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姜黄素对小鼠离体十二指肠平滑肌舒缩活动的影响*

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摘要 目的:本研究采用小鼠离体十二指肠平滑肌观察姜黄素对胃肠道蠕动的影 响,探讨其作用机制。**方法:**取小鼠离体十二指肠平滑肌条,放入 37℃ Krebs 液浴槽中,通入 95%氧气和 5%二氧化碳混合气体,分组进行下列实验:对照组和分别加入 10-40 M 姜黄素组,测量记录十二指肠平滑肌的自主收缩变化;另取一组平滑肌条,分对照组、乙酰胆碱组、乙酰胆碱+姜黄素组、阿托品组、阿托品+姜黄素组,采用张力换能器连接多通道生理信号采集处理系统,测量比较十二指肠平滑肌舒缩的变化。**结果:**小鼠十二指肠平滑肌加入姜黄素孵育后,其自主收缩幅度有明显下降($P<0.01$),而且降低的幅度与姜黄素剂量相关;给与乙酰胆碱引起十二指肠收缩后,再加姜黄素孵育,十二指肠平滑肌的收缩幅度明显的下降($P<0.01$);给予阿托品引起小鼠平滑肌舒张后,再给予姜黄素孵育,平滑肌收缩幅度进一步降低。**结论:**姜黄素对小鼠离体十二指肠平滑肌具有直接舒张作用。

关键词:姜黄素;平滑肌;十二指肠;蠕动

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Effects of Curcumin on the Activity of Isolated Duodenal Smooth Muscle of Mice*

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ABSTRACT Objective: This study was to observe the effects of curcumin on the activity of isolated duodenal smooth muscle of mice. **Methods:** The duodenal smooth muscle strips of healthy mice were immediately removed and suspended in thermostatically control organ bath containing Krebs solution and to maintain continuously gassed with 95% O₂ and 5% CO₂. The experimental groups were divided into: Control and 10-40 M curcumin group individually. The spontaneous contraction of the strips was observed after incubated with different concentration of curcumin. Another duodenal smooth muscle strips were divided into: Control, acetylcholine (Ach), Ach+curcumin, atropine, and atropine+curcumin groups. The changes of duodenal contraction or relaxation were observed and compared by tonotransducer connected with signal acquisition system. **Results:** After the duodenal smooth muscle strips were incubated with curcumin in 20 μ mol/L-40 μ mol/L, the mean contractile amplitude of the duodenal smooth muscle strips was significantly reduced ($P<0.05$) in a dose-dependent fashion. After adding Ach to induce duodenal contraction, the mean contractile amplitude of the duodenal smooth muscle was obviously reduced by curcumin ($P<0.05$ or $P<0.01$). After adding atropine to induce duodenal relaxation, the mean contractile amplitude of the duodenal smooth muscle was also reduced ($P<0.05$). **Conclusion:** Curcumin directly induce relaxation on isolated duodenal smooth muscle of mice.

Key words: Curcumin; Smooth muscle; Duodenum; Peristalsis

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前言

本室前期研究显示,姜黄素整体灌胃给药可以显著减轻胆

铂、阿托品等引起的小鼠胃肠蠕动功能障碍,促进胃排空和小肠蠕动^[1,2],这种作用是通过姜黄素吸收代谢后产生,还是姜黄素本身对胃肠道有刺激作用目前还不清楚。本研究采用姜黄素

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直接作用于小鼠离体十二指肠平滑肌条,拟观察姜黄素是否对肠道运动有直接刺激作用,以及在肠道收缩和舒张时姜黄素的影响,以推断姜黄素的作用途径和机制。

1 材料和方法

1.1 实验动物和平滑肌条制备

选用雄性昆明种小鼠,体质量 22-25 g,购自山东鲁抗医药股份有限公司质监中心实验动物室(合格证号 0016092)。实验前禁食十二小时后脱臼处死小鼠,分离和剪取距幽门 2-4 cm 处一段十二指肠,刮除肠段表面肠系膜,制成 2.5 cm× 0.5 cm 的平滑肌条。

