Intravenous magnesium for cardiac arrhythmias: jack of all trades

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Abstract. Intravenous magnesium has been used to prevent and treat many different types of cardiac arrhythmia. It has diverse electrophysiological actions on the conduction system of the heart; including prolonging sinus node recovery time, and reducing automaticity, atrioventricular nodal conduction, antegrade and retrograde conduction over an accessory pathway, and His-ventricular conduction. Intravenous magnesium can also homogenise transmural ventricular repolarisation. Because of its unique and diverse electrophysiological actions, intravenous magnesium has been reported to be useful in preventing atrial fibrillation and ventricular arrhythmias after cardiac and thoracic surgery; in reducing the ventricular response in acute onset atrial fibrillation, including for patients with Wolff-Parkinson-White syndrome; in the treatment of digoxin induced supraventricular and ventricular arrhythmias, multifocal atrial tachycardia, and polymorphic ventricular tachycardia or ventricular fibrillation from drug overdoses. Intravenous magnesium is, however, not useful in monomorphic ventricular tachycardia and shock-resistant ventricular fibrillation. Large randomised controlled studies are needed to confirm whether intravenous magnesium can improve patient centre outcomes in different cardiac arrhythmias.

Key words: antiarrhythmics, atrial fibrillation, rhythm control

Magnesium has many significant physiological and pharmacological effects on different organ systems. Intravenous magnesium has a high therapeutic to toxic ratio and minimal negative inotropic effect [1], and as such, it has been used in the prevention and treatment of many different types of cardiac arrhythmia. Cardiac arrhythmia is, however, a common presentation of a diverse spectrum of diseases. Even within the same class of arrhythmia, such as atrial fibrillation or ventricular tachycardia, it can still be caused by different arrhythmogenic mechanisms from different underlying diseases. It is, therefore, unrealistic to expect intravenous magnesium to be useful in preventing or treating all types of cardiac arrhythmias. Furthermore, animal studies have shown that both the pro-arrhythmic effects of hypomagnesaemia and the anti-arrhythmic effects of magnesium depend on the underlying causes of the arrhythmia and the condition of the heart [2-4]. This review aims to briefly summarise the electrophysiological effects of intravenous magnesium and its effects on different types of cardiac arrhythmia. While intravenous magnesium chloride may have different actions from magnesium sulphate [5], magnesium sulphate is the most widely available intravenous preparation and almost exclusively used in many of the studies cited in this review.

Electrophysiological effects of intravenous magnesium

Intravenous magnesium has been shown to have a number of electrophysiological actions on the conduction system of the heart. The mechanism of its actions may include calcium antagonism at the L- and T-type calcium channels [6], regulation of energy transfer, and in supraphysiological doses, magnesium decreases the outward potassium current density resulting in membrane stabilisation and it also acts as an indirect antagonist of digoxin at the sarcolemma Na(+)-K(+)-ATPase pump [7, 8].
In the supraventricular conduction pathway, magnesium can reduce automaticity [9], increase sinus node recovery time (at high doses) [10], and reduce atrioventricular nodal conduction without affecting atrial-atrial conduction [11]. Magnesium can also block the antegrade and retrograde conduction over an accessory pathway [12-14], and has a dominant effect on the slow atrioventricular nodal (AVN) pathway in patients with dual AVN physiology [15].

In the ventricular conduction pathway, magnesium suppresses prematurely triggered activity, prolongs the His-ventricular conduction [16], and homogenises transmural ventricular repolarisation [4, 17] without affecting autonomic nervous activity [18]. Homogenisation of ventricular repolarisation is believed to explain the anti-arrhythmic effect of magnesium in prolonged QT syndrome [17]. Magnesium appears to have no effect on excitable gap arrhythmias associated with a fixed anatomic substrate (e.g. monomorphic ventricular tachycardia) [4, 19].

Table 1. Possible indications for intravenous magnesium as an anti-arrhythmic agent.

