

氟对大鼠NK细胞和IL-2的影响 以及硼对氟的拮抗作用*

同济医科大学职业医学研究所 (430030) 徐增光 陈荣安 幸孟本 郑红燕
工业氟病防治研究协作组 夏亨生 胡超 王泽国 南涤飞

提 要 本文研究了氟对大鼠自然杀伤(NK)细胞和白细胞介素-2(IL-2)的影响以及硼对氟的拮抗作用。大鼠饮用含氟水(110mgF⁻/L)和氟硼混合水(110mgF⁻+44mgB³⁺/L)4个月,以饮用自来水为对照。研究结果表明氟可抑制大鼠脾脏NK细胞和IL-2的活性;硼在体外与氟混合后饮用,可拮抗氟引起的NK细胞和IL-2活性的降低,并使尿氟排出增加,骨氟含量下降,提示硼可拮抗氟的毒性。

关键词 氟 硼 拮抗作用 自然杀伤细胞 白细胞介素-2

氟进入机体可引起广泛的损伤,目前,国内外学者仍在不断探索有效的防治药物和方法。硼作为一种拮抗药物,其基础研究和临床应用已取得了一定的进展,我们在原有研究基础上,对氟与免疫细胞(NK细胞)和细胞因子(IL-2)的关系进行了研究,并进一步探索了硼抗氟毒性的效果。

1 材料和方法

1.1 动物分组: Wistar 大鼠36只,体重120~130g,饲养观察一周,随机分为A组(阴性对照组)、B组(阳性对照组)、C组(硼实验组)(以下简称A、B、C组)。每组12只,雌雄各半。

1.2 给药剂量与途径: A组饮用自来水;B组用NaF配成含110mgF⁻/L的饮用水;C组用NaF和硼砂配成含110mgF⁻+44mgB³⁺/L的氟硼混合水,自由饮用,实验期4个月。

1.3 指标: 每天观察动物饮食、外观等一般状况,两周称重一次,绘制体重增长曲线。实验第1、8、16周收集24小时尿,用BF₄⁻选择性电极法测尿BF₄⁻含量。实验结束,大鼠断头,取右侧股骨,用消化法测骨氟含量⁽¹⁾。断头后无菌取脾,用LDH释放法测NK细胞活性⁽²⁾;取配制的脾细胞悬液,用MTT比色分析法测IL-2的活性⁽³⁾。

2 结果

2.1 B组大鼠自第3周开始,出现少动、萎靡不振;第6周起体重增长明显低于A、C组($P<0.05$),C组体重增长慢于A组,但差异无显著性($P>0.05$)。

2.2 尿中BF₄⁻含量测定结果表明(表1),C组动物尿BF₄⁻含量明显增高($P<0.01$),且随实验期延长更加明显($P<0.01$)。A、B两组间无显著差异($P>0.05$)。

表1 各组大鼠尿BF₄⁻含量 ($\bar{X} \pm S$ 单位mg/L)

组别	n	第1周	第8周	第16周
A	12	3.79±1.48	4.88±1.61	5.26±1.58
B	12	4.42±0.57	5.58±0.89	6.92±1.84
C	12	6.34±1.42**▲	10.83±1.07**▲▲	10.61±1.62**▲▲

C组与A、B组比较 * $P<0.05$, ** $P<0.01$; C与B组比较▲ $P<0.05$, ▲▲ $P<0.01$ (下同)

2.3 从表2可见,各组动物骨氟以B组最高,A组最低;与B组比较,C组骨氟明显降低,差异极显著($P<0.01$)。

2.4 脾NK细胞和IL-2活性检测结果显示

(表2),与A组比较,C组动物NK细胞和IL-2活性下降($P<0.05$),但明显高于B组大鼠的NK细胞和IL-2活性($P<0.01$)。

* 中国有色金属总公司“八·五”项目。

表2 各组大鼠骨氟含量以及NK细胞和 IL-2 活性($\bar{X} \pm S$)

