventricular rate during AF is influenced by sympathetic nervous system activity in patients with WPW syndrome. When a paroxysm of AF occurs in patients with WPW syndrome, the first priority is to convert it to sinus rhythm.

This case illustrates the risk of life-threatening tachyarrhythmias produced by an anticholinesterase drug in patients with WPW syndrome. We suggest that antagonism of non-depolarizing neuromuscular blocking drugs should be avoided when a paroxysm of AF occurs in these patients. AF should be treated rapidly to restore sinus rhythm before administration of an anticholinesterase. In addition, if antagonism of a non-depolarizing neuromuscular blocking drug is indicated during normal sinus rhythm, an anticholinesterase drug should be used with caution as autonomic nervous system imbalance during anaesthesia in these patients may convert sinus rhythm to AF.

References