THERAPY AND PREVENTION
ARRHYTHMIA

Treatment of torsade de pointes with magnesium sulfate

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ABSTRACT Twelve consecutive patients who developed torsade de pointes (polymorphous ventricular tachycardia with marked QT prolongation, TdP) over a 4 year period were treated with intravenous injections of magnesium sulfate. In nine of the patients a single bolus of 2 g completely abolished the TdP within 1 to 5 min, and in three others complete abolition of the TdP was achieved after a second bolus was given 5 to 15 min later. Nine of the patients also received continuous infusion of MgSO4 (3 to 20 mg/min) for 7 to 48 hr until the QT interval was below 0.50 sec. In nine of the 12 patients the TdP was induced by antiarrhythmic agents. The QT interval preceding TdP ranged from 0.54 to 0.72 sec. After the MgSO4 bolus, which prevented the recurrence of TdP, no significant changes were observed in the QT interval. There were no side effects of this treatment. In eight of the 12 patients potassium levels before the TdP were below 3.5 meq/liter; magnesium levels were available in eight patients before TdP, and were normal in all. Five additional patients with polymorphous ventricular tachycardia but normal QT intervals (non-TdP patients) received two to three boluses of MgSO4. This treatment was ineffective in all, but they responded to conventional antiarrhythmic therapy. Thus, MgSO4 is a very effective and safe treatment for TdP, and its application is rapid and simple. Its use is therefore recommended as the first line of therapy for TdP.


TORSADE DE POINTES (TdP) is a distinct form of ventricular tachycardia occurring in patients with marked QT prolongation. The conventional treatment is aimed at shortening the QT interval by accelerating the heart rate with isoproterenol infusion or by cardiac pacing.

Three years ago we first reported our experience with magnesium sulfate as a treatment for TdP in three patients.¹ Now with extended experience the role of magnesium sulfate seems to be well established in the treatment of patients with TdP.

Patients and methods

Twelve consecutive patients who developed TdP with QT prolongation between March 1982 and December 1986 were treated with magnesium sulfate. There were 10 women and two men. Their ages ranged from 46 to 87 years (mean, 69 years). Six patients had chronic ischemic heart disease, two had valvular rheumatic heart disease, two had atrial arrhythmia, and two had no signs of organic heart disease. Of the 12 patients nine were on antiarrhythmic therapy: six received type 1 antiarrhythmic drug only (quinidine, three patients; procainamide, three patients), one received amiodarone alone, and two received a combination of quinidine or procainamide with amiodarone. Of the remaining three patients, one tried to commit suicide with imipramine and thioridazine, one received furosemide alone, and one had psychogenic polydipsia. Eight of the 12 patients were on diuretic therapy.

Five additional patients with chronic ischemic heart disease (two had acute myocardial infarction and three chronic congestive heart failure) developed polymorphous ventricular tachycardia with normal QT interval and received magnesium sulfate therapy, and their response was compared with that in the TdP group.

TdP was diagnosed as a recurrent polymorphous ventricular tachycardia in which the peaks of the QRS complexes twisted around the isoelectric line in a set up of marked QT interval prolongation (figure 1). The QT intervals were measured in the limb leads of the electrocardiogram when possible, from the sinus beat immediately preceding the TdP. The corrected QT interval (QTc) was calculated according to Bazett's formula.

Solutions of 25% or 50% MgSO4 were used. The magnesium was given as an intravenous bolus of 2 g within 1 to 2 min and in most patients this was followed by a continuous infusion (3 to 20 mg/min).

Results

Magnesium sulfate was given intravenously to all 12 patients. Four of the patients received other modes of therapy before the administration of magnesium sulfate. Two of them had received lidocaine because the ventricular tachycardia was not diagnosed initially as TdP, and the drug was ineffective in both.

