

金蛤口服液对环磷酰胺所致血虚模型小鼠外周血象及记忆功能的影响^Δ

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摘要 目的:研究金蛤口服液对血虚模型小鼠外周血象及记忆功能的影响。方法:给予小鼠腹腔注射环磷酰胺 50 mg/kg 和照射 X 射线复制血虚模型。实验分为空白对照(等容生理盐水)、模型(等容生理盐水)、红参黄芪(10 g/kg)与金蛤口服液高、中、低剂量(53、26.5、13.3 g/kg)组,灌胃给药,每天 1 次,连续 21 d。给药第 14 天和第 21 天测定小鼠外周血象。血虚模型小鼠腹腔注射氢溴酸东莨菪碱 4 mg/kg 致记忆受损,记录小鼠跳台实验中潜伏期、错误次数。结果:给药第 14 天,与空白对照组比较,模型组白细胞(WBC)、红细胞(RBC)显著减少($P < 0.05$);与模型组比较,金蛤口服液高、中、低剂量组小鼠 WBC 显著增加,金蛤口服液高、中剂量组 RBC 显著增加($P < 0.05$)。给药第 21 天,与空白对照组比较,模型组 WBC、RBC、血红蛋白(HGB)显著减少($P < 0.05$);与模型组比较,金蛤口服液高、中、低剂量组小鼠 WBC 显著增加,金蛤口服液高剂量组 RBC 显著增加,金蛤口服液高、低剂量组 HGB 显著增加($P < 0.05$)。与空白对照组比较,模型组潜伏期显著缩短,错误次数显著增加($P < 0.05$);与模型组比较,金蛤口服液高、中、低剂量组潜伏期显著延长,错误次数显著减少($P < 0.05$)。结论:金蛤口服液对血虚模型小鼠外周血细胞状况尤其是白细胞有明显的改善作用,对小鼠记忆功能可能有改善作用。

关键词 金蛤口服液;外周血象;记忆功能;血虚模型

Influences of Jinha Oral Liquid on Peripheral Blood and Memory Function in Model Mice of Hematopenia Induced by Cyclophosphamide

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ABSTRACT OBJECTIVE: To study the influences of Jinha oral liquid on peripheral blood and memory function in model mice of hematopenia induced by cyclophosphamide. METHODS: Deficiency of blood mice model was induced by cyclophosphamide 50 mg/kg intraperitoneally and irradiated with X-rays cyclophosphamide. Mice were divided into blank control group (constant volume of normal saline), model group (constant volume of normal saline), *Panax ginseng* Astragali Radix group (10 g/kg) and Jinha oral liquid high-dose, medium dose and low-dose groups (53, 26.5, 13.3 g/kg). They were given medicine intragastrically once a day for consecutive 21 days. Peripheral hemogram of mice was determined on 14th and 21th day. Memory impairment blood model mice was given scopolamine hydrobromide 4 mg/kg intraperitoneally, latent period and error number of step-down test were recorded. RESULTS: Compared with blank control group, white blood cells and red blood cells counts in model group were significantly lowered ($P < 0.05$) on 14th. Compared with model group, white blood cells in Jinha oral liquid high-dose, medium dose and low-dose groups were significantly highered, and red blood cells counts Jinha oral liquid high-dose, medium dose groups were significantly highered ($P < 0.05$) on 14th. Compared with blank control group, white blood cells, red blood cells and hemoglobin counts in model group were significantly lowered ($P < 0.05$) on 21th. Compared with model group, white blood cells counts in Jinha oral liquid high-dose, medium dose and low-dose groups were highered significantly highered, red blood cells counts Jinha oral liquid high-dose dose group were highered significantly highered, and hemoglobin counts in Jinha oral liquid high-dose and low-dose groups were highered significantly ($P < 0.05$) on 21th. Compared with blank control group, latent period in model group were shortened and error number of step-down test were increased significantly ($P < 0.05$). Compared with model group, latent period were longhened in Jinha oral liquid high-dose, medium dose and low-dose groups, and error number of step-down test were decreased significantly ($P < 0.05$). CONCLUSION: Jinha oral liquid can improve peripheral blood of mice model of hematopenia induced by cyclophosphamide, especially white blood cells, and also improve the memory function.

