

# “拮氟锐”对氟拮抗作用的现场试验研究\*

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**提 要** 80名连续氟暴露5年以上的工人,按班组分为A、B两组;同样以非氟暴露工人20名为C组。A组42人口服拮氟锐复方剂,B组38人未服药,均不脱离生产岗位,进行为期一个月的现场试验观察。结果表明,与未服药对照组比较,服药组工人尿中氟及氟硼酸根含量及排出量明显增高,血清碱性磷酸酶活性下降,血清Zn、Cu含量增加,红细胞免疫粘附能力明显增强。提示拮氟锐有较明显的预防氟损伤效应。

**关键词** 氟暴露 拮氟锐 抗氟作用

过量氟可引起机体多功能、多系统损伤。在我国,不仅地氟病流行严重,且工业性氟暴露所引起的氟损伤亦愈来愈为人们重视。目前,对氟病的防治,尤其是药物防治仍是一个亟待解决的环节。我们研制的拮氟锐复方剂,经动物实验研究结果表明,拮氟锐有明显的抗氟毒性作用<sup>[1]</sup>。为此,本文进一步对氟暴露工人在不脱离生产岗位情况下,进行现场试验观察,目的在于探讨拮氟锐有否预防性抗氟损伤的作用。

## 1 对象与方法

**1.1 对象** 某厂电解铝车间防护措施较差,车间空气氟浓度平均在1.46~2.30mg/m<sup>3</sup>。选择连续氟暴露工龄5年以上男性电解工80名,按班次分为A、B两组,A组42例为服药组,B组38例为未服药组;非氟暴露工龄5年以上的修配车间男性工人20名为C组。

**1.2 药物剂量与用法** (1) 药物剂量是经实验筛选,并观察药物毒性与功效后确定的;(2) 本药物是由中药煎剂、硼及微量元素等

成份配制而成的复方剂。均不脱离生产岗位,服药组每人每天一剂,每剂40ml,在上班时跟班送药,5班4倒,休息天停药,连续一个月,由专人负责追踪观察。

**1.3 观察指标** 各组统一时间收取24小时尿样和班前血样进行组间比较分析:(1) 24小时尿 F<sup>-</sup>、BF<sub>4</sub><sup>-</sup> 含量(离子选择性电极法);(2) 血清碱性磷酸酶活性(金氏法试剂盒);(3) 血清红细胞免疫粘附抑制因子及促进因子活性(花环法);(4) 血清微量元素 Cu、Zn、Ca、Mg 含量(原子吸收法)。

## 2 结果

**2.1 24小时尿F<sup>-</sup>、BF<sub>4</sub><sup>-</sup>测定** 收集较全的62例尿样检测结果表明,氟暴露组24小时尿F<sup>-</sup>、BF<sub>4</sub><sup>-</sup>含量及排出量均明显高于非氟暴露组(P<0.01)。在氟暴露工人中,服药组工人尿氟较高于未服药组,但差异不显著(P>0.05);服药组尿BF<sub>4</sub><sup>-</sup>含量及排出量则明显高于未服药组(表1),差异非常显著(P<0.01),使尿氟总排出量明显增加。

表1 各组24小时尿氟及氟硼酸根测定结果比较( $\bar{X} \pm S$ )

组别	例数	尿F <sup>-</sup>		尿BF <sub>4</sub> <sup>-</sup>	
		μmol/L	μmol/d	μmol/L	μmol/d
A	23	58.95 ± 25.79	95.79 ± 56.32	71.89 ± 10.83*	110.14 ± 16.94*
B	31	48.42 ± 11.58	70.53 ± 35.26	36.29 ± 5.53	54.26 ± 8.29
C	8	26.84 ± 5.63	46.68 ± 18.42	28.80 ± 2.19	48.96 ± 3.11