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patients were treated with intravenous isoproterenol (1 to 5 \( \mu \)g/min), which was effective in only one, and because of intolerable palpitations had to be stopped. Cardiac pacing was tried in one patient and was not effective. In the other eight patients magnesium sulfate was the only treatment given. A bolus of 2 g of MgSO\(_4\) was given intravenously to all 12 patients (table 1). In nine of the patients the TdP was completely abolished after this initial treatment. Three other patients who did not respond completely to the first MgSO\(_4\) bolus received a second bolus within 5 to 15 min. In nine patients MgSO\(_4\) infusion was given at rates of 3 to 20 mg/min. In three of these patients the infusion was given after a second bolus of MgSO\(_4\) was required, while in the other six, it was given preventively. In two patients the TdP recurred 1 to 6 hr after the intravenous infusion of magnesium was begun; therefore another bolus was given that was effective in both. Intravenous infusion of MgSO\(_4\) was continued in nine of the patients until the QT interval was shortened below 0.50 sec (7 to 48 hr).

Table 2 details the QT, QTc, potassium, and magnesium levels in all patients before and after administration of magnesium. The QT intervals ranged from 0.54 to 0.72 sec (mean, 0.61 sec) and the QTc intervals ranged from 0.53 to 0.80 sec (mean, 0.64 sec). No significant changes in the QT or QTc intervals were observed in most patients immediately after magnesium therapy (table 2, figure 2). Serum potassium levels before the development of TdP were below 3.5 meq/liter in eight of 12 patients. These patients received oral and intravenous potassium supplements after magnesium therapy was given. Magnesium levels were within normal limits (1.6 to 2.5 meq/liter) at the time of the arrhythmia in all eight patients in whom magnesium levels were available.

### TABLE 1

**Magnesium therapy for TdP**

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>MgSO(_4) administration</th>
<th>Infusion (mg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bolus 1 (g)</td>
<td>Bolus 2 (g)</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>4</td>
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<tr>
<td>3</td>
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<td>11</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>12</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

![Figure 1](image-url)

**FIGURE 1.** A rhythm strip of TdP induced by quinidine. Note the marked QT prolongation before the ventricular arrhythmia, the twisting of the QRS axis, and the spontaneous termination.
Magnesium sulfate in patients with polymorphous ventricular tachycardia and normal QT interval. Five other patients suffering from ischemic heart disease developed recurrent polymorphous ventricular tachycardia with normal QT intervals (figure 3). Four patients had recurrent nonsustained polymorphous ventricular tachycardia and one had sustained polymorphous ventricular tachycardia (more than 30 sec) requiring several direct-current shocks. Three of the patients were on antiarrhythmic therapy; one received ajmaline, one disopyramide, and one lidocaine. The QT intervals ranged from 0.38 to 0.49 sec (mean, 0.46). The potas-

### TABLE 2
QT, QTc, potassium, and magnesium levels before and after magnesium therapy of TdP

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Before MgSO₄ therapy</th>
<th>After MgSO₄ therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>QT (sec)</td>
<td>QTc (sec)</td>
</tr>
<tr>
<td>1</td>
<td>0.60</td>
<td>0.69</td>
</tr>
<tr>
<td>2</td>
<td>0.68</td>
<td>0.80</td>
</tr>
<tr>
<td>3</td>
<td>0.72</td>
<td>0.63</td>
</tr>
<tr>
<td>4</td>
<td>0.56</td>
<td>0.62</td>
</tr>
<tr>
<td>5</td>
<td>0.60</td>
<td>0.55</td>
</tr>
<tr>
<td>6</td>
<td>0.54</td>
<td>0.56</td>
</tr>
<tr>
<td>7</td>
<td>0.64</td>
<td>0.53</td>
</tr>
<tr>
<td>8</td>
<td>0.60</td>
<td>0.73</td>
</tr>
<tr>
<td>9</td>
<td>0.60</td>
<td>0.69</td>
</tr>
<tr>
<td>10</td>
<td>0.60</td>
<td>0.63</td>
</tr>
<tr>
<td>11</td>
<td>0.56</td>
<td>0.57</td>
</tr>
<tr>
<td>12</td>
<td>0.60</td>
<td>0.66</td>
</tr>
<tr>
<td>Mean</td>
<td>0.61</td>
<td>0.64</td>
</tr>
</tbody>
</table>

