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比较间硝苯地平 and 硝苯地平十二指肠给药对犬冠状动脉血流量、心肌 O₂ 和 CO₂ 的影响¹

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Effects of *m*-nifedipine and nifedipine given intraduodenally on coronary flow, myocardial oxygen, and carbon dioxide metabolism in dogs¹

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ABSTRACT In anesthetized dogs intraduodenal administration of *m*-nifedipine (*m*-Nif) 0.4 mg·kg⁻¹, coronary flow increased from 708±72 to 880±150 ml·min⁻¹·kg⁻¹ (+24%) at 5 min, to 1976±350 ml·min⁻¹·kg⁻¹ (+179%) at 30 min, and to 998±250 ml·min⁻¹·kg⁻¹ (+41%) at 4 h. At the dose of nifedipine (Nif), coronary flow increased from 778±91 to 1080±90 ml·min⁻¹·kg⁻¹ (+39%) at 3 min

and to 1836±280 ml·min⁻¹·kg⁻¹ (+136%) at 90 min. *m*-Nif was more 43% potent than Nif and the duration of action of *m*-Nif was longer. *m*-Nif reduced heart rate by -39%, while Nif reduced only -11%. *m*-Nif increased coronary sinus O₂ content and reduced MVO₂, and no difference was seen between these 2 drugs. However, the rate of CO₂ production with *m*-Nif was reduced to a greater degree than that of Nif. The results indicated that *m*-Nif was more beneficial in alleviating myocardial ischemia than that of Nif.

KEY WORDS *m*-nifedipine; nifedipine; coronary circulation; heart rate; oxygen consumption

摘要 开胸麻醉犬十二指肠给药, *m*-Nif 0.4 mg·kg⁻¹ 增加冠脉流量+179%, 较 Nif +135% 强而持久, (给药 20 min, $P < 0.01$). *m*-Nif 减慢心率-39%, 强于 Nif -11% ($P < 0.001$). *m*-Nif 减少冠状窦 CO₂ 含量-25%, 较 Nif -2.6% 强 ($P < 0.001$). 二药对动脉压、MVO₂, O₂ 摄取率影响无组间差异. 提示 *m*-Nif 对心肌缺血的供血与缺血敏感指标 CO₂ 产生均优于 Nif.

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关键词 间硝苯地平; 硝苯地平; 冠状动脉循环; 心率; O₂消耗

间硝苯地平(*m*-Nif)抑制心肌较硝苯地平(Nif)弱,而松弛血管平滑肌则较之强^[1,2],表现在前者增强心肌泵血功能,降低舒张压及TTI较后者强而持久。*m*-Nif iv增加冠状窦O₂含量弱于Nif,但降低O₂摄取率和CO₂产生率则较强。本文采取十二指肠给药方法,比较二药对冠脉血流量、心肌O₂和CO₂代谢的影响。

MATERIALS AND METHODS

m-Nif和Nif以聚乙二醇400作为溶剂,配成0.2%的浓度,另配不含药物的溶剂作为溶剂对照。实验数据以 $\bar{x} \pm s$ 表示,以*t*检验比较给药前后差别的显著性,组间差别以方差分析。

实验方法参照文献^[1],计算O₂及CO₂代谢指标参照文献^[3]。于右肋下切一小口,将细塑料管插入十二指肠,周围缝一小荷包袋固定之,全部手术结束后待标本稳定30 min,连续测定所需指标三次,作为给药前的正常值。通过小塑料管分别注入*m*-Nif或Nif 0.4 mg·kg⁻¹,以聚乙二醇400 0.2 ml·kg⁻¹作为溶剂对照,溶剂对照组共观察3例,观察期240 min内无显著影响。

RESULTS

对冠状窦血流量的影响 *m*-Nif给药后5 min,冠状窦血流量由708±72 ml·min⁻¹·kg⁻¹增加到880±150 ml·min⁻¹·kg⁻¹ (+24%),给药后30 min,作用达峰值(1976±350 ml·min⁻¹·kg⁻¹) (+179%),作用持续到240 min,血流量仍高于正常水平的41%。Nif给药后3 min血流量明显增加,较*m*-Nif吸收及发挥作用快,由778±91 ml·min⁻¹·kg⁻¹增加到1080±90 ml·min⁻¹·kg⁻¹ (+39%),90 min时达峰值(1836±280 ml·min⁻¹·kg⁻¹) (+136%),Nif的峰值时间较*m*-Nif迟,增加血流量的幅度也较弱,20,30,60 min二药组间差异显著(*P* < 0.05或0.01) *m*-Nif在180 min时冠脉血流量高于原水平55.4%,而Nif已接近原水平。说明*m*-Nif增加冠脉流量较

Nif强而持久(Fig 1)。

对血压、心率的影响 *m*-Nif给药后5 min,平均动脉压开始下降,180 min时下降到最低值,为原水平的52%,同样时间Nif降低到原水平的50%,二者无显著差别。*m*-Nif给药后10 min心率逐渐减慢,至210 min时心率降低到原水平的39%,而Nif减慢心率的作用在60 min时达最低,为原水平的11%,方差分析二药组间差显著。此结果与文献^[4]报道离体心房结果一致。