\* A组与B、C组比较P<0.01

**2.2 血清AKP及BUN测定** 结果表明,非氟暴露组工人血清碱性磷酸酶活性为12.98 ± 2.13金氏单位,氟暴露工人AKP较高(14.47 ±

\* 中国有色金属总公司“八五”项目

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2.31),而服药组工人AKP明显降低(11.40±2.80);A组与B组比较,差异有极显著性(P<0.01),C组与B组比较差异亦有显著意义(P<0.05),但A组与C组无明显差异(P>0.05)。BUN在各组间无明显差异。

2.3 红细胞免疫粘附因子活性测定 结果表明(表2):(1)氟暴露工人血清红细胞免疫粘附抑制因子活性明显增高,与非氟暴露组比较差异非常显著(P<0.01);而服药组工人血清RFIR明显低于氟暴露组(P<0.01),说明拮氟锐对其的抑制作用。(2)红细胞免疫粘附促进因子(RFER)活性在各组间无明显差异(P>0.05)。

表3 各组血清微量元素检测结果( $\bar{X} \pm S$ )

组别	例数	Cu <sup>++</sup> ( $\mu\text{mol/L}$ )	Zn <sup>++</sup> ( $\mu\text{mol/L}$ )	Ca <sup>++</sup> (mmol/L)	Mg <sup>++</sup> (mmol/L)
A	37	18.88±3.46*	20.19±6.73**	2.69±0.97***	0.79±0.28
B	20	16.84±3.77	14.21±7.14	2.62±0.77***	0.91±0.23
C	20	17.31±4.12	15.48±7.09	2.06±0.45	0.94±0.30

A组与B组比较 \* P<0.05, \*\* P<0.01; \*\*\* A、B组与C组比较P<0.05

3 讨论

对氟拮抗剂的研究认为硼有一定的排氟作用<sup>[27]</sup>,摄入一定量的硼对健康人并无直接影响<sup>[4~6]</sup>。Grunewald的研究认为,氟暴露工人每天摄入10~20mgB<sup>+++</sup>能以硼络合物形式从尿排出<sup>[6]</sup>。而过量氟摄入,对机体可产生多功能、多系统的损伤。为探讨既能排氟又有抗氟损伤的拮抗剂,本文经实验筛选<sup>[1]</sup>,对提出的拮氟锐复方剂,进一步在现场进行预防性治疗中,观察其抗氟效应。

据报道氟致骨代谢紊乱的早期表现为血清AKP和尿羟脯氨酸的增高<sup>[17]</sup>,本研究结果可见氟暴露组工人血清AKP有所增高,但幅度不大;虽服药组工人血清AKP有明显下降,但能否说明其氟暴露引起的AKP改变,以及拮氟锐纠正其改变,有待进一步观察。口服拮氟锐工人的尿BF<sup>-</sup>含量明显增加,促进了尿氟的排出,使体内氟负荷降低,从而减轻了氟的毒性。Marier的研究认为<sup>[8]</sup>,血清Zn的下降是氟损伤的一个直接表现,Zn是人体必需微量元素,有的金属酶含有Zn,并对免疫功能也起重要作用。

表2 各组血清红细胞C<sub>3</sub>b受体花环抑制率及促进率(%)比较( $\bar{X} \pm S$ )

组别	例数	RFIR	RFER
A	40	28.20±10.78	205.14±58.12
B	29	40.03±10.04*	201.17±72.20
C	20	26.02±9.58	228.40±58.10

\* B组与A、C组比较P<0.01

2.4 血清微量元素测定 结果见表3,氟暴露工人血清Cu、Zn有所下降,但与对照组差异不显著(P>0.05);血清Ca的增高,与对照组有明显差异(P<0.01)。服药组工人血清Cu、Zn有明显增高,与未服药组比较差异显著(P<0.01)。血清Mg在各组间无明显差异(P>0.05)。

