OBSTETRICS

Effects of magnesium on central arterial compliance in preeclampsia

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OBJECTIVE: The objective of the study was to investigate the effect of $MgSO_4$ infusion on central arterial compliance, using radial artery applanation tonometry in women with preeclampsia.

STUDY DESIGN: Seventy women with preeclampsia were prospectively recruited. Radial pulse waveforms were obtained and the aortic waveforms constructed. The arterial compliance surrogates, augmentation pressure (AP) and augmentation index (AIx-75), were derived from the aortic waveform and then compared: prior to $MgSO_4$ (t1), 1 hour after $MgSO_4$ bolus (t2), 4 hours after $MgSO_4$ infusion (t3), and 24 hours after $MgSO_4$ cessation (t4). Statistical analysis was performed using differences of least squared means with Tukey Kramer adjustments.

RESULTS: The AP and AIx-75 at t2-t4 were significantly lower compared with t1, with the greatest decrease in arterial stiffness at t3 ($P <$ .05).

CONCLUSION: In preeclampsia, $MgSO_4$ improved central arterial compliance. This effect was most exaggerated after 4 hours of infusion and remained 24 hours following $MgSO_4$ completion, suggesting either a sustained arterial compliance effect or resolution of the vasoconstrictive effect of preeclampsia.

Key words: arterial compliance, magnesium sulfate, preeclampsia

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In normal pregnancy, arterial compliance adaptively increases by 30% in the first trimester and remains elevated thereafter, returning to normal levels by 8 weeks postpartum.[1] This enhancement of arterial compliance has been suggested to constitute part of the vascular adaptation to increased intravascular volume.[2] In pregnancies complicated by preeclampsia, this mechanism of adaptation is blunted and women with preeclampsia exhibit decreased arterial compliance.[2,3]

With each heart beat, a pulse wave travels away from the heart along the arterial tree but is reflected back toward the heart and meets the next advancing wave. Under normal circumstances, the reflected wave reaches the aorta during diastole increasing the diastolic portion of the wave, allowing perfusion of the coronary arteries and maintenance of the mean arterial pressure.[4] However, when the arterial wall stiffness is increased (ie, decreased compliance), the arterial pulse wave travels more rapidly away from the heart, while the reflected wave returns more quickly.

This causes early return of the wave reflection such that the diastolic portion of the wave moves into systole, producing a second (late) systolic peak that is higher than the first.[5] The resultant systolic augmentation of the aorta can be assessed by analyzing the radial pulse waveform with the simple noninvasive method of applanation tonometry.[6]

This technique has been validated in various populations and is an accepted measurement for various central pressure and arterial compliance indices.[7] It has been used to quantify alterations in central arterial compliance associated with age, renal disease, diabetes, and chronic hypertension.[8-10] Preeclampsia is a disorder of vascular endothelium, and recent studies have utilized applanation tonometry to further characterize this condition.

Pulse wave analysis in women with hypertensive disorders of pregnancy has consistently demonstrated the association of poor arterial compliance in preeclamptic and hypertensive gravidas.[11-13] Yet few studies have addressed methods to improve arterial compliance during preeclampsia.[14] It has been proposed that magnesium sulfate ($MgSO_4$) use causes transient effects on blood pressure;[15] however, the effect of $MgSO_4$ on arterial compliance has not been well studied. It may be that $MgSO_4$ affects the central pressure and arterial stiffness, thus making its use beneficial beyond seizure prophylaxis in women with preeclampsia.

The purpose of our study was to investigate the effect $MgSO_4$ infusion has on central arterial stiffness in women with preeclampsia. We hypothesized that women with preeclampsia would have a decrease in augmentation pressure (AP) and augmentation index (AIx-75), an indication of improved central arterial stiffness and central blood pressure, while undergoing $MgSO_4$ therapy for seizure prophylaxis.

MATERIALS AND METHODS

This was a prospective observational study at the University of Illinois Hospi-

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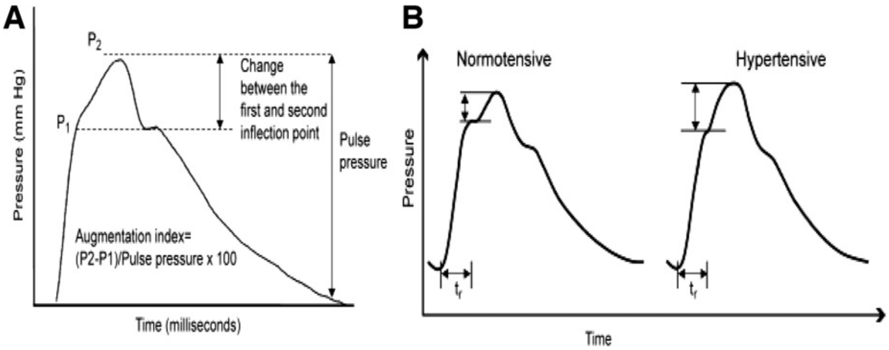
FIGURE 1
Example of aortic pulse waveforms



