Magnesium: Haemodynamics

Acute haemodynamic actions of intravenous magnesium in patients with heart disease

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Zusammenfassung

Calcium-Antagonisten sind eine heterogene Substanzklasse mit unterschiedlichen Wirkungen auf das kardiovaskuläre System. Anorganische Kationen wie Mangan, Koblat, Lanthan und Magnesium können ebenfalls als Calcium-Antagonisten wirken.
Hämodynamische Wirkungen nach intravenöser Gabe von Magnesium in relativ hoher Konzentration wurden bei 12 Patienten untersucht, die zur kardialen Diagnostik eingewiesen worden waren. Nach Einstellung stabiler hämodynamischer Parameter wurden 0,1 mmol $MgSO_4$ pro Kilogramm Körpergewicht während ca. 40 Sekunden intravenös infundiert. Alle Patienten berichteten über eine vorübergehende Wärmeempfindung der Haut. Es fand sich eine signifikante Abnahme des systemischen und pulmonalen Gefäßwiderstandes. Der arterielle Druck im großen und im Lungenkreislauf blieb jedoch praktisch unverändert aufgrund einer erhöhten Herzfrequenz und eines geringen Anstieges des Schlagvolumens. Der mittels Einschwemmkatheter in einer Verzweigung der Pulmonalarterie gemessene Druck in den Lungenkapillaren („Pulmonary Wedge Pressure") änderte sich nicht. Die hämodynamischen Wirkungen waren kurzfristig und liefen nicht synchron mit dem beträchtlich langsamer abfallenden Plasma-Mg-Spiegel.
Es wird geschlossen, daß für Patienten mit mäßig erniedrigter Herzfunktion eine Auffüll-Dosis an Mg „sicher" ist. Die mögliche therapeutische Bedeutung dieses natürlichen Calcium-Antagonisten erfordert weitere Aufmerksamkeit; Vorsicht ist bei Patienten mit stenosierenden Klappenerkrankungen oder schwerer kardialer Dekompensation geboten.

Summary

Calcium antagonists are a heterogenous class of agents with dissimilar effects on the cardiovascular system. Inorganic cations, such as manganese, cobalt lanthanum and mangnesium, may also function as calcium antagonists.
The haemodynamic effects of an intravenous loading dose of magnesium was studied in twelve patients referred for cardiac evaluation. Following baseline haemodynamic measurements, 0,1 mmol magnesium sulphate per kilogram body weight was infused during approximately 40 seconds. All patients reported a transient sensation of cutaneous warmth. There was a significant fall in systemic and pulmonary vascular resistance. Systemic and pulmonary artery pressure, however, both remained virtually unchanged because of a rise in heart rate and a minute increase in stroke volume. There was no significant change in pulmonary capillary wedge pressure. The haemodynamic changes were short-lasting and did not parallel the considerably slower fall in plasma magnesium.
It is concluded that an intravenous loading dose of magnesium can be safely given in patients with moderately depressed cardiac function. The therapeutic potential of this naturally occuring calcium antagonist deserves further attention, but caution should nevertheless be exercised in patients with stenotic valve lesions or severe cardiac decompensation.

Résumé

Les inhibiteurs calciques forment une classe hétérogène de médicaments, dont les effets sur le système cardio-vasculaire sont dissemblables. Des cations inorganiques, tels que le manganèse, le cobalt, le lanthanum et le magnésium, peuvent également se comporter comme des inhibiteurs calciques.
Les auteurs ont étudié les effets hémodynamiques d'une charge de magnésium administrée par voie intraveineuse chez 12 patients leur ayant été adressés pour une évaluation de leur état cardiaque. Après un bilan hémodynamique initial, on a perfusé 0,1 mmol de sulfate de magnéésium par kilogramme de poids corporel pendant environ 40 secondes. Tour les patients ont fait part d'une sensation transitoire de réchauffement cutané. Il y a eu une chute significative des résistances vasculaires pulmonaires et systémiques. En revanche, la pression artérielle globale et la pression artérielle pulmonaire sont restées pratiquement inchangées, en raison d'une augmentation de la fréquence cardiaque et d'une accroissement discret du volume d'éjection systolique. On n'a pas observé de modification significative de la pression capillaire pulmonaire. Ces modifications hémodynamiques ont été de courte durée et n'ont pas été corrélées à la diminution considérablement plus lente de la magnésémie.
Les auteurs concluent qu'il est possible d'administrer, en toute sécurité, une dose de charge de magnésium par voie intraveineuse chez des patients présentant une insuffisance cardiaque modérée. Le potentiel thérapeutique de cet inhibiteur calcique naturel mérite une attention accrue, mais il semble indispensable d'exercer une vigilance toute particulière chez les patients atteints de lésions valvulaires sténosées ou de sévère décompensation cardiaque.