用。本研究表明,氟暴露有引起微量元素Zn、Cu下降趋势,而拮氟锐明显提高了血清Zn、Cu水平。实验研究和人群观察结果均表明,氟暴露可引起机体免疫功能下降<sup>[9]10]</sup>。以红细胞作为免疫细胞,探讨氟对红细胞免疫功能的影响,迄今尚未见报道,本文通过红细胞花环试验,观察氟暴露对工人血清红细胞免疫粘附因子活性的影响,以及拮氟锐的拮抗效应。结果发现氟能增加抑制因子的活性,使红细胞免疫粘附功能下降,而拮氟锐确实表现了明显的抗氟效应。

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组注入等量的生理盐水,正常组未作处理。染尘组与生理盐水对照组于处理后1、2、4及12周各处死6只,作支气管肺灌洗,收集BALF备用。

1.3 HA及CP测定 HA试剂盒购自上海海军医学研究所,放免分析法测定,可测限为10μg/L。CP用

对苯二胺盐酸盐法测定。结果用光密度值表示。

1.4 统计方法 显著性T检验及直线相关分析。

## 2 结果

2.1 BALF及血清中HA测定 结果见表1。

表1 BALF及血清HA水平测定结果(μg/L) ( $\bar{X} \pm S$ )

组别		1W	2W	4W	12W
NS组	B	≤10.67 ± 1.48	≤13.61 ± 5.85	≤11.16 ± 2.60	≤10.33 ± 0.75
	S	124.17 ± 49.02	125.33 ± 47.49	81.20 ± 6.88	123.60 ± 31.95
SiO <sub>2</sub> 组	B	81.17 ± 30.07*	79.33 ± 37.34*	60.00 ± 21.98*	49.71 ± 21.42**
	S	167.5 ± 38.26	121.67 ± 34.16	105.67 ± 67*	109.57 ± 28.45

B: BALF; S: 血清; BALF, HA 正常对照组 ≤13.3 μg/L, 血清HA正常对照组为100.83 ± 12.6; \*P < 0.05, \*\*P < 0.001。

由表1可见BALF及血清HA,在生理盐水对照组与正常对照组间差异均无显著性(P > 0.05)。染尘后不同时间组BALF HA与对照组相比均具有极显著性差异(P < 0.001)。染尘组较对照组平均增高6.26倍。

血清HA除染尘4W时与对照相比差异有显著性(P < 0.05)外,余各组差异均无显著性(P > 0.05)。

2.2 BALF中CP测定结果

表2 BALF中CP活性测定结果(光密度值) ( $\bar{X} \pm S$ )

	1W	2W	4W	12W
NS组	0.0108 ± 0.0071	0.0167 ± 0.0043	0.0195 ± 0.0061	0.0074 ± 0.0016
SiO <sub>2</sub> 组	0.074 ± 0.0295**	0.0557 ± 0.0188*	0.055 ± 0.0115*	0.0506 ± 0.0078*

\* P < 0.05 \*\* P < 0.001

由表2可见染尘后各组BALF CP活性与对照组相比,差异也十分显著(P < 0.05),前者较后者平均增加4.99倍, BALF中HA与CP间呈正相关(r = 0.6209, P < 0.01)。

## 3 讨论

HA为直链高分子多糖,是结缔组织基质的重要组成部分。在肺内主要由成纤维细胞合成。本文观察到大鼠矽肺纤维化过程中BALF HA增高。有报道HA可使巨噬细胞聚集,而矽肺正是以巨噬细胞聚积为起点的疾病,推测矽肺过程中增多的HA可通过巨噬细胞聚积、释放纤维母细胞增殖因子最终导致纤维

化而参与矽肺纤维化过程。HA可能是成纤维细胞活化的一种标志物。

CP为一种含铜的糖蛋白,能促胶原发生交联反应,是尘肺辅助检查中一重要生化指标。本实验BALF中CP活性在染尘后各期均较对照显著增加,但增加幅度似不及HA高,二者间有很好的相关性,HA可能是一项较CP更敏感的指标。

本实验血清中HA除4W外,余各时间与对照相比差异均无显著性,表明BALF中HA测定较血清HA更敏感。

(感谢北医大公卫学院秦孝发的帮助。)

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## Abstracts of Original Articles

### **P<sub>300</sub> in 32 Patients with Acute Carbon Monoxide Poisoning**

**Wang Yuping, et al**

Event-related potential (P<sub>300</sub>) and neurobehavioral core test battery (NCTB) have been widely used for reflecting the dysfunction of central nervous system.