KEY WORDS Jinha oral liquid; Peripheral blood; Memory function; Hematopenia model

金蛤口服液配方源于壮族地区,为民间验方,由金鱼、河

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蚌、刺参、银耳等组成,具有补虚解毒、止血止痛、软坚散结之功效,主要用于白血病等恶性肿瘤的治疗^[1]。该制剂已被广西食品药品监督管理局批准为医院制剂,临床上已用于 60 例急性白血病(AL)的治疗,在缓解 AL 临床症状方面疗效确切,毒副作用低。多数肿瘤患者经过长期的放、化疗,会出现免疫抑制、骨髓抑制等毒副作用,思维、学习与记忆方面也会有一定减弱^[2]。而按壮医理论,白血病多为气血虚弱所致^[3],故笔者运

用注射环磷酰胺致化学损伤法和照射X射线致放射性损伤法复制小鼠血虚模型,给药后测定各项指标变化,以研究金蛤口服液对小鼠放射损伤的保护作用及对记忆功能的改善作用,为临床应用提供可靠的实验依据。

1 材料

1.1 仪器

Tu-1901型双光束紫外-可见分光光度计(北京普析通用仪器有限公司)。

1.2 药品

金蛤口服液(南宁市第二人民医院制备,批号:20120704,规格:10 ml/支);注射用环磷酰胺(山西普德药业有限公司,批号:20080101,规格:0.2 g/支);氢溴酸东莨菪碱注射液(上海禾丰制药有限公司,批号:20090302,规格:0.3 mg/支)。

1.3 动物

昆明种纯系小鼠144只,♀♂兼半,体质量(20±2)g,由广西中医学院实验动物中心提供[动物生产合格证号:(桂)医动字11004]。

2 方法

2.1 金蛤口服液对模型小鼠外周血象的影响

2.1.1 分组与给药 实验分为6组,即空白对照(等容生理盐水)、模型(等容生理盐水)、红参黄芪(10 g/kg)与金蛤口服液高、中、低剂量(53、26.5、13.3 g/kg)组。ig给药,每天1次,连续21 d。

2.1.2 模型的复制 ig给药7 d后,第8天除空白对照组外其余各组小鼠照射X射线。照射剂量:2 Gy;照射距离:100 cm;照射时间:2 min 16 s。每天1次,连续14 d。ig给药3 d后,第4天除空白对照组外其余各组小鼠ip环磷酰胺50 mg/kg,每天1次,连续3 d。

2.1.3 指标的测定 ig给药14 d后,眼球取血测血常规[白细胞(WBC)、红细胞(RBC)、血红蛋白(HGB)、血小板(PLT)]。末次给药1 h后,小鼠称体质量,眼球取血测血常规。

2.2 金蛤口服液对模型小鼠在跳台实验中潜伏期和错误次数的影响

2.2.1 分组与给药 分组、给药方法同“2.1.1”项下。

2.2.2 血虚小鼠记忆受损模型的复制 模型的复制方法同“2.1.2”项下。训练前10 min ip氢溴酸东莨菪碱(4 mg/kg)致小鼠记忆受损。空白对照组ip生理盐水。

2.2.3 跳台法 末次给药1 h后开始训练。20 min后将小鼠放入未通电的铜栅上,先适应环境3 min,再通以36 V交流电,训练5 min并记录5 min内的错误次数(两前足同时接触铜栅而遭到电击)和触电潜伏期(将小鼠放在载台上,通电后小鼠第一次跳下台的时间)。24 h后重新测试并记录触电潜伏期和5 min内的错误次数。

2.3 统计学方法

采用SPSS 10.0统计软件,结果以 $\bar{x} \pm s$ 表示,组间比较采用t检验。 $P < 0.05$ 为差异有统计学意义。

3 结果

3.1 小鼠外周血象检测结果

ig给药14 d后,与空白对照组比较,模型组小鼠血液WBC、RBC显著减少($P < 0.05$);与模型组比较,金蛤口服液高、中、低剂量组小鼠血液WBC显著增加,金蛤口服液高、中剂量组RBC显著增加($P < 0.05$)。ig给药21 d后,与空白对照

组比较,模型组小鼠血液WBC、RBC、HGB显著减少($P < 0.05$);与模型组比较,金蛤口服液高、中、低剂量组小鼠血液WBC显著增加,金蛤口服液高剂量组小鼠血液中RBC显著增加,金蛤口服液高、低剂量组HGB显著增加($P < 0.05$)。小鼠外周血象检测结果见表1、表2。

表1 第14天小鼠外周血象检测结果($\bar{x} \pm s, n = 12$)