对O₂及CO₂的影响 从冠状窦O₂分压升高情况分析,给药10 min后,*m*-Nif作用略强于Nif,从10—180 min,*m*-Nif升高O₂分压28%,Nif升高O₂分压20%,二者无组间差别,按O₂摄取率,心肌耗O₂量比较,二药作用强度接近。

10—180 min,*m*-Nif使冠状窦CO₂含量平均下降25%,而Nif为2.6%。*m*-Nif降低CO₂产生率的作用强于Nif (*P* < 0.01)。

DISCUSSION

Gross等^[5]报道Nif舌下含服0.43 mg·kg⁻¹后,3—5 min内,清醒犬冠脉左旋支流量增加64.4%,心率增加62.4%,主动脉压降低5.8%。本文通过十二指肠给药,其吸收发挥作用几乎与舌下给药相似。本文所用Nif剂量与Gross等相近,但冠脉流量增加的幅度(+136%)远大于前者,这是由于本文所用的是麻醉犬,取消了反射的代偿机制且测定的是全心血流量。Nif在扩张外周血管,血压下降时反射性使交感张力升高,部分抵消了它的直接扩张冠脉流量的作用,并使心率加快,但在麻醉状态下,心率却轻度减慢。本文证明麻醉状态下,*m*-Nif减慢心率的作用显著大于Nif,与文献^[4,6]结果一致。*m*-Nif增加冠脉流量显著强于Nif,作用时间长而持久,心率明显减慢,对治疗缺血性心脏病不仅增加供血,而且降低心肌耗O₂量,对缺O₂较敏感的指标,冠状

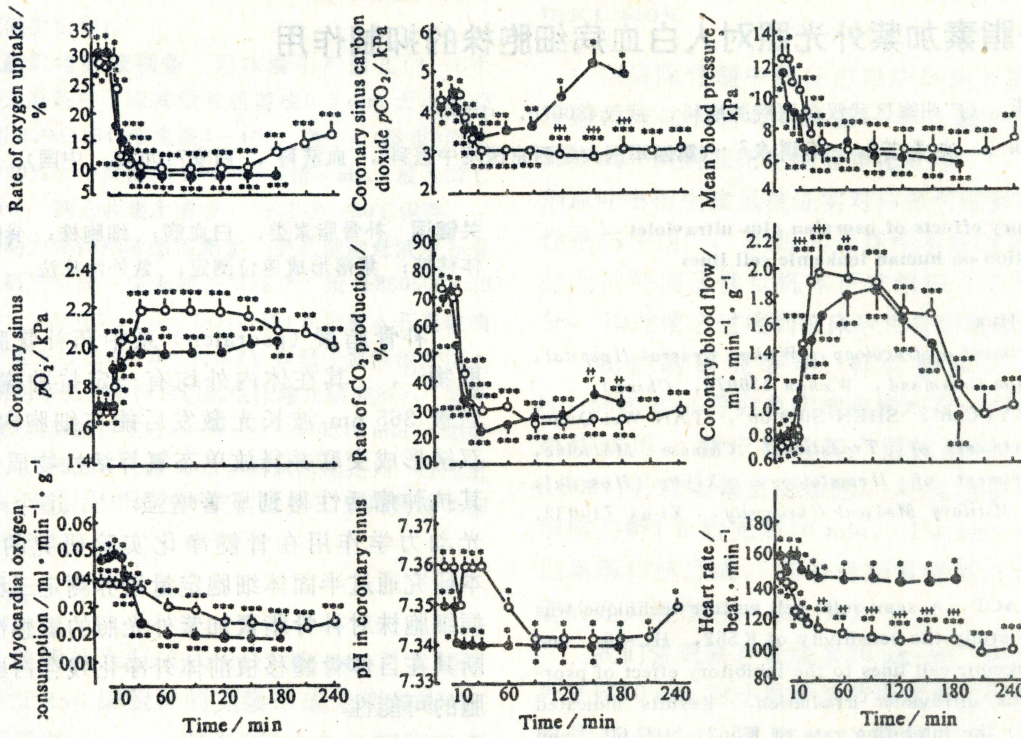


Fig 1. Effects of *m*-Nif (○) and Nif (●) $0.4 \text{ mg} \cdot \text{kg}^{-1}$ given intraduodenally on coronary blood flow, oxygen and carbon dioxide metabolism in 8 anesthetized dogs. $\bar{x} \pm s$. * $P > 0.05$, ** $P < 0.05$, *** $P < 0.01$ vs control. + $P > 0.05$, ++ $P < 0.05$, +++ $P < 0.01$ between two group.

窦 CO_2 含量及 CO_2 产生率的研究结果进一步证实了上述论点, *m*-Nif 改善缺血性心脏病将优于 Nif. 尽管 *m*-Nif 对冠状窦 O_2 含量、心肌耗 O_2 量、 O_2 摄取率的影响与 Nif 无显著差别, 但 Nif 在清醒状态下, 心率加快可部分抵消了其它耗 O_2 降低的作用, 而 *m*-Nif 则否.

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