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High-dose intravenous magnesium sulfate in the management of life-threatening status asthmaticus

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Abstract. In severe status asthmaticus basic medical treatment often fails to improve the patient's condition. Mechanical ventilation in this situation is associated with a high incidence of serious complications. After the bronchodilating effect of moderate-dose magnesium sulfate in asthmatic patients had been demonstrated in previous studies we treated five mechanically ventilated patients with refractory status asthmaticus successfully with high dosages of $MgSO_4$ IV (10–20 g within 1 h depending on the bronchodilating effect). $MgSO_4$ resulted in a significant decrease of peak airway pressure (43.0±6.8 to 32.0±8.0 cmH_2O) and inspiratory flow resistance (22.7±7.0 to 11.9±6.0 $cmH_2O \cdot l^{-1} \cdot s^{-1}$) within 1 h. The resulting serum magnesium levels after one hour were up to threefold of the normal serum levels. Although a maintainance dose of 0.4 g/h had been administered continuously during the following 24 h serum magnesium decreased towards normal values within this time. The only relevant side-effect was a mild to moderate arterial hypotension in two of the five patients during the high dose administration period of $MgSO_4$ which responded readily to dopamine treatment.

Key words: Status asthmaticus – Artificial respiration – Magnesium sulfate – Bronchodilator agents

Life-threatening status asthmaticus is defined as a prolonged asthmatic attack unresponsive to conventional conservative treatment including therapy with β2-agonists, methylxanthines, corticosteroids and oxygen. Patients with status asthmaticus often need tracheal intubation and mechanical ventilation. However, mechanical ventilation in status asthmaticus is associated with a high incidence of complications including barotrauma, cardiovascular impairment, and a mortality rate of 22% [1]. Sedatives and muscle relaxants are usually required to facilitate mechanical ventilation, but they have no intrinsic bronchodilating properties; on the contrary some have bronchoconstrictor effects. When conventional measures fail there are only few remaining "unconventional" alternatives such as halothane anesthesia, ketamine infusion, controlled hypoventilation or even extracorporeal membrane oxygenation all of which are neither always effective nor without marked side-effects. The bronchodilating effect of moderate-dose magnesium sulfate ($MgSO_4$) in spontaneously breathing asthmatic patients and in two mechanically ventilated asthmatic patients has been demonstrated previously [2, 3, 4]. We decided to apply even larger dosages of $MgSO_4$ (up to 20 g within 1 h depending on the bronchodilating effect) in patients with refractory status asthmaticus as an adjunctive therapy to conventional measures. The results in five patients whose bronchoconstriction was treated successfully with this high-dose intravenous $MgSO_4$ regimen after maximal conservative treatment had failed are described.

Methods

All patients had the following routine intensive care monitoring: continous ECG monitoring, continuous monitoring of hemoglobin oxygen saturation by pulse oximetry, and online measurement of arterial blood pressure via an indwelling arterial cannula (all Hewlett Packard Component Monitoring System, Palo Alto, CA.). All patients were mechanically ventilated in a volume constant mode with constant inspiratory flow and an inspiratory pressure plateau (0.5–1 s). Tidal volume and minute ventilation as well as inspiratory flow rate were kept constant during the period of observation. The maximal flow resistance (R_{max}) of the total respiratory system was calculated with the following equation: R_{max} = (peak airway pressure – inspiratory plateau airway pressure)/inspiratory flow. Serum magnesium concentrations were measured by atomic absorption spectrometry (SL7, Zeiss, Kochel, Germany). The basic bronchodilating therapy as described individually in the text was given continuously during the whole observation period.

Case reports

Patient 1

A 25-year-old, 70-kg male with a 10-year-history of allergic asthma was scheduled for elective inguinal herniorrhaphy. He was asymptomatic preoperatively and receiving no medication. After induction of anesthesia with 0.25 mg fentanyl and 100 mg methohexital a flush was observed