组别	WBC, $\times 10^9 L^{-1}$	RBC, $\times 10^{12} L^{-1}$	HGB, g/L	PLT, $\times 10^9 L^{-1}$
空白对照组	6.165 ± 0.88	9.064 ± 0.44	130.933 ± 5.97	1 226.533 ± 110.38
模型组	3.179 ± 1.41 [*]	8.425 ± 0.60 [*]	131.625 ± 12.60	1 129.375 ± 125.90
金蛤口服液高剂量组	5.665 ± 1.66 [#]	9.606 ± 0.67 [#]	140.500 ± 11.60	1 176.750 ± 125.08
金蛤口服液中剂量组	4.220 ± 0.56 [#]	9.504 ± 0.46 [#]	137.800 ± 9.51	1 154.000 ± 94.42
金蛤口服液低剂量组	6.482 ± 1.21 [#]	9.061 ± 1.42	134.412 ± 18.34	1 154.235 ± 102.88
红参黄芪组	4.235 ± 0.41 [#]	9.894 ± 1.11 [#]	145.643 ± 10.49 [#]	1 079.500 ± 104.40

与空白对照组比较: * $P < 0.05$;与模型组比较: # $P < 0.05$

vs. blank control group: * $P < 0.05$; vs. model group: # $P < 0.05$

表2 第21天小鼠外周血象检测结果($\bar{x} \pm s, n = 12$)

组别	WBC, $\times 10^9 L^{-1}$	RBC, $\times 10^{12} L^{-1}$	HGB, g/L	PLT, $\times 10^9 L^{-1}$
空白对照组	6.097 ± 1.26	9.606 ± 1.35	148.929 ± 24.18	1 246.571 ± 258.19
模型组	2.904 ± 1.22 [*]	8.489 ± 0.56 [*]	135.500 ± 12.88 [*]	1 236.071 ± 243.17
金蛤口服液高剂量组	4.300 ± 0.77 [#]	9.630 ± 0.94 [#]	151.176 ± 16.92 [#]	1 176.529 ± 180.42
金蛤口服液中剂量组	4.621 ± 1.38 [#]	9.116 ± 0.86	141.059 ± 10.91	1 034.647 ± 174.29
金蛤口服液低剂量组	5.462 ± 0.73 [#]	8.741 ± 0.58	150.353 ± 12.90 [#]	1 041.353 ± 198.42
红参黄芪组	3.815 ± 1.25 [#]	9.452 ± 0.70 [#]	151.786 ± 12.94 [#]	1 225.571 ± 160.41

与空白对照组比较: * $P < 0.05$;与模型组比较: # $P < 0.05$

vs. blank control group: * $P < 0.05$; vs. model group: # $P < 0.05$

3.2 小鼠跳台实验结果

两次记录中,与空白对照组比较,模型组小鼠潜伏期显著缩短,错误次数显著增加($P < 0.05$);与模型组比较,金蛤口服液高、中、低剂量组小鼠潜伏期显著延长,错误次数显著减少($P < 0.05$)。小鼠跳台实验结果见表3。

表3 小鼠跳台实验结果($\bar{x} \pm s, n = 12$)

组别	n	第1次记录		第2次记录	
		潜伏期, s	错误次数, 次	潜伏期, s	错误次数, 次
空白对照组	12	126.08 ± 91.91	1.83 ± 1.59	102.27 ± 45.54	2.455 ± 2.07
模型组	12	62.42 ± 31.49 [*]	4.00 ± 1.91 [*]	60.27 ± 25.08 [*]	5.091 ± 3.18 [*]
金蛤口服液高剂量组	12	107.42 ± 53.50 [#]	1.83 ± 1.53 [#]	105.82 ± 55.43 [#]	2.818 ± 2.18 [#]
金蛤口服液中剂量组	12	116.17 ± 63.84 [#]	2.33 ± 1.97 [#]	106.00 ± 54.56 [#]	2.545 ± 1.69 [#]
金蛤口服液低剂量组	12	107.33 ± 60.70 [#]	2.67 ± 2.67 [#]	106.27 ± 53.85 [#]	2.727 ± 2.49 [#]
红参黄芪组	12	125.67 ± 81.37 [#]	1.00 ± 1.29 [#]	109.55 ± 63.39 [#]	2.667 ± 2.38 [#]

