# Effects of Magnesium on Isolated Canine Coronary Arterial Tension

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The effects of magnesium on the tension of isolated canine coronary arterial strips were studied.

In the solution containing $K^+$ of 20 mEq·$l^{-1}$, $Ca^{2+}$ of 4 mEq·$l^{-1}$, and $Na^+$ of 127 mEq·$l^{-1}$, the tension was 811 ± 111 mg with $Mg^{2+}$ of 1 mEq·$l^{-1}$, 494 ± 135 mg with $Mg^{2+}$ of 10 mEq·$l^{-1}$, 272 ± 126 mg with $Mg^{2+}$ of 20 mEq·$l^{-1}$, −52 ± 63 mg with $Mg^{2+}$ of 30 mEq·$l^{-1}$, −69 ± 80 mg with $Mg^{2+}$ of 40 mEq·$l^{-1}$. In the solution containing $K^+$ of 20 mEq·$l^{-1}$, $Na^+$ of 12 mEq·$l^{-1}$ and $Ca^{2+}$ of 0 mEq·$l^{-1}$, the tension was 102 ± 22 mg with $Mg^{2+}$ of 1 mEq·$l^{-1}$, 3 ± 35 mg with $Mg^{2+}$ of 10 mEq·$l^{-1}$, −49 ± 33 mg with $Mg^{2+}$ of 20 mEq·$l^{-1}$, −59 ± 49 mg with $Mg^{2+}$ of 30 mEq·$l^{-1}$, −65 ± 54 mg with $Mg^{2+}$ of 40 mEq·$l^{-1}$.

The data demonstrated that $Mg^{2+}$ above 30 mEq·$l^{-1}$ inhibited the increase in tension caused by $Ca^{2+}$ and $Mg^{2+}$ above 20 mEq·$l^{-1}$ inhibited the increase in tension caused by low $Na^+$ concentration. (Key words: coronary artery, contraction, magnesium, calcium, sodium)

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The electrolyte composition is the important factor which affect the tension of the smooth muscle. In the earlier study, we confirmed that in high-$K^+$ solution, an increase in $Ca^{2+}$ and a reduction in $Na^+$ produces a dose-dependent increase in the tension of the isolated canine coronary artery[1,2]. On the other hand, it is known that $Mg^{2+}$ successfully competes with $Ca^{2+}$ for the Ca-binding site on myosin[3].

In this study, the effects of $Mg^{2+}$ in the extracellular fluid on the tension caused by $Ca^{2+}$ and low-$Na^+$ on isolated canine coronary artery were studied.

## Methods

The preparation of muscle strips and the experimental procedure were the same as those described in the earlier study[1,2]. The anterior descending coronary arteries taken from dogs (10 ~ 14 kg, either sex) anesthetized with thiamylal natrium (25 mg·$kg^{-1}$, i.v.). The coronary artery was dissected and its surrounding tissue was removed under a microscope. Helical strips of about 3 mm in width and 15 mm in length

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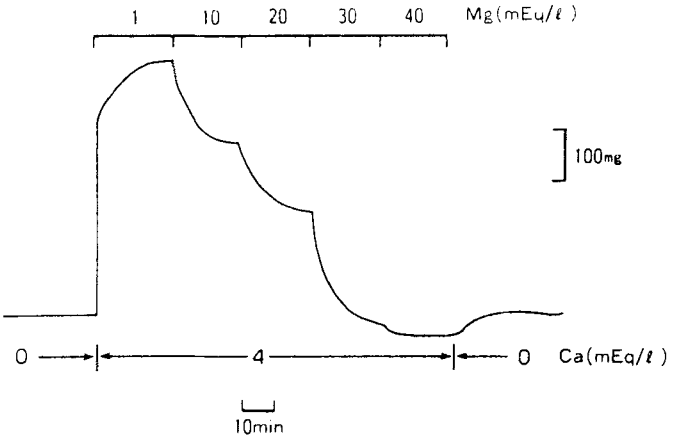


**Fig. 1.** Effects of Mg in the high-K, 4 mEq·$l^{-1}$ Ca solution.
The tension was reduced gradually by cumulation of Mg.

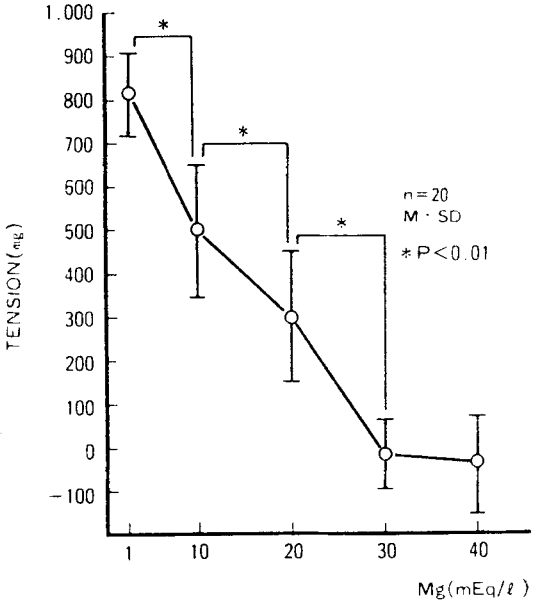


**Fig. 2.** Mg concentration-tension curve in the high-K, 4 mEq·$l^{-1}$ Ca solution.
Wilcoxon rank-sum test was adopted.
Mg suppressed the tension in a dose-dependent manner, but there was no statistical significance between 30 and 40 mEq·$l^{-1}$ Mg.