on the chest, ventilation with the face mask was nearly impossible, and the patient became hypoxic. Wheezing was heard on auscultation and severe bronchospasm (perhaps by an anaphylactoid reaction) was diagnosed. The patient was paralyzed with pancuronium bromide, he was intubated, mechanically ventilated and inhalation anaesthesia was started with halothane at an inspired concentration of up to 2%. Bronchospasm with high airway pressures persisted despite administration of theophylline (0.48 g IV), methylprednisolone (250 mg). Adrenaline or other IV sympathomimetics were not given because of halothane anaesthesia. A bilateral tension pneumothorax with massive mediastinal and skin emphysema developed within 15 min. Surgery was cancelled, and after bilateral chest tubes were inserted the patient was transferred to our ICU. Here administration of theopylline via infusion pump (0.96 g/24 h; the initial theophylline serum level was 12.4 μg/ml) and muscle relaxation with vecuronium (16 mg) was continued. Salbutamol (5 mg in 5 ml saline in 10 min) was administered via a nebulizer. Due to poor response to this bronchodilator therapy treatment with a $MgSO_4$ infusion was initiated. Based on our experience with $MgSO_4$ for deliberate hypotension we started with an infusion rate of 10 g/h for 1 h. After less than 30 min of infusion the peak airway pressure (Paw) had decreased from an initial value of 45 cmH_2O to 32 cmH_2O. Blood pressure decreased from 140/80 mmHg to 100/55 mmHg, heart rate decreased from 110 to 100/min. After reducing the infusion rate to 0.4 g/h the blood pressure increased to 130/80 mmHg) and heart rate increased again to 110/min within 30 min while Paw continued to decrease. The patient was extubated 12 h later.

Patient 2

A 47-year-old, 75-kg male with a 6-year-history of intrinsic asthma was admitted to the emergency unit suffering from pneumonia leading to severe bronchospasm and rapidly worsening respiratory insufficiency. Bronchodilator therapy with inhaled salbutamol, theophylline, methylprednisolone (250 mg) and O_2 via face mask in the emergency room was unsuccessful (O_2 saturation by pulse oximetry 80–83%). The patient was then transferred to our ICU for mechanical ventilation. He was unconscious and tachypneic (35 breaths/min) with tachycardia (128/min) and hypertension (200/100 mmHg). After tracheal intubation the patient was ventilated using a volume constant mode. The initial arterial blood gases at $FIO_2 = 1.0$ were PaO_2 160 mmHg, $PaCO_2$ 87 mmHg and pH 7.00. Theophylline (0.96 g/24 h) and salbutamol (25 μg/min) were administered via an infusion pump. Despite heavy sedation with midazolam and muscle relaxation with pancuronium bromide and theophylline serum level of 21.3 μg/ml high airway pressure (>50 cmH_2O) persisted. Halothane anesthesia was begun with initial success, but four hours later severe bronchospasm refractory to halothane recurred during an attempt to obtain bronchial secretions and we began treatment with $MgSO_4$ with an initial infusion rate of 10 g/h for 1 h. At this time salbutamol had been administered for more than 13 h. At 15 min after starting the $MgSO_4$ infusion the bronchospasm had resolved completely on auscultation and the Paw had decreased from 35 to 25 cmH_2O (inspiratory flow 0.27 l/s; tidal volume 540 ml). Blood pressure and heart rate also decreased (see Table 1). The serum concentrations of magnesium are given in Table 2. After discontinuing the $MgSO_4$ infusion the blood pressure increased slightly but Paw remained low and mechanical ventilation was now unproblematic. However, further mechanical ventilation and later spontaneous breathing on CPAP were necessary because of ongoing pneumonia. The patient was extubated 6 days later and was discharged from the ICU on day 8.

Following these promising results with a therapy which had been instituted as a treatment of last resort in patients with status asthmaticus who were being mechanically ventilated a formal study protocol was developed and accepted by the Ethical Committee of our Medical Faculty. The $MgSO_4$ infusion was to be started at a rate of 10 g/h for 10 min and thereafter decreased or increased depending on the bronchodilating effect. The infusion was limited to a maximum total dose of 20 g of $MgSO_4$ in the first hour. After the first hour a maintenance rate of 0.4 g/h was given for the next 24 h. Hemodynamic effects were treated with dopamine if necessary. Inclusion criteria were high Paw (at tidal

Table 1. Respiratory mechanics, systolic arterial pressure, heart rate, and blood gas parameters ($PaCO_2$ and PaO_2/FIO_2) at various times before and after onset of the magnesium sulfate infusion. Note that the variables at the time "onset" of magnesium infusion were measured directly at onset of magnesium infusion. It must be observed that these measurements differ from those obtained at admission which are described in the text. The respiratory mechanics of patient no. 1 could only be estimated until 4 h after magnesium infusion because thereafter the ventilatory mode was changed to a pressure support ventilation (PSV) mode and the patient was extubated 12 h after magnesium infusion