Introduction

More than 20 years have passed since the introduction of calcium antagonists, and they have established their therapeutic potential in a variety of cardiovascular diseases [1–3]. Their effects involve coronary arterial tone, vascular resistance, myocardial contractility, and cardiac impulse formation and conduction [2–4]. Several inorganic cations, such as manganese, cobalt, lanthanum and magnesium may also function as general calcium antagonists and are effective in blocking a wide variety of cal-

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cium dependent processes [4, 5]. While the circulatory effects of pharmacological agents with calcium blocking properties have been extensively evaluated, magnesium has been insufficiently studied in this respect. The present study was therefore undertaken to clarify the haemodynamic response to a loading does of magnesium sulphate.

Patients

Twelve patients, referred for evaluation of suspected angina pectoris or aortic valve disease, were included in the study. Their ages ranged from 18 to 68 years (mean 52), and they were in class II or III according to the functional classification of New York Heart Association. Eight had coronary artery disease verified by angiography, three had atypical chest pain with normal coronary arteriograms, and one had moderate aortic reguritation. Patients with significant valvular stenosis or severe congestive failure (class IV) were excluded. Digitalis, betablockers, and calcium antagonists were withheld at least 48 hours before cardiac catheterisation. Informed consent was obtained from every patient. The design of the study was approved by the local ethics committee.

Methods

Cardiac catheterisation was performed without premedication in accordance with the routine of the hospital. A modified Seldinger technique for catheter introduction was used, and pressures were recorded using liquid-filled catheters. An ECG and systemic and pulmonary artery pressure were continuously recorded. Following baseline haemodynamic measurements, 0.1 mmol of magnesium sulphate per kilogram body weight, diluted in 100 ml is-