were excised from the segments of coronary artery of 0.8 to 1.2 mm in diameter. Each strip was mounted in an organ bath (37°C) through which the normal solution (see below) was perfuse at a constant rate of 2 ml·min$^{-1}$. The tension was isometrically recorded by using a strain gauge. After 30 min or more equilibration, the strip was stretched by the tension of approximately 0.5g and the normal solution was changed to high-$K^+$, $Ca^{2+}$-free solution (see below).

In the first experiment, external $Ca^{2+}$ concentration was increased to 4 mEq·$l^{-1}$ and $Mg^{2+}$ concentrations were varied between 1 mEq·$l^{-1}$ and 40 mEq·$l^{-1}$ after the tension was stabilized. In the second experiment, external $Na^+$ concentration was reduced to 12 mEq·$l^{-1}$ and $Mg^{2+}$ concentrations were varied between 1 mEq·$l^{-1}$ and 40 mEq·$l^{-1}$. In both experiments, the changes in the tension were measured in each solution.

The composition of the normal solution was as follows: Na 127 mM, K 5.9 mM, Ca 4.7 mM, Mg 1.0 mM and 11.8 mM glucose. The high-$K^+$, $Ca^{2+}$-free solution was made by removing $Ca^{2+}$ with 0.5 mM EGTA from the normal solution and adjusting $K^+$ to 20 mEq·$l^{-1}$. When $Na^{2+}$ concentration decreased, $Na^{2+}$ was replaced with saccharose on an equiosmolar basis (337m 0 sm·$l^{-1}$).

Statistical evaluation was performed by using Wilcoxon ranksum test. A probability value less than 1% was regarded as statistically significant.

**Table.** The tension at various Mg concentration with 4 mEq·l$^{-1}$ Ca or 12 mEq·l$^{-1}$ Na

| Mg (mEq·l$^{-1}$) / Electrolyte | 1 | 10 | 20 | 30 | 40 |
|---|---|---|---|---|---|
| Ca | 811 ± 111 | 494 ± 135 | 272 ± 126 | −52 ± 63 | −69 ± 80 |
| Na | 102 ± 22 | 3 ± 35 | −49 ± 33 | −59 ± 49 | −65 ± 54 |

The values are mean ± SD (mg), and n=20 (Ca) or 22 (Na).
Mg suppressed the tension caused by Ca or low-Na.

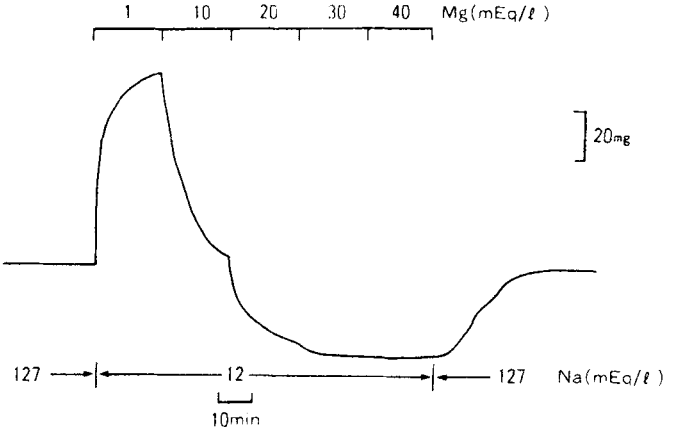


**Fig. 3.** Effects of Mg in the high-K, 12 mEq·$l^{-1}$ Na solution.
The tension was suppressed by cumulation of Mg.

## Results

As shown in figure 1, the tension increased in $Ca^{2+}$ of 4 mEq·$l^{-1}$. The tension decreased in proportion to the increases in $Mg^{2+}$ ranging from 1 mEq·$l^{-1}$ to 40 mEq·$l^{-1}$. The tensions were 811 ± 111 mg with $Mg^{2+}$ of 1 mEq·$l^{-1}$, 494 ± 135 mg with $Mg^{2+}$ of 10 mEq·$l^{-1}$, 272 ± 126 mg with $Mg^{2+}$ of 20 mEq·$l^{-1}$, −52 ± 63 mg with $Mg^{2+}$ of 30 mEq·$l^{-1}$ and −69 ± 80 mg with $Mg^{2+}$ of 40 mEq·$l^{-1}$ (table). Negative values mean relaxation. The statistical significance was found between $Mg^{2+}$ of 1 mEq·$l^{-1}$ and 30 mEq·$l^{-1}$, but not between $Mg^{2+}$ of 30 mEq·$l^{-1}$ and 40 mEq·$l^{-1}$ (fig. 2).