Time	Pat. 1	Pat. 2.	Pat. 3	Pat. 4	Pat. 5	Mean ± SD
Peak airway pressure (cmH_2O)						
Onset	45.0	35.0	55.0	39.0	41.0	43.0 ± 6.8
1 h	32.0	25.0	45.0	23.5	33.5	32.0 ± 8.0*
2 h	25.0	25.5	44.0	25.0	33.0	30.5 ± 7.4
4 h	22.0	26.0	48.0	25.5	38.0	31.9 ± 9.7
8 h	14.0 (PSV)	26.0	45.0	28.5	35.0	27.7 ± 10.2
12 h	spontaneous	22.0	40.0	26.0	34.5	30.6 ± 7.0
Flow resistance ($cmH_2O \cdot l^{-1} \cdot s^{-1}$)						
Onset	22.5	18.7	12.6	33.2	26.6	22.7 ± 7.0
1 h	9.4	10.1	5.2	11.5	23.2	11.9 ± 6.0*
2 h	7.5	5.6	4.6	15.0	27.8	12.1 ± 8.6
4 h	6.7	7.5	5.9	15.0	27.4	12.5 ± 8.1
8 h	n.e. (PSV)	6.7	5.3	18.8	24.3	13.8 ± 8.0
12 h	spontaneous	8.2	3.6	14.9	24.7	14.8 ± 10.9
Systolic arterial pressure (mmHg)						
Onset	140	130	110	140	158	135.6 ± 15.7
1 h	100	100	80	117	93	98.0 ± 12.0*
2 h	140	100	80	147	104	114.2 ± 25.4
4 h	140	120	95	154	102	122.2 ± 22.3
8 h	150	120	110	151	114	129.0 ± 17.8
12 h	160	140	110	140	116	133.2 ± 18.1
Heart rate (/min)						
Onset	110	145	140	86	97	115.6 ± 23.3
1 h	100	130	112	75	103	104.0 ± 17.9
2 h	110	130	120	74	103	107.4 ± 19.0
4 h	104	120	132	84	103	108.6 ± 16.3
8 h	112	110	120	88	109	107.8 ± 10.6
12 h	92	100	130	96	97	103.0 ± 13.7
$PaCO_2$ (mmHg)						
Onset	57	49	86	60	35	57.4 ± 16.7
1 h	m.v.	43	73	49	34	49.8 ± 14.4
2 h	56	m.v.	59	47	36	49.8 ± 9.2
4 h	43	38	51	44	38	42.8 ± 4.8
8 h	45	35	58	42	38	43.6 ± 8.0
12 h	m.v.	38	45	45	37	41.3 ± 3.8
PaO_2/FIO_2 (mmHg)						
Onset	101	178	192	157	204	166.4 ± 36.1
1 h	m.v.	223	136	247	167	193.1 ± 43.8
2 h	111	m.v.	110	220	245	171.6 ± 61.5
4 h	159	245	106	250	250	201.8 ± 59.4
8 h	372	220	164	270	265	258.3 ± 68.4
12 h	m.v.	228	220	300	253	250.0 ± 31.3

m.v., Missing value; spontaneous, spontaneous breathing (room air); n.e., not estimated. Time: onset, onset of high-dose $MgSO_4$ infusion; 1 h, 1 hour after starting $MgSO_4$ infusion (end of high-dose $MgSO_4$ infusion; see table 2 for amount of $MgSO_4$); 2 h, 4 h, 8 h, 12 h, hours after starting $MgSO_4$ infusion (maintaining infusion rate of $MgSO_4$: 0.4 g/h)

*$p < 0.05$ between "onset" and "1 h" (Wilcoxon matched-pairs test)

Table 2. Serum magnesium concentrations following magnesium sulfate infusion

Patient	$MgSO_4$ dose		Serum magnesium concentrations (mM/l) Hours after beginning $MgSO_4$ infusion						
	During 1st h	Total in 24 h	0	1	2	4	8	12	24
1	10	14[a]	1.2	2.4	–	data missing	–	1.1	0.9
2	10	20	–	–	data not determined			–	–
3	17	27	1.1	3.2	2.3	1.9	1.4	1.2	1.0
4	15	25	0.9	3.0	2.4	2.2	1.7	1.6	1.3
5	20	30	0.8	2.8	2.6	2.3	1.7	1.6	1.5

Magnesium concentrations (mM/l) in serum determined at various times after starting the magnesium sulfate infusion. Normal values for healthy patients are from 0.65 to 1.1 mM/l in our institution. The data for patient 2 were not determined. Note that the patients had a normal serum magnesium before magnesium infusion

[a] $MgSO_4$ had been administered only for 10 h

volume < 10 ml/kg and inspiratory flow < 0.5 l/s) and/or severe air trapping refractory to maximal conventional medical treatment (as outlined above) including sedation and paralysis in patients requiring mechanical ventilation. Air trapping was clinically assessed by ongoing exhalation for several seconds after occasional end-expiratory disconnections of the respirator. Patients with known AV-block, bradycardia or renal insufficiency were excluded from the study. The following three patients were studied under this protocol.