<table>
<thead>
<tr>
<th>Rhythm and clinical condition</th>
<th>Benefits</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Atrial fibrillation (AF)</strong></td>
<td></td>
<td></td>
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<tr>
<td>- Prevention in cardiac and thoracic surgery</td>
<td>Reduces the incidence of AF</td>
<td>[20, 21]</td>
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<tr>
<td>- Treatment of chronic AF</td>
<td>Reduces rapid ventricular response</td>
<td>[8]</td>
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<tr>
<td>- Digoxin toxicity with Wolff-Parkinson-White syndrome</td>
<td>Reduces rapid ventricular response</td>
<td>[14, 23]</td>
</tr>
<tr>
<td>- Treatment of acute onset AF</td>
<td>Reduces rapid ventricular response</td>
<td>[22, 24, 25]</td>
</tr>
<tr>
<td>- Improved conversion to sinus rhythm and reduces the incidence of torsades de pointes polymorphic ventricular tachycardia when used with ibutilide</td>
<td></td>
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</tr>
<tr>
<td><strong>Multifocal atrial tachycardia</strong></td>
<td>Reduces rapid ventricular response and converts some patients to sinus rhythm</td>
<td>[26]</td>
</tr>
<tr>
<td><strong>Paroxysmal supraventricular tachycardia</strong></td>
<td>Converts to sinus rhythm (less effective than adenosine but may help if no response to adenosine)</td>
<td>[12, 27, 28]</td>
</tr>
<tr>
<td><strong>Ventricular premature complexes</strong></td>
<td></td>
<td></td>
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<tr>
<td>- Prevention in cardiac surgery</td>
<td>Reduces the incidence</td>
<td>[29, 30]</td>
</tr>
<tr>
<td>- Treatment in heart failure patients with hypomagnesaemia</td>
<td>Reduces the incidence</td>
<td>[31]</td>
</tr>
<tr>
<td><strong>Ventricular tachycardia (VT)</strong></td>
<td></td>
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<tr>
<td>- Digoxin toxicity</td>
<td>Converts to stable junctional rhythm</td>
<td>[32]</td>
</tr>
<tr>
<td>- Class Ic anti-arrhythmic toxicity (e.g. pilsicainide)</td>
<td>Converts to sinus rhythm</td>
<td>[33]</td>
</tr>
<tr>
<td><strong>Polymorphic VT (torsades de pointes)</strong></td>
<td></td>
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<tr>
<td>- Prolonged QT (congenital and acquired) (e.g. haloperidol, amiodarone)</td>
<td>Converts to sinus rhythm</td>
<td>[34-36]</td>
</tr>
<tr>
<td><strong>Ventricular fibrillation (VF)</strong></td>
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<td></td>
</tr>
<tr>
<td>Amitriptyline poisoning</td>
<td>Converts to sinus rhythm</td>
<td>[37]</td>
</tr>
<tr>
<td><strong>Intravenous magnesium was reported to be not useful in the following conditions</strong></td>
<td></td>
<td></td>
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<tr>
<td>Community cardiac arrest with shock-resistant VF</td>
<td></td>
<td>[38, 39]</td>
</tr>
<tr>
<td>Monomorphic VT</td>
<td></td>
<td>[4, 19]</td>
</tr>
</tbody>
</table>

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Effects of intravenous magnesium on different types of cardiac arrhythmia

Due to its unique but diverse electrophysiological effects, intravenous magnesium has been reported to be effective in the prevention and treatment of a variety of cardiac arrhythmias (table 1).

Intravenous magnesium is useful in preventing atrial fibrillation and ventricular arrhythmias after cardiac and thoracic surgery [20, 21], reducing the ventricular response in acute onset atrial fibrillation [22] (including in patients with Wolff-Parkinson-White syndrome [23]), improving rhythm control with ibutilide [24, 25], treatment of digoxin induced supraventricular and ventricular arrhythmias, multifocal atrial tachycardia [26], polymorphic ventricular tachycardia with a prolonged QT interval, and ventricular fibrillation from amitriptyline overdoses. Intravenous magnesium can also be considered as a second line drug in the treatment of supraventricular tachycardia when adenosine is not effective [27]. Intravenous magnesium is, however, not useful in monomorphic ventricular tachycardia and shock-resistant ventricular fibrillation.

Apart from being effective in controlling many cardiac arrhythmias, intravenous magnesium also has less significant detrimental haemodynamic effects on the cardiovascular system compared to other anti-arrhythmic agents, including amiodarone or calcium channel blockers; although minor symptoms of flushing, tingling, and dizziness are common after intravenous magnesium [22]. Evidence that supports the use of intravenous magnesium in many different types of cardiac arrhythmias is, however, based on case reports, animal studies, and randomised controlled studies that evaluated physiological endpoints only [20, 22]. None of the published randomised controlled studies on intravenous magnesium have demonstrated a significant reduction in mortality.

Conclusion

Intravenous magnesium appears to be useful in the prevention and treatment of a variety of cardiac arrhythmias. It is, however, not useful in monomorphic ventricular tachycardia and shock-resistant ventricular fibrillation. We must also be aware that the successful prevention or treatment of cardiac arrhythmias is only, at best, a surrogate end-point of effectiveness. Large randomised controlled studies are needed to confirm whether intravenous magnesium can improve patient centre outcomes in different cardiac arrhythmias.

References


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