牛甲状旁腺素 1–34 舒张兔主动脉的作用

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关键词：牛甲状旁腺素 1–34，BAY k 8644，抗凝血，舒张血管，钙离子

牛甲状旁腺素 (parathyroid hormone, PTH) 可减少外周血管张力，降低动脉血压，增加血管血流。PTH 通过其受体介导的信号通路引起血管平滑肌舒张，我们以往的研究发现 PTH 的作用可能与其对 Ca2+ 运动的改变有关。

本试验选用盲肠横管平滑肌 BAY k 8644 作血管收缩剂，将 BPTH1–34（含牛 PTH 氨基末端 34 个氨基酸的合肽段，具 PTH 全肽的某些生物活性）与已知的钙通道阻断剂硝苯地平 (nitrendipine, NID) 和维拉帕米 (verapamil, VM) 比较，探讨了 BPTH1–34 舒张血管的特性和可能机制。

H2N–Ala–Val–Ser–Glu–Hle–Gln–Phe–Met–His–
Asp–Val–His–Asn–Phe

Bovine parathyroid hormone 1–34

（bPTH1–34）

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材料和方法

bPTH1–34 为 Sigma 公司产品，分子量 4108.7，BAY k 8644 为 Bayer 药物公司，NID 为 Sigma 公司产品，VM 为天坛中药制药厂生产，去甲肾上腺素（N）为美国 Sigma 布南公司产品，其余试剂均为 AR 级。

取大鼠 1 尾，体重 200 g，颈总动脉取血后取胸主动脉，剪成 30×3 mm 之纵切片条，置 37℃ Krebs 溶液，平衡 90 min，每 15min 漓洗一次，置 95% O2 + 5% CO2，pH 7.5±0.1，负荷 0.5 g，无氧条 件作用不含 Ca2+ 并加 EDTA 1 mmol/L 的 Krebs 溶液 10 min，张力变化经机械–电位读数输入生理记录仪。

结果

BAY k 8644 收缩血管的特点

在正常 Krebs 溶液中，BAY k 8644 对离体主动脉条表现双相作用，于 1–1000 mmol/L 范围内收缩血管，强度与剂量相关，约 1 mmol/L 时达最大效应（计 100%），ED50 0.1 mmol/L，r = 0.98，浓度为 2 mmol/L，收缩作用逐渐降低，于 30 mmol/L 时可使主动脉内小剂量 BAY k 8644 诱发的收缩完全恢复。

在含 EDTA 的无 Ca2+ Krebs 溶液中，BAY k 8644
Fig. 1. Effects of BAY k 8644 on rabbit isolated aortic strip in normal (A) or Ca²⁺-free (B) Krebs solutions.

BAY 8644 14不引起收缩, 此时加入CaCl₂, 收缩迅速

Fig. 2. (A) Inhibition effect of BAY 8644 on both the basal tension and contraction induced by BAY 8644 in rabbit isolated aortic strips. (B) A typical recording of the relaxation of aortic strips to BAY 8644 following the contraction induced by BAY 8644.

BAY 8644 降低基础张力和对机BAY 8644

Fig. 3. Inhibition of BAY 8644-induced contraction of rabbit isolated aortic strips by BAY 8644, nifedipine and verapamil. n = 4-6, y ± SD.

BAY 8644 与 Nif、Ver 肾血管作用的比较

BAY 8644 诱导

Fig. 4. Inhibition of 2,8 μmol/L BAY 8644-induced contraction of rabbit isolated aortic strips by BAY 8644, nifedipine and verapamil. n = 4-6, y ± SD.

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Fig 5. (A) Contraction of rabbit isolated aortic strips induced by BAY k 8644 plus 100 mmol/L PTH, 0, 50 or 100 mmol/L in normal Krebs solution, n = 4–5, **P<0.01 vs control.

(B) Double-reciprocal plots

By BAY k 8644 in the largest contractions in terms of strain and time observed with 100 mmol/L PTH, whereas BAY k 8644 alone had only a minor effect. The results suggest that BAY k 8644 may inhibit the activity of calcitonin receptors by a mechanism different from that of PTH.

Discussion

The effects of BAY k 8644 on the responsiveness of aortic strips isolated from rabbits were investigated. The compound exhibited a dose-dependent inhibition of PTH-induced contractions, with an IC50 of approximately 10 μmol/L. In addition, BAY k 8644 was found to be effective in blocking the agonist-induced contractions of aortic strips from rats, with an IC50 of about 1 μmol/L.

References

Relaxation effect of bovine parathyroid hormone 1–34 on rabbit aorta

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ABSTRACT Bovine parathyroid hormone 1–34 (bPTH(1–34)) was studied in rabbit isolated aortic strips. It was found that bPTH(1–34) lowered the basal tension of the aortic strips (IC50 48 μmol/L). Like nifedipine and verapamil, bPTH(1–34) inhibited the contraction induced by BAY K 8644 (1.4 μmol/L) with an IC50 value of 0.95 μmol/L. In contrast, its inhibition of contraction induced by norepinephrine was weak. It is suggested that bPTH(1–34) reduces the tension in vascular smooth muscle by acting mainly on potential sensitive calcium channels to decrease calcium transmembrane influx.

KEY WORDS parathyroid hormone 1–34; BAY K 8644; nifedipine; verapamil; calcium; aorta; vascular smooth muscle