Patient 3

A 25-year-old, 70-kg female with a 18-year-history of allergic bronchial asthma required mechanical ventilation in an external hospital after rapid detoriation of status asthmaticus due to pneumonia. After failure of conventional treatment (theophylline, β2-agonists IV, corticosteroids) including halothane anesthesia the patient was transferred to our ICU with a persisting high Paw. On admission she had a severe bronchospasm with a Paw of 60 cmH_2O and arterial blood gases under $FIO_2 = 1.0$ showed a severe respiratory acidosis (pH 7.1, $PaCO_2$ 96 mmHg) and an A-aDO_2 > 500 mmHg. The observed arterial hypotension in combination with tachycardia (120 to 150/min) was probably caused by the marked hyperinflation of the lungs shown in the X-ray. Dopamine (20 $\mu g \cdot kg^{-1} \cdot min^{-1}$) and IV fluids were administered to maintain the systolic blood pressure above 80 mmHg. Theophylline (0.72 g/24 h) and salbutamol 25 μg/min) were administered continuously. Theophylline serum level was 17.3 μg/ml at this time. β2-agonists had been given for more than 48 hrs (included the treatment in the external hospital). The $MgSO_4$ infusion was started at an infusion rate of 10 g/h which was increased to 20 g/h after 15 min because of an initially insufficient effect on the bronchomotor tone measured as the absence of significant airway pressure reduction at constant ventilatory settings. At the higher $MgSO_4$ infusion rate auscultation of the lungs showed decreasing rhonchi and wheezes simultaneously with decreasing Paw from an initial 55 cmH_2O to 45 cmH_2O one hour later with unchanged tidal volume and flow rate settings on the respirator. During this period $PaCO_2$ decreased from 86 mmHg to 73 mmHg and further to 60 mmHg within the next hour. After 1 hour the $MgSO_4$ infusion was reduced to a maintenance rate of 0.4 g/h for the following 24 h. The X-ray picture of the lungs showed a reduction of hyperinflation and mechanical ventilation was uncomplicated with Paw decreasing further to 30 cmH_2O within 24 h. Due to the pneumonia mechanical ventilation of the lungs was necessary for further four days after which the patient was extubated and recovered completely.

Patient 4

A 61-year-old, 80-kg obese female with a history of intrinsic asthma suffered a hypoxic cardiocirculatory arrest and following tracheal intubation she was resuscitated in her home (with IV epinephrine), where the bronchospasm had been treated with 80 mg triamcinolone, 0.24 g theophylline, and a salbutamol infusion 10–30 μg/min by an emergency physician. In addition she had arterial hypertension and diabetes mellitus. On admission to our ICU she had bronchospasm with marked air-trapping (uncongested, hyperinflated lungs in the chest X-ray). Theophylline serum level was 10.2 μg/ml at the time of admission. Changing the ventilator settings and further application of theophylline, corticosteroids, salbutamol (25 μg/min via infusion pump) and relaxants (vecuronium) failed to improve the patients condition. $MgSO_4$ infusion was started 1 h after admission. Total duration of salbutamol infusion before $MgSO_4$ infusion was 2.5 h. Initial arterial blood gases with FIO_2 1.0 before $MgSO_4$ therapy revealed a respiratory acidosis (pH 7.24, $PaCO_2$ 60 mmHg) and an A-aDO_2 > 450 mmHg. With an increased infusion rate (total $MgSO_4$ 15 g in the first hour) the auscultatory signs of bronchospasm disappeared almost completely within 15 min and Paw decreased from 39.0 to 23.5 cmH_2O with unchanged ventilator settings. Airway resistance decreased from initial 33.2 to 23.2 $cmH_2O \cdot l^{-1} \cdot s^{-1}$ within 15 min after starting the $MgSO_4$ infusion and was 11.5 $cmH_2O \cdot l^{-1} \cdot s^{-1}$ after 1 h (see Table 1). The A-aDO_2 improved rapidly to 150 mmHg and the $PaCO_2$ decreased to 47 mmHg with improving ventilation. Under high-dose $MgSO_4$ the systolic BP decreased to 117 mmHg within 10–15 min rising again to 140 mmHg approximately 30 min after reducing the $MgSO_4$ dosage to 0.4 g/h for the following 24 h. Subsequent mechanical ventilation was uncomplicated and the circulation was stable, but the patient did not regain consciousness. After repeated neurological examinations 2 weeks later revealed severe and irreversible hypoxic brain damage due to the primary resuscitation the decision was made to discontinue intensive therapy and mechanical ventilatory support. A nosocomial pneumonia developed, and the patient died three weeks later from hypoxic cardiac failure.