**FIGURE 2.** Rhythm strip 5 min after 2 g of intravenous magnesium sulfate, which suppressed the TdP. Note the marked QT prolongation.
sium levels at the time of the ventricular tachycardia ranged from 3.1 to 4.3 meq/liter (mean, 3.7). Serum magnesium levels before the ventricular tachycardia were available in two of the patients, and were normal in both. MgSO₄ was given as a 2 g bolus to all patients and was ineffective in all. A second bolus was therefore given and two of the patients received a third bolus that was also ineffective; another antiarrhythmic drug was therefore administered. Three patients responded to intravenous lidocaine and two to procainamide.

Discussion

Since the first description of TdP by Dessertenne,² controversy has existed as to whether polymorphous ventricular tachyarrhythmias associated with a normal QT interval should also be called TdP. Our group³ and others⁴-⁷ have expressed their opinion that the term Torsade de pointes should be reserved only for a ventricular tachycardia with a polymorphous appearance that is associated with marked prolongation of the QT interval, since the presence of the QT prolongation mandates completely different therapy.

The treatment of TdP was the subject of many reports. The aim of the treatment has been to shorten the delayed repolarization by increasing the heart rate with the infusion of isoproterenol,⁸ atrial or ventricular pacing,⁹,¹⁰ or atropine. Isoproterenol is an effective mode for accelerating the heart rate and thereby shortening the QT interval. However, this drug is contraindicated in patients with acute myocardial infarction, angina pectoris, or hypertension. In some patients it may cause intolerable side effects, such as severe palpitations, and in others it may be ineffective.¹¹,¹² Furthermore, use of isoproterenol may be fatal if it is given to patients with a ventricular tachycardia that is not TdP (without QT prolongation). Cardiac pacing is an effective and safe method for treating TdP,⁸,⁹ but its application requires certain skills and equipment and therefore it can not be applied in an ambulance or in every emergency room, and even if skilled personnel and equipment are available there is a considerable delay between the time of diagnosis of TdP and the initiation of cardiac pacing.

The role of magnesium in ventricular tachyarrhythmias has been the subject of several clinical investigations.¹¹-¹³ Magnesium sulfate was used empirically for many years as a treatment for atrial and ventricular arrhythmias in patients with normal or low magnesium levels,¹⁴-¹⁷ in patients with digitalis toxicity, and in alcoholics.
In 1984 we reported the first three patients with TdP who were successfully treated with MgSO4. In the present report we describe our extended experience in 12 patients with TdP, all of whom responded to intravenous magnesium sulfate. In eight of the patients magnesium was the only therapy given, while in four others initial therapy failed and therefore magnesium sulfate was given. The treatment with magnesium sulfate consisted of an initial bolus of 2 g, given within 1 to 2 min. In nine of the 12 patients this was associated with complete eradication of TdP and most ventricular premature beats. In three patients, only a partial response was observed and therefore a second bolus was given 5 to 15 min later. Infusion of magnesium sulfate (3 to 20 mg/min) was given to nine of the patients after the initial bolus. In three of them it was given because of partial response to the initial bolus, while in the others it was given preventively. It seems to us that if a complete response is observed after the first bolus of 2 g no further therapy is required, while in patients with no or a partial response a second bolus is indicated together with continuous infusion of 3 to 10 mg/min. In two of our patients TdP recurred after few hours of continuous infusion of magnesium and another bolus abolished it. In the nine patients in whom a continuous infusion of magnesium was given, the indication for cessation of infusion was shortening of QT below 0.50 sec, which occurred within 7 to 48 hr. Except for flushing sensations during the bolus injection no side effects were noted.