A, Typical ascending aortic pulse waveform, showing 2 systolic peaks (P1 and P2). Augmentation index is calculated as the difference between P2 and (△P), expressed as percentage of the pulse pressure. The designation P1 is the first inflection point; P2 is the second inflection point. **B**, In hypertensive disorders, arterial wall stiffness is increased; the arterial pulse wave travels faster, so the resulting wave reaches the advancing wave in systole, resulting in greater augmentation of the systolic peak. Time, t_r is the time to reach the reflected wave.

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tal (Chicago, IL) from November 2008 to August 2009, approved by the institutional review board prior to subject recruitment. All gravidas 16 years or older, diagnosed with preeclampsia, designated to receive $MgSO_4$ for seizure prophylaxis were deemed eligible and approached to participate. Written informed consent was obtained prior to obtaining the initial measurement. Those presenting with eclampsia or magnesium contraindication or already on $MgSO_4$ were excluded.

The diagnoses of severe, superimposed, and mild preeclampsia are based on the criteria established by the National High Blood Pressure Education Program Working Group[16] and the American College of Obstetricians and Gynecologists.[17] However, when a 24 hour urine collection was not feasible, a spot protein to creatinine ratio of 0.30 or greater satisfied criteria for proteinuria because this methodology is 92% sensitive and 84% specific.[18]

At our institution, $MgSO_4$ is administered to all women meeting criteria for severe preeclampsia and also typically for those with mild preeclampsia, although at the discretion of the provider. Routinely, a 4 g loading dose over 30 minutes is administered, followed by a 2 g/h maintenance infusion until 24 hours after delivery. Magnesium levels were not routinely obtained.

The central hemodynamic values were obtained using the SpyghmoCor device (AtCor Medical Inc, Itasca, IL), with incorporated supporting software that performs the analysis of direct applanation tonometry. The tonometer captures the pattern of the radial pulse wave and then synthesizes the aortic wave form using an internal generalized transfer function that describes the arterial properties between the ascending aorta and peripheral recording sites. The aortic pressure waveform is then analyzed, and multiple central hemodynamic parameters are calculated, including the estimates of arterial compliance: AP and AIx-75 along with other determinants of the central aortic waveform.

The augmentation is the increase provided to the late systolic pressure after the initial systolic shoulder (Figure 1).[14] When expressed in terms of millimeters of mercury (pulse pressure/p1), it is defined as the AP. When expressed in terms relative to a percentage of the pulse pressure (p1-p2/pulse pressure × 100), the augmentation index (AIx) is defined.[6] The AIx has a linear relationship with heart rate and therefore is standardized to a heart rate of 75 beats/min or the AIx-75.

All applanation tonometry measurements were made by 1 of 5 operators, each trained to ensure accurate measurements. Training incorporated theoretical and technical aspects, including identification of the maximum radial artery pulsation, application of the sensor, and recognition of appropriate arterial waveforms. Pulse wave analysis was accepted when the arterial pressure waveforms had the greatest attainable amplitude and maintained the same character, consistently beat to beat, for a minimum of 12 seconds throughout the measurement.

In addition, SpyghmoCor software (AtCor Medical) incorporates an internal quality control, the operator index, displayed simultaneously with study results, which correlates with the adequacy of the data input from the radial artery. The score ranges from 0 (poor study) to 100 (perfect study), with a score of 65 considered adequate for data input. We chose a higher standard for adequate data input and demanded an operator index of 85 or greater, ensuring that high-quality data were collected and analyzed.

All measurements were performed after admission to the hospital, immediately following the standard brachial artery blood pressure measurement, using the available nonintravenous arm while the patient was quiet, in semifowler's position and between contractions. Based on previously published studies on magnesium pharmacokinetics in preeclamptic patients,[19] we chose measurements at 4 specific time points: T1, prior to magnesium sulfate bolus; T2, 1 hour following magnesium sulfate bolus; T3, 4 hours after magnesium infusion began; and T4, 24hours after magnesium infusion cessation. All women were followed up until the final measurement was obtained.

The primary outcome measures of interest, which are surrogates of arterial stiffness, were AP and AIx-75. These variables were collected and the means compared across each time point in the analysis. A planned subgroup analysis of AIx-75 and AP was performed on