Patient 5

A 33-year-old, 65-kg female with a 13-year-history of intrinsic bronchial asthma required mechanical ventilation in an outside hospital after rapid detoriation of status asthmaticus due to a viral pneumonia. The patient was transferred to our ICU due to worsening gas exchange and a persisting bronchospasm with high Paw. On admission the patient had a severe respiratory acidosis (pH 7.09, $PaCO_2$ 89 mmHg) and a PaO_2 of 67 mmHg at FIO_2 of 1.0. The chest X-ray showed a marked hyperinflation of the left lung with a mediastinal shift to the right and a mediastinal and skin emphysema. During the first few hours we were able to maintain IPPV using conventional broncholytic therapy (theophylline 0.96 g/24 h; methylprednisolone 250 mg all 6 h; salbutamol 15–25 μg/min) deep sedation (midazolam) and muscle relaxation (vecuronium). Theophylline serum level was 16.7 μg/ml at this time. Severe refractory bronchospasm occurred during an attempt to obtain bronchial secretions for bacteriology, and $MgSO_4$ therapy was subsequently started with an initial infusion rate of 10 g/h and increased after 15 min (total $MgSO_4$ dose 20 g in first hour). At this time IV β2-agonists had been given for more than 3 days. The Paw decreased from 41 to 33 cmH_2O within 20 min after onset of the $MgSO_4$ infusion. Dopamine (6–12 $\mu g \cdot kg^{-1} \cdot min^{-1}$) was administered to maintain the blood pressure above 85 mmHg. With a maintainance infusion of $MgSO_4$ (0.4 g/h) for the next 24 h no further sedation or muscle relaxation was necessary. Paw remained stable during IPPV (30–33 cmH_2O), the respiratory acidosis was corrected and we were able to reduce the FIO_2 to 0.3. Further mechanical ventilation was unproblematic and the patient was extubated two days later. The patient was discharged to a normal ward 10 days after admission.

Urine output remained stable between 70 and 200 ml/h in all patients during the high-dose $MgSO_4$ infusion. In three patients diuresis increased three to five hours after the high-dose $MgSO_4$ period with urine output up to 600 ml/h. Low dose dopamine (3 $\mu g \cdot kg \cdot min^{-1}$) was administered to all patients for the entire duration of mechanical ventilation, but only patient 3 and 5 received a higher dosage of dopamine during hypotensive periods. Neither rebound hypertension nor reflex tachycardia were seen during or after $MgSO_4$ therapy. Since the

electrocardiogram was monitored continuously in all patients we were able to exclude bradycardia, arrhythmias and AV-block with certainty. Except for the 2 cases of arterial hypotension no adverse side-effects of $MgSO_4$ were seen in our patients.

Discussion

The treatment of status asthmaticus is usually difficult and often requires multiple approaches. Using unconventional measures (i.e. halothane anesthesia, ketamine infusion, controlled hypoventilation) the mortality rate in mechanically ventilated asthmatics can be decreased (in our institution 3% [5]). Magnesium sulfate as a further adjunct to the therapeutic regimen offers some promising properties. Its bronchodilating effect was described recently by studies in spontaneously breathing asthmatics and in two mechanically ventilated patients who had mild or moderate airway obstruction [2–4]. In the latter studies 0.4–0.615 mM/min $MgSO_4$ was administered for 20 min (= 2.0–3.0 g total dose). In the study of Okayama et al. [4] two patients with moderate increase of airway resistance were treated in this manner after having been anesthetized with ketamine. In both patients airway resistance decreased to the greatest extent within one minute after beginning the $MgSO_4$ infusion and increased again to nearly initial values 20 minutes after terminating the infusion. In contrast to the findings of Okayama et al. [4] our five patients with severe bronchospasm requiring mechanical ventilation did not respond as promptly although they had been given a larger $MgSO_4$ dose (10–20 g in 1 h versus 2.5 g in 20 minutes). This might be taken as an indication that our patients were more severely ill. In spite of the risks of high serum magnesium concentrations described in older studies [comprehensive review in 6] we considered this regimen to be feasible due to our experience with high-dose intravenous $MgSO_4$ for controlled hypotension [7]. In some patients we observed a slight increase of airway resistance with decreasing serum magnesium concentrations. This finding would agree with the results of Lindeman et al. [8] who recently demonstrated a dose dependent ability of $MgSO_4$ to attenuate hypcapnia-induced bronchoconstriction in dogs.