32 cases of acute carbon monoxide poisoning were examined with P<sub>300</sub> and NCTB.

The results showed that the latency of P<sub>300</sub> was extended and the amplitude was lowered in poisoning group extended than that of control group. It was found that the latency of P<sub>300</sub> of 9 cases were significantly delayed among 17 cases whose coma-time lasted more than 12 hours during acute period. It was suggested that P<sub>300</sub> might be used for predict the occurrence of the toxic delayed encephalopathy by CO.

The results also showed that there was a good correlation between NCTB and P<sub>300</sub>.

Key words: acute carbon monoxide poisoning, event-related potential (P<sub>300</sub>), neurobehavioral core test battery (NCTB)

### **Effect of Extracts of Dunaliella salina (EDS) on Antioxidation and Cellular Immune Functions in Patients with Pneumoconiosis**

**Zhang Huizhen, et al**

The effect of EDS on antioxidation and cellular immune function in patients with pneumoconiosis who took EDS capsules (15mg each, twice a day) for 30 days was observed in the study. The results showed that while serum beta-carotene and vitamin A levels increased, blood lipid peroxides (LPO) content markedly decreased ( $P < 0.01$ ), and the activities of superoxide dismutase (SOD) and glutathione per-

oxidase (GSH-Px) were significantly increased ( $P < 0.01$ ) than those before administration of EDS. Cellular immune functions, such as the activity of tumor necrosis factor (TNF) and lymphocyte transformation rate (LCTR) improved, that was TNF activity increased ( $P < 0.01$ ) and LCTR raised ( $P < 0.05$ ). It was suggested that was effective in improving antioxidation and immunologic functions of pneumoconiosis patients and was safe at the dose tested, and that it is worthy to do further study on the action of this drug in prevention and treatment of pneumoconiosis.

Key words: pneumoconiosis, beta-carotene (BC), extracts of dunaliella salina (EDS), antioxidation, immunologic function

### **A Field Trial of Anti-fluoride Effect of Jiefurui**

**Chen Rongan, et al**

80 workers who had continuous exposure to fluoride for 5 or more than 5 years were divided into two groups: group A 42 workers and group B 38 workers. The workers in group A took jiefurui, a mixture made of boron, trace elements, and chinese traditional herbs, for one month. Group B was served as control. In addition, group C of 20 workers was served as an unexposed control group. All workers were observed for one month during exposure to fluoride. The results showed that the concentrations of urinary fluoride and tetrafluoroborate in workers of group A, as compared with two control groups, were significantly increased, the alkaline phosphatase activity reduced, the content of zinc, copper, iron in serum increased, the ability of red cell immune adherence was enhanced. It suggested that jiefurui might have an

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Peng Shanzhuo, et al ..... (265)

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effect of preventing fluoride damage.

Key words: exposure to fluoride, jiefurui, antifuoride damage

**Study on the Relationship Between the Copper Containing Enzymes and Serum Copper Content in Silicosis**

**Peng Shanzhuo, et al**

The whole blood superoxide dismutase activity, the serum copper content, the serum

ceruloplasmin activity and the serum lipid peroxide level were determined in 83 cases of silicosis and those complicated with tuberculosis and other respiratory diseases as well as in healthy controls. The results showed that these biological indices in the patients with silicosis and complicated silicosis were significantly higher than those in healthy subjects.

Key words: silicosis, whole SOD activity, serum copper