与空白对照组比较: * $P < 0.05$;与模型组比较: # $P < 0.05$

vs. blank control group: * $P < 0.05$; vs. model group: # $P < 0.05$

4 讨论

放、化疗是目前治疗白血病的主要手段,在治疗过程中往往联合使用,但其副作用如免疫抑制、骨髓抑制等严重,以致患者身体无法承担。金蛤口服液作为民间验方,可治疗白血病,但其具体的作用机制仍不清楚。笔者通过给予小鼠注射环磷酰胺与照射X射线复制免疫低下模型,研究了金蛤口服液对放、化疗中血虚模型小鼠的保护作用。

环磷酰胺作为临床常用抗肿瘤化疗药物,其作用在于破坏骨髓造血微环境,从而导致外周血细胞数量减少,而外周血细胞数量变化在一定程度上反映了骨髓造血功能变化^[4-6]。放

黄芩素滴丸对大鼠的急性毒性实验研究[△]

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摘要 目的:研究黄芩素滴丸对大鼠的急性毒性。方法:实验分为对照(等容纯化水)与黄芩素滴丸高、中、低剂量(1.0、0.5、0.25 g/kg)组。灌胃给药,每天1次,连续12周。测定给药12周和停药4周后大鼠各项指标。结果:在12周给药期间,黄芩素滴丸高、中、低剂量组大鼠一般状况良好,行为活动正常,无异常外观体征,大鼠排尿、排便、饮水、摄食量及一般体征与对照组比较无显著性差异。给药12周后,黄芩素滴丸中剂量组血红蛋白显著高于对照组($P<0.05$),血糖、总胆红素显著低于对照组($P<0.01$ 或 $P<0.05$)。停药4周后,黄芩素滴丸高剂量组总蛋白显著低于对照组($P<0.05$)。结论:黄芩素滴丸在1.0、0.5、0.25 g/kg剂量下连续给药12周,对大鼠排尿、排便、饮水、摄食量、血常规、尿常规、血液生化学指标无明显影响。

关键词 黄芩素;滴丸;口服给药;生化指标

Study on Acute Toxicity of Baicalin Dripping Pills on Rats

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ABSTRACT OBJECTIVE: To study on acute toxicity of Baicalin dripping pills on rats. METHODS: The experimental rats were divided into control group (constant volume of purified water), Baicalin dripping pills high-dose, medium-dose and low-dose groups (1, 0.5, 0.25 g/kg). They were given medicines intragastrically once a day, for 12 consecutive weeks. The indexes were tested after 12 weeks of administration and 4 weeks after drug withdrawal. RESULTS: During 12 weeks, rats of Baicalin dripping pills high-dose, medium-dose and low-dose groups were in good condition, and the activities of them were normal without abnormal signs and appearance. There was no significant difference in defecation, urination, drinking water, food and general symptoms between high-dose, medium-dose and low-dose groups and control group. Compared with control group, HGB in Baicalin dripping pills medium-dose groups increased significantly ($P<0.05$), Glu and TBili decreased significantly ($P<0.01$, $P<0.05$) after 12 weeks of administration. TP in Baicalin dripping pills high-dose groups decreased significantly ($P<0.05$) 4 weeks after drug withdrawal. CONCLUSION: Baicalin dripping pills 1, 0.5 and 0.25 g/kg have no obvious effect on the urination, defecation, drinking water and food intake after 12 weeks continuous administration.

KEY WORDS Baicalin; Dripping pills; Oral administration; Biochemical index

射治疗因其“敌我不分”的特点,在杀死肿瘤细胞的同时,亦对正常细胞造成损伤,尤其是分裂、增殖比较快的细胞如骨髓造血细胞、胃肠道黏膜上皮细胞等。本研究结果显示,金蛤口服液对模型小鼠的血细胞降低有明显的改善作用,说明其可有效地降低放、化疗对血虚小鼠造血功能的抑制作用。

记忆过程依次为记忆获得、巩固,最后是再现,多次反复予以刺激往往会加强记忆。跳台实验主要反映动物空间位置感和方向感的学习记忆能力。根据记忆形成的特点,模型组出现相对于空白对照组潜伏期缩短和错误次数增加的现象;金蛤口服液高、中、低剂量组与模型组比较,潜伏期延长,错误次数减少,证实了金蛤口服液对血虚模型小鼠记忆认知的改善作用。

本研究结果显示,金蛤口服液对血虚模型小鼠外周血血细胞状况尤其是白细胞有明显的改善作用,对小鼠认知记忆

能力可能有一定改善作用。

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