The theoretical basis for the therapeutic effect is the fact that magnesium acts principally as a "physiological" calcium antagonist by displacing calcium from its binding sites, thereby either preventing its actions as a second messenger or impeding transmembrane calcium flux. There is evidence that magnesium acts on airway smooth muscles in a nifedipine-like manner by blocking voltage-sensitive calcium channels [8].

It is unsusal for $MgSO_4$ to be administered in such high doses as those employed in our patients. There are reports of severe cardiovascular complications such as bradycardia, AV-block and cardiac arrest associated with serum magnesium concentrations above 7.5 mM/l [9]. However, these complications were all observed either in patients with concomitant renal failure and hyperkalaemia, or in spontaneously breathing patients receiving magnesium infusions who might have become hypercapnic and hypoxic as a result of the relaxant effect of magnesium [9]. In mechanically ventilated patients hypoxia usually does not occur (none of our patients were hypoxic during the magnesium infusion). More convincing evidence against the reported dangers of high-dose $MgSO_4$ is provided by the data gathered in patients who had serum magnesium concentrations far in excess of 7.5 mM/l (up to 13.6 mM/l) while still retaining their cardiovascular stability under general anesthesia and during mechanical ventilation [7].

We did observe a dose dependent, reversible decrease of arterial blood pressure during the high-dose $MgSO_4$ infusion, but this required treatment with dopamine only in two patients. This implies that high-dose $MgSO_4$ infusions should only be administered with continuous on-line blood pressure monitoring. In previous studies a decrease in peripheral resistance during $MgSO_4$-infusion was demonstrated while pulmonary vascular resistance only showed an insignificant decrease [7]. The muscle relaxant effect of magnesium must be kept in mind, especially in combination with benzodiazepine sedation [7], since the time to sufficient spontaneous breathing may be prolonged.

There is some criticism about IV $MgSO_4$ as a bronchodilating therapy in asthmatics. Kufs [10], in a comment on a study of Skobeloff et al. [2], stated that he sees no need for IV magnesium because acute bronchoconstriction can be resolved by β-agonist inhalations if provided sufficiently. There is even evidence that the bronchodilating effect of β-agonists may be more pronounced than that of magnesium [3]. However, it can be argued that indeed inhalational β-agonists can only be effective when delivered adequately to the lower airways. The problem of insufficient application of β-agonists can be avoided by the intravenous application route independent of the bronchoconstricted airways.

We are not advocating intravenous $MgSO_4$ as a basic measure but consider it to be a further adjunct to manage severe bronchoconstriction in mechanically ventilated patients. However, if edema is not the main cause of high airway resistance, the IV application of magnesium could offer a therapeutic advantage in patients no longer responsive to adequate β-agonist therapy. Certainly it is difficult to evaluate the special benefit of magnesium in patients who are being treated simultaneously with several other bronchodilating drugs. This is a general problem in clinical experiments in very ill patients. In our study the continuing infusion of β2-agonists in four of five patients could hypothetically have led to an increasing bronchodilating effect over time due to the increasing plasma levels of β2-agonists. However, because of the observed bronchodilating effect time related to the short high-dose $MgSO_4$ infusion the latter seems to be the more plausible mechanisms. Nevertheless, controlled randomized blind studies on a larger number of patients are necessary to confirm our results.

Our data suggest that high dose IV $MgSO_4$ can be an effective therapy in patients suffering from life-threatening status asthmaticus requiring mechanical ventilation, if conventional treatment is insufficient. The only relevant side-effect in mechanically ventilated patients is the mild to moderate arterial hypotension which responds readily to treatment.

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