1.2 离体平滑肌条实验

将小鼠离体十二指肠平滑肌条,放入 37℃ Krebs 液浴槽中,通入 95%氧气和 5%二氧化碳混合气体,分组进行下列实验:对照组、10、20、30、40 μM 的姜黄素组(Sigma 公司),通过多道生理信号采集处理系统测量记录十二指肠平滑肌的张力变化;另取十二指肠平滑肌条分为对照组、乙酰胆碱组、乙酰胆碱 + 姜黄素(20 μM)组、阿托品组和阿托品 + 姜黄素(20 μM)组,然后通过生理信号采集系统观察比较十二指肠平滑肌的张力变化。

1.3 统计学分析

实验数据以均数± 标准差 ($\bar{X}+S$) 表示,运用 Graphpad Prism 3.0 软件分析,方差齐性采用 LSD 检验,姜黄素处理前后收缩波振幅数值构成配对资料应用配对 t 检验。多组资料之间指标两两比较采用单因素方差分析 (ANOVA), $P<0.05$ 有统计学意义。

2 结果

2.1 姜黄素对十二指肠自主收缩活动的影响

20 μM/40 μM 姜黄素孵育能够显著的抑制十二指肠肌条的自主收缩活动,小鼠十二指肠平滑肌条自主收缩波平均振幅明显降低($P<0.05$ or $P<0.01$)(表 1)。

2.2 姜黄素对 Ach 收缩十二指肠的影响

Ach 孵育的十二指肠离体平滑肌条收缩兴奋,收缩曲线波振幅增大($P<0.05$),加入 20 μM 姜黄素后小鼠离体肌条收缩波振幅明显减小($P<0.01$),而更换新鲜 Krebs 液后离体肌条收缩波振幅恢复(表 2)。

2.3 姜黄素对阿托品舒张十二指肠的影响

阿托品孵育的十二指肠离体平滑肌条舒张,收缩曲线波振幅明显减小($P<0.01$),加入 20 μM 姜黄素后小鼠离体肌条收缩波振幅进一步减小($P<0.05$),而更换新鲜 Krebs 液后离体肌条收缩波振幅恢复(表 2)。

表 1 不同浓度姜黄素对小鼠十二指肠肌条收缩平均振幅的影响($\bar{X}+S$; n=6)

Table 1 Effects of different concentrations of curcumin on the contracted average amplitude of duodenal muscle strips in mice($\bar{X}+S$; n=6)

Group	Contracted average amplitude(g)
Control	0.33± 0.05
Curcumin10 μM	0.28± 0.07
Curcumin20 μM	0.22± 0.07*
Curcumin30 μM	0.19± 0.06*
Curcumin40 μM	0.17± 0.05**

注:*.与对照组比, $P<0.05$,**.与对照组比, $P<0.01$ 。

Note*:Compared with control group, $P<0.05$,**:Compared with control group, $P<0.01$.

表 2 姜黄素对 Ach/ 阿托品诱导的十二指肠收缩 / 舒张波平均振幅的影响($\bar{X}+S$; n=6)

Table 2 Effect of curcumin on the average amplitude of contraction/ diastole induced by Ach/ atropine($\bar{X}+S$; n=6)

Group	Contracted average amplitude(g)
Control	0.33± 0.05
Ach	0.42± 0.07*
Curcumin+ Ach	0.29± 0.06##
Atropine	0.21± 0.07**
Curcumin+Atropine	0.13± 0.04\$

注:*.与对照组比, $P<0.05$,**.与对照组比, $P<0.01$ 。

Note*:Compared with control group, $P<0.05$,**:Compared with control group, $P<0.01$.