As in many previously reported cases of TdP, eight of our 12 patients suffered from hypokalemia (K level below 3.5 meq/liter). Therefore, in addition to the administration of MgSO4, these patients received intravenous and oral potassium supplements. Serum magnesium levels were available in eight of the 12 patients and in all it was within normal range. Thus, the TdP could not be attributed to serum hypomagnesemia. Intracellular magnesium levels were not available in our study.

The effect of magnesium sulfate was assessed in five additional patients with polymorphous ventricular tachycardia and a normal QT interval. Two to three boluses of magnesium sulfate were given (4 to 6 g) to these patients without any response. Subsequent conventional therapy for ventricular tachycardia with lidocaine or procainamide was given with satisfactory results. Thus, MgSO4 is not effective in the treatment of patients with polymorphous ventricular tachycardia without QT prolongation.

The mechanism of action of MgSO4 is not understood. Unlike isoproterenol infusion and cardiac pacing, MgSO4 prevented the recurrence of TdP without shortening the QT interval. The fact that the QT interval remained unchanged despite the suppression of the ventricular arrhythmia suggests that the salutary effect of magnesium is not related to shortening of repolarization. Since magnesium is a cofactor in the sodium-potassium ATPase activity, it may have prevented the TdP by facilitating influx of potassium into the cells, thereby stabilizing membrane potential, correcting the dispersed repolarization process without shortening it.

It is well known that various drugs that cause QT interval prolongation are capable of inducing TdP. It has been suggested that asynchronous recovery of excitability is a predisposing factor for reentrant ventricular arrhythmias. Dispersion of refractoriness has been demonstrated in a number of conditions, such as left stellate ganglion stimulations, myocardial ischemia, hypothermia, and also after premature stimulation or pacing at a long cycle length. The recently described observation that the last supraventricular beat (before the initiation of TdP) is almost always preceded by a long cycle length (either postextrastysolic pause or bradycardia) favors this hypothesis. On the other hand, the inability to induce TdP in the laboratory by premature electrical stimulation is a serious argument against a reentrant mechanism for TdP.

Dessertenne, in his original description of TdP, suggested that this arrhythmia may be a result of the activity of two automatic foci. Naumann et al., who succeeded in building a model of Tdp-like arrhythmia in isolated pig hearts by simultaneous pacing from both ventricles, also suggested that the tachycardia is a result of the interference of two separate foci acting at two different rates. On the other hand, Bhargava et al. presented evidence against the multiple focal cause for TdP, based on their results of spectral-analysis data of the electrocardiograms of three patients with TdP; they suggested that the origin of the tachycardia is in a single ectopic center, migrating around the ventricles in a periodic way. Triggered activity and afterdepolarization may play a role in the initiation and/or perpetuation of TdP. Jackman et al. succeeded in inducing TdP in dogs with cesium chloride, which in vitro prolongs repolarization and induces bradycardia-dependent early afterdepolarization and triggered activity. The ionic mechanism responsible for afterdepolarization is not clear. Intracellular calcium may play a role as an oscillatory modulator of inward currents that are not specific and are probably responsible for the afterdepolarization.

Kass et al. suggested that the phasic movement of calcium in and out the sarcoplasmic reticulum as a
result of intracellular gain of sodium and loss of potassium might cause transient inward currents and transient depolarization and that high magnesium levels block, and low magnesium levels potentiate, the phasic movement. It is possible also that magnesium deficiency may lead to influx of calcium and may be the primary cause of intracellular potassium loss. 28, 29

Because of the properties of magnesium as a modulator of calcium ions it has been called “nature’s physiologic calcium blocker.” 30 In the light of the above discussion it seems to us that the effectiveness of intravenous magnesium therapy in patients with TdP might be related to suppression of oscillatory currents responsible for afterdepolarization.

From our experience with the above-described 12 patients with TdP who were effectively treated with MgSO4, it is our recommendation that this treatment should be used as the first line of therapy for patients suffering from this disorder. This treatment is not only very effective, but is also safe and easily applied, and the response is very rapid.

References

Treatment of torsade de pointes with magnesium sulfate.
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