The tension increased in the solution containing $Na^{+}$ of 12 mEq·$l^{-1}$, and decreased gradually with the increase in $Mg^{2+}$ (fig. 3). The tensions were 102 ± 22 mg with $Mg^{2+}$ of 1 mEq·$l^{-1}$, 3 ± 35 mg with $Mg^{2+}$ of 10 mEq·$l^{-1}$, −49 ± 33 mg with $Mg^{2+}$ of 20 mEq·$l^{-1}$, −59 ± 49 mg with $Mg^{2+}$ of 30 mEq·$l^{-1}$ and −65 ± 54 mg with $Mg^{2+}$ of 40 mEq·$l^{-1}$ (table). The statistical significances were found between $Mg^{2+}$ of 1 mEq·$l^{-1}$ and 10 mEq·$l^{-1}$, and between $Mg^{2+}$ of 10 mEq·$l^{-1}$ and 20 mEq·$l^{-1}$. There were no statistical significance $Mg^{2+}$ above 20 mEq·$l^{-1}$ (fig. 4).

## Discussion

The tension of the coronary artery is affected by electrolyte composition of extracellular fluid. We reported that an increase in Ca or a decrease in Na produced a dose-dependent increase in the tension of the isolated canine coronary artery in high-K solution[1,2].

The initial phasic response of K-contracture of teania coli is insepara-

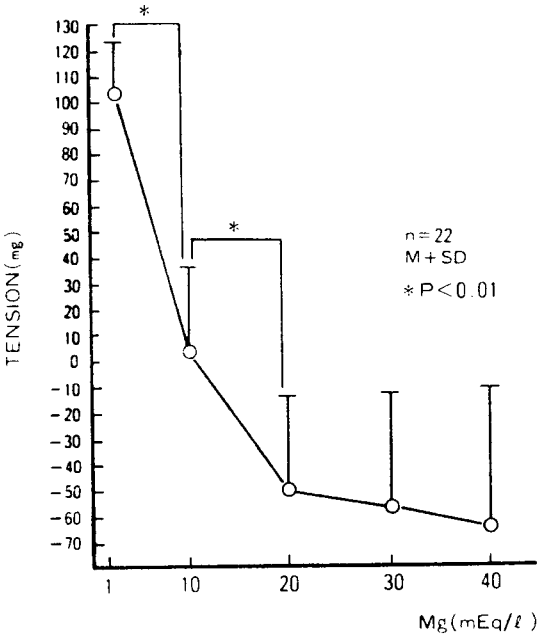


**Fig. 4.** Mg concentration-tension curve in the high-K, 12 mEq·$l^{-1}$ Na solution.

Wilcoxon rank-sum test was adopted.

Mg suppressed the tension, and the relaxation was occured above 20 mEq·$l^{-1}$ Mg.

bly associated with the spike potential and hence with the Ca-influx, which functions as the trigger and somehow liberates the bound Ca into the muscle fibres[4]. A portion of the ensuing tonic phase is dependent upon the inward movement of Ca from the extracellular space, while the rest is brought about by the release of bound Ca due to the sustained membrane depolarization[4]. It is generally agreed that the concentration of free intracellular $Ca^{2+}$ is the main determinant of the degree of activation of the contractile apparatus in smooth muscle[5]. Therefore, in high-K solution, an increase in extracellular Ca develop tension.

It has been reported that in Ca-free solution or in the presence of verapamil, Na removal can still produce some mechanical response. The magnitude of this response remains nearly constant when Na removal is repeated in Ca-free solution containing 0.1–0.5 mM-EGTA, and it is independent of the duration of pre-treatment with Ca-free solution[6]. Na removal might increase the sensitivity of postsynaptic receptors to vasoconstrictive agents and might alter permeability to $Ca^{2+}$[7].

Mg probably stabilize the cell membrane by binding to the outer surface of the membrane and increasing the electrical potential gradient in the region of the activating gates for the voltage-dependent Na channels[8]. Extracelular $Mg^{2+}$ can modulate membrane permeability to $Ca^{2+}$ and their distribution and exchange in vascular smooth muscle[9]. Therefore the dilator effect of Mg may not the results of a direct action on $\beta$-adrenoreceptors, histamine $H_2$ or cholinergic receptors, and this effect may require the presence of an intact endothelium. It has been suggested that Mg exerts relaxant activity by interfering with not only Ca permeability in the cellular membrane but also translocation of Ca within the cell, and there may be an interaction between Mg and Ca during the activity of the contractile proteins[10]. Indeed, Mg in hign concentration can compete with Ca in binding to actomyosin of chicken gizzard[3]. Mg relaxes the contractile proteins of skeletal and cardiac muscle by competing with Ca for their Ca binding sites[11]. These mechanisms are probably true in arterial smooth muscle.

In conclusion, $Mg^{2+}$ suppressed the increase in tension caused by $Ca^{2+}$ or low-$Na^{+}$. And high concentration $Mg^{2+}$ completely inhibited this increase in tension, above 30 mEq·$l^{-1}$ $Mg^{2+}$ inhibited the increase in tension caused by $Ca^{2+}$ and above 20 mEq·$l^{-1}$ $Mg^{2+}$ inhibited the increase in tension caused by low-$Na^{+}$ concentration.

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