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注射用双黄连类过敏反应物质及作用机制研究

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中文摘要:目的:探讨注射用双黄连(SHLI)发生类过敏反应的物质基础及其作用机制。方法:①类过敏反应和致类过敏物质研究:ICR小鼠随机分成不同实验组,分别一次性静脉注射含有0.4%伊文思蓝的不同浓度的SHLI、黄芩苷溶液、连翘苷溶液、绿原酸溶液、Compound 48/80溶液或生理盐水给药后30 min记录各组药物耳廓血管通透性增高反应的阳性和进行耳廓蓝染程度评分并定量测定耳廓伊文思蓝染出量。②类过敏机制研究:将小鼠分别预先口服不同剂量的连翘苷、黄芩苷注射环磷酰胺或Compound 48/80后,再静脉注射含有0.4%伊文思蓝的SHLI,同前述方法观察耳廓蓝染情况,将预处理组与同剂量SHLI组比较。结果:① SHLI 300,600 mg · kg<sup>-1</sup> (分组相当)于耳廓重量的加倍和2倍剂量静脉注射均可引起小鼠耳廓血管通透性增高,耳廓明显蓝染,但相当于SHLI临床2倍剂量的连翘苷、黄芩苷和绿原酸静脉注射均未造成小鼠耳廓血管通透性增高。②预先口服连翘苷或黄芩苷600 mg · kg<sup>-1</sup> (造成的小鼠耳廓血管通透性增高程度明显减轻)预先腹腔注射环磷酰胺后,血管通透性增高程度有轻度减轻,而预先腹腔注射Compound 48/80后,血管通透性增高程度没有明显变化。结论:SHLI在临床等效剂量和2倍临床剂量下有明显增高血管通透性的作用,提示有致类过敏作用。由SHLI的主要成分为连翘苷、黄芩苷和绿原酸可能不是造成SHLI发生类过敏反应的主要物质,SHLI发生类过敏反应的主要机制可能与直接刺激组胺的生成增加有关,白细胞激活可能参与了SHLI的致类过敏反应。抗组胺药可部分预防SHLI的类过敏反应。

中文关键词:类过敏反应 注射用双黄连 物质基础 反应机制 血管通透性

## Material and mechanisms for evaluation of Shuanghuanglian injection induced pseudoanaphylactoid reactions

**Abstract:** Objective: To investigate the substance basis and the mechanism of pseudoanaphylactoid reactions (PR) induced by Shuanghuanglian injection (SHLI). Method: (1)The study of PR and the substance basis of PR of SHLI: ICR mice were divided into different test groups, the mice were intravenously injected with solutions of different concentration of SHLI, baicalin, frysophytin, caffetoinic acid, positive control Compound 48/80 and normal sodium. All test substances were mixed with 0.4% Evans blue. The reaction and vascular permeability of the ears were observed and measured 30 min after SHLI injection. (2)The study of mechanisms: Mice were pretreated with an oral administration of Astemizol, intraperitoneal injection of cyclophosphamide 75 mg · kg<sup>-1</sup> or Compound 48/80 4 mg · kg<sup>-1</sup>, then mice were orally administered with SHLI. At last, vascular permeability of the ears in pretreated groups was compared with SHLI treatment alone group. Result: SHLI of 300 mg · kg<sup>-1</sup> and 600 mg · kg<sup>-1</sup> caused obvious vascular hyperpermeability, but baicalin, frysophytin and caffetoinic didn't cause vascular hyperpermeability in the ears. The Astemizol can decrease the degree of SHLI-induced vascular hyperpermeability of the ears in the mice. After intraperitoneal injected with cyclophosphamide, there was a slight decrease in the degree of SHLI-induced vascular hyperpermeability, but there was no marked changes in the degree of the SHLI-induced vascular hyperpermeability after the mice were pretreated with Compound 48/80. Conclusion: SHLI in clinic equivalent dose can cause vascular hyperpermeability. Baicalin, frysophytin and caffetoinic may not result in the PR of SHLI. The mechanism of the PR maybe relate to that SHLI stimulates histamine release, the activation of leucocyte maybe take part in the SHLI-induced PR, too. Antihistamine drug can prevent the genesis of PR which induced by SHLI.

Keywords: pseudoanaphylactoid reactions Shuanghuanglian injection sensitizer mechanism vasopermeability

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