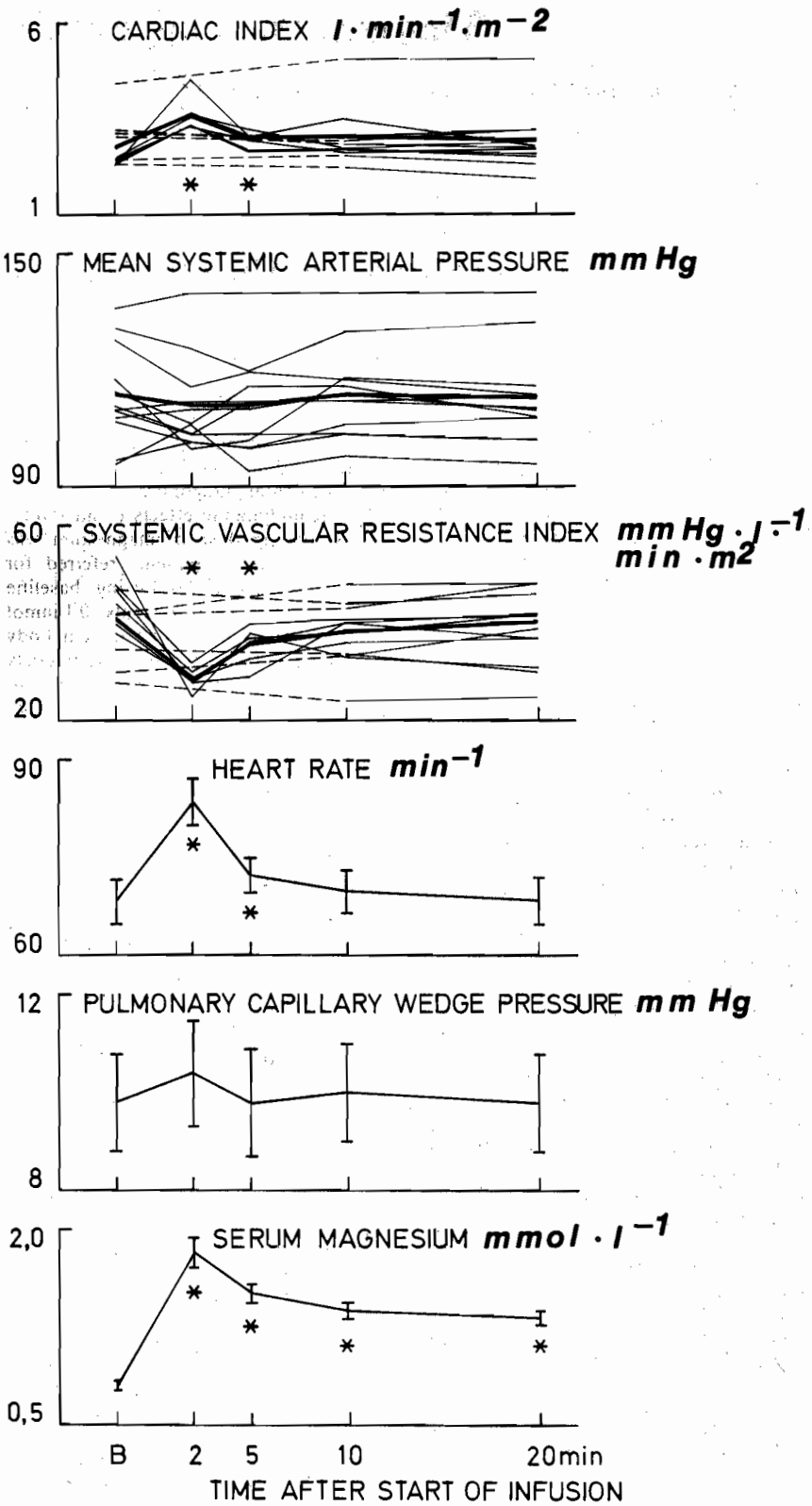

Fig. 1: Haemodynamic findings and plasma magnesium before (B), 2, 5, 10, and 20 minutes after an intravenous infusion of 0.1 mmol magnesium sulphate per kg body weight in twelve patients. Thick lines represent mean values and thin lines individual patients. Unbroken lines indicate measurements of cardiac index by the thermodilution technique and broken lines by the Fick method

otonic saline, was infused intravenously during approximately 40 seconds. Pulmonary capillary wedge pressure was registered and blood samples for magnesium analysis were taken before, 2, 5, 10 and 20 minutes after the start of infusion. Cardiac output was determined by the direct Fick method in six patients and measurements were performed before, 10 and 20 minutes after the infusion with five minutes of oxygen sampling. In the other six patients cardiac output was determined by the thermodilution technique as an average of four measurements before, 2, 5, 10 and 20 minutes after the start of infusion. Haemodynamic variables were calculated as follows: Cardiac index (CI) = cardiac output ÷ body surface area; Systemic vascular resistance index = {mean brachial artery pressure — mean right atrial pressure} ÷ CI; Pulmonary vascular resistance index = {mean pulmonary artery pressure — mean pulmonary capillary wedge pressure} ÷ CI.

Statistical analysis was performed by Wilcoxon's signed rank test, with $p < 0,05$ considered as the level of significance.

Results

The haemodynamic effects of the magnesium infusion as well as plasma magnesium concentrations are summarised in the Table and Figure. There was a significant reduction of systemic and pulmonary vascular resistance. Cardiac output increased owing to a marked rise in heart rate and a small rise in stroke volume. There were no significant changes in systemic or pulmonary artery pressure, and pulmonary capillary wedge pressure also remained unchanged. The alterations observed were transient, with maximal deviation from initial values 2 minutes after the start of infusion, and baseline values were reached within 10 minutes in all patients.

There was also a sharp increase in plasma magnesium concentration, followed by a gradual decline, but baseline values were in

Tab. 1: Hemodynamic findings and plasma magnesium in twelve patients. Values are presented as mean ± SEM

Variables	Before magnesium	2 minutes	5 minutes	10 minutes	20 minutes
		After magnesium			
Heart rate (min^{-1})	68,3 ± 3,4	83,6 ± 3,5*	72,3 ± 2,7*	69,8 ± 3,4	68,4 ± 3,7
Systemic artery pressure (mm Hg)					
Systolic	160,5 ± 7,0	151,5 ± 7,8	155,2 ± 6,9	158,4 ± 7,3	158,3 ± 6,6
Diastolic	83,2 ± 3,8	82,2 ± 3,5	81,3 ± 3,6	82,3 ± 3,5	84,3 ± 3,6
Mean	113,9 ± 3,6	110,9 ± 3,4	110,9 ± 3,6	114,3 ± 3,4	112,7 ± 3,6
Pulmonary artery pressure (mm Hg)					
Systolic	24,8 ± 1,4	25,7 ± 1,7	25,0 ± 1,6	24,8 ± 1,5	25,1 ± 1,5
Diastolic	10.6 ± 0.9	11.1 ± 1.2	10.8 ± 1.0	11.2 ± 1.0	11.0 ± 1.0
Mean	17,0 ± 1,0	17,7 ± 1,4	16,6 ± 1,2	16,5 ± 1,0	16,4 ± 1,2
Pulmonary capillary wedge pressure (mm Hg)	9,8 ± 1,0	10,4 ± 1,1	9,8 ± 1,1	10,0 ± 1,0	9,8 ± 1,0
Cardiac index ($l \cdot min^{-1} \cdot m^{-2}$ BSA)	2,7 ± 0,2	3,6 ± 0,2*†	3,0 ± 0,1*†	3,0 ± 0,2	2,9 ± 0,2
Stroke volume (ml)	74,4 ± 4,4	82,0 ± 6,7†	79,5 ± 4,4*†	78,5 ± 5,5	77,0 ± 5,7
Systemic vascular resistance index (mm $Hg \cdot l^{-1} \cdot min \cdot m^2$ BSA)	45,1 ± 2,4	28,7 ± 1,0*†	35,5 ± 1,6*†	38,0 ± 1,2	40,0 ± 1,0
Pulmonary vascular resistance index (mm $Hg \cdot l^{-1} \cdot min \cdot m^2$ BSA)	2,8 ± 0,3	2,1 ± 0,3*†	2,2 ± 0,3*†	2,1 ± 0,2	2,6 ± 0,4
Plasma magnesium ($mmol \cdot l^{-1}$)	0,81 ± 0,03	1,84 ± 0,12*†	1,52 ± 0,07*†	1,38 ± 0,06*	1,33 ± 0,05*