3 讨论

姜黄素是从姜黄中提取的一中酚类化合物,在我国主要被用于食物色素。研究显示姜黄素具有抗炎、抗氧化、抗肿瘤等多种作用,而且不良反应少,无毒、副作用已成为世界卫生组织和美国食品药品监督管理局等组织认定的安全药物^[3,4]。姜黄素对于胃

肠道的影响,国内外有少量研究显示,姜黄素可以减轻大、小鼠胃溃疡模型的胃粘膜损伤^[5-8]、肠炎模型肠粘膜的损伤^[9-11]。国内学者在复制的大鼠小肠炎模型中发现姜黄素可以改善肠黏膜的通透性^[12],对大鼠小肠炎具有保护作用。本实验室先前实验研究发现姜黄素灌胃能够显著改善化疗药物顺铂所致的小鼠胃肠道功能障碍,减轻胃内容物残留,增加胃肠蠕动^[1,13],提示姜

黄素整体给药有改善胃肠运动的功能,进一步研究显示,预先给予姜黄素灌胃,可以减轻阿托品和一氧化氮造成的胃肠蠕动减慢^[2],说明在胃肠蠕动功能障碍时姜黄素有促进胃肠运动的功能。为了验证姜黄素是否有直接刺激胃肠蠕动的作用,本研究采用离体十二指肠平滑肌条直接给予姜黄素孵育,观察和记录了平滑肌张力的变化。结果显示,姜黄素呈剂量依赖性的抑制小鼠十二指肠的自发收缩活动,而且在乙酰胆碱收缩十二指肠和阿托品舒张十二指肠的情况下,姜黄素都能使平滑肌张力减弱,说明姜黄素对于十二指肠的直接作用是舒张平滑肌,从而减弱其蠕动能力。这与整体灌胃给药的结果相反,说明姜黄素局部和整体给药会产生不同的作用。整体灌胃给药,姜黄素要经历胃肠道的消化和吸收,在体内的代谢产物可能产生了与姜黄素直接作用于肠道平滑肌不同的作用。整体实验结果中同等剂量灌胃 1-5 天无效,10-15 天才产生了明显的改善胃肠蠕动的作用^[14],也充分说明整体给药所产生的功能可能不是姜黄素的直接作用所致。

国内外关于姜黄素对胃肠蠕动作用研究报道极少,机制研究几乎是空白。巴勒斯坦学者研究发现姜黄粗提物舒张兔离体空肠自主性和 K^+ 诱导的收缩,同时改变 $CaCl_2$ 浓度反应曲线,姜黄的这种作用主要是由钙通道阻滞介导的^[15]。近期意大利学者离体实验发现,姜黄提取物能够减少小鼠回肠和结肠平滑肌条自发收缩活动^[16],虽然并没有揭示姜黄的作用机制,但是至少证明不是通过抗炎作用。上述离体研究结果与本研究结果类似,说明姜黄素直接作用于离体十二指肠平滑肌具有舒张的作用。日本学者研究发现,食入含姜黄的米饭可以增加人肠道呼吸氢浓度,小肠运输时间缩短,认为姜黄素可增强小肠运动^[17]。姜黄素对胃肠活动在整体和离体状态下的差异,提示我们今后在姜黄素的实验研究和临床应用中要充分考虑姜黄素的给药方式和剂型^[18],才能真正发挥姜黄素应有的作用。近期国内外学者利用纳米技术研究的姜黄素剂型^[19,20]给姜黄素的应用提供了广阔的前景。

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而下降,为防止老年 2 型糖尿病低血糖的发生,应提高血糖监测的重视程度,根据患者病情的实际需要来制定血糖监测的频率以及时间。⑤心理护理及健康指导 有关糖尿病的调查^[19,20]显示,多数患者存在焦虑、忧郁等心理障碍,医护人员应加强对患者及其家属的指导及心理护理,帮助他们正确认识糖尿病,接受规范的治疗;需告知家属常探视老人,让老人感受到亲人的陪伴和支持,使患者树立战胜疾病的信心。

综上所述,老年 2 型糖尿病患者住院期间血糖的控制需患者本人主观努力,更需医护人员的指导、帮助和关注以及对患者血糖水平的及时有效的检测,从而将老年 2 型糖尿病患者的血糖控制在理想水平。

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