† = six patients; * = $p < 0,05$ (compared with pre-infusion value)

no case reached after 20 minutes. Although magnesium was infused with isotonic sodium chloride, there were no significant changes in the plasma concentration of sodium, calcium, or potassium.

Apart from sinus tachycardia, no arrhytmias were monitored during the study. A sensation of heat, which subsided after a few minutes, was experienced by all patients. No serious side effects were observed.

Comments

An intravenous loading dose of magnesium has powerful vasodilatatory properties, as indicated by the considerble decrease in systemic and pulmonary vascular resistance observed in this study. The alterations in heart rate and cardiac output observed were probably reflex in origin, induced by the fall in vascular resistance. Magnesium itself has been claimed to reduce the heart rate [8, 9]. No significant decrease in systemic blood pressure was, however, observed, in agreement with previous experience of acute administration of calcium antagonists in normotensive and hypertensive subjects. A reduction of blood pressure is usually observed in the latter group only [10–12]. The haemodynamic effects of magnesium are thus similar to those reported for conventional calcium antagonists [13–16].

Although magnesium is reported to exert a myocardial depressant effect [5, 6], there were no changes in pulmonary artery or pulmonary capillary wedge pressure, and no reduction of cardiac output occured in patients with raised pulmonary wedge pressure. No patients was in functional class IV, however, and all had a basal wedge pressure below 20 mm Hg. Thus, it is possible that a reduction in cardiac output may occur in patients with more severely impaired ventricular funtion, or if larger doses of magnesium are given.

There was no clear relation between plasma magnesium concentrations, on one hand, and haemodynamic alterations, on the other. The haemodynamic changes were of brief duration and could be demonstrated only by the thermodilution technique, since the Fick method requires steady state during the period of oxygen sampling for accurate determinations. The haemodynamic changes induced by the sharp rise of plasma magnesium were rapidly counteracted. A continuous infusion of magnesium, however, might produce a more protracted reduction of vascular tone.

Our results agree with those reported by *Mroczek* et al. [12]. These authors examined haemodynamics in healthy volunteers and subjects with uncomplicated essential hypertension. About 16 mmol magnesium sulphate was given during ten minutes, and an increase in cardiac output and a decrease in systemic vascular resistance resulted. There was a slight fall in blood pressure in hypertensive patients, but no appreciable change in normotensive subjects.

Our data are, however, somewhat at variance with those reported by *Mori* [17], who infused 0,05 mmol magnesium aspartate per kg body weight during five minutes in normotensive volunteers and hypertensive subjects. There was a slight increase in peripheral resistance in hypertensives, the mean blood pressure and heart rate rose in both normotensives and hypertensives, but cardiac index was not altered. The dose of magnesium given was, however, small and the rise in plasma magnesium was considerably lower than that registered in our study and in the study of *Mroczek* et al. [12].

There may be several potential therapeutic applications for magnesium. There is now considerable evidence that magnesium protects against some of the changes induced by myocardial ischemia and reduces complications in acute myocardial infarction [6, 7, 18]. Arrhythmias, in particular those related to digitalis toxicity and acute myocardial infarction, have been associated with magnesium deficiency [6, 7, 19–21], and rapid magnesium supplementation might be beneficial. Our results indicate that intravenous loading of magnesium is safe in patients with moderatly impaired ventricular function. Caution should nevertheless be exercised in patients with severe myocardial decompensation, and a reduction of vascular resistance may be detrimental in patients with a significant valvular stenosis.

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