组别	n	骨氟含量(mgF ⁻ /kg干骨)	NK细胞活性(%)	IL-2活性(OD ₅₇₀₋₆₃₀)
A	12	626.28 ± 60.94	40.82 ± 7.99	0.76 ± 0.020
B	12	4271.42 ± 233.49**	22.70 ± 6.90**	0.611 ± 0.035**
C	12	3643.34 ± 273.20***Δ	31.94 ± 9.16***Δ	0.715 ± 0.022***Δ

3 讨论

氟病是全身性疾病,实验结果表明氟可影响动物的生长发育^[47]。Elsair进行了硼对氟的拮抗作用研究,提出硼与氟在体内可能形成毒性低的BF₄⁻随尿排出^[6];李健学的研究证明,硼与氟在体内形成BF₄⁻可增加体内氟的排出量^[7]。本文结果进一步表明,硼与氟在体内络合形成BF₄⁻而减少氟进入靶器官——骨组织的数量,并使沉积于骨中的氟明显降低,减轻氟的毒性。

有实验表明,氟暴露大鼠溶菌酶水平降低,白细胞吞噬指数下降,使机体自然免疫(非特异)功能降低^[8];而氟化钠可减少淋巴细胞数目,抑制特异性免疫^[9]。对豚鼠的研究显示,氟可降低淋巴细胞转化功能^[5]。NK细胞主要功能是非特异杀灭外来异物、抗感染、抗肿瘤、释放淋巴因子参与免疫应答。IL-2是特异性免疫中重要的细胞因子,由T_H细胞分泌的糖蛋白,其主要功能是促进T细胞和B细胞以及CTL细胞的增殖和分化,并增强其活性,促进NK细胞和T细胞分泌淋巴因子。本研究结果表明,慢性氟暴露可明显降低NK细胞和IL-2的活性。在体外,硼与氟混合进入体内,硼可一定程度地拮抗氟引起的

NK细胞和IL-2活性的降低。

4 参考文献

- 白雪涛,等。锌、锰、铜对大鼠氟骨沉积的阻断作用。中国地方病防治杂志 1993;8(5):267
- 王甫厚,等。LDH释放法测NK细胞毒的方法学研究。中国免疫学杂志 1990;6(2):115
- 郑永唐,等。测定细胞存活和增殖的MTT方法的建立。免疫学杂志 1992;(4):266
- Elsair J, et al. Effects of a subacute fluorine intoxication of several months on hemostasis in rabbits in presence and absence of an antidote (boron). Fluoride, 1979; 12(3):136
- 宋世震,等。氟化物免疫毒性的实验研究。职业医学 1988;15(4):4
- Elsair J, et al. Boron as a preventive antidote in acute and subacute fluoride intoxication in rabbits; Its action and fluoride and calcium-phosphorous metabolism. Fluoride, 1980; 13(3): 129
- 李健学,等。四硼酸钠对氟致肾损伤的拮抗作用及其机理研究。中国工业医学杂志 1989;2(1):13
- IRPTC. Scientific Reviews of Soviet Literature on Toxicity and Hazards of Chemicals, Sodium Fluoride. United Nations Environment Programme, 38, Centre of International Projects, GK-NT, Moscow, 1983; 5~35
- Jain SK & Susheela AK. An experimental study in rabbits, Proceeding of the fifteenth conference of international society for fluoride research, 1985; 42

(感谢李健学博士、杨一清硕士的帮助和支持。)

征 稿 通 知

中华预防医学会职业病专业委员会于1994年11月12日召开常委会, 决定第九届职业病学术大会于1995年11月在贵州省贵阳市召开。会议学术交流中心议题以农药中毒为主。

欢迎各地寄交有关农药中毒的临床总结、基层实践、农药毒性与人体作用关系、农药中毒流行病学研究、包括地区中毒发病态势研究、特殊品种的临床问题、特殊综合征的认识与处理经验等方面的论文到大会交流。

论文请用稿纸誉写, 一式两份, 附加500字以内的摘要。加单位审查证明, 于1995年7月底前邮寄贵州省贵阳市大水沟省职业病防治院(邮编: 550006)王明启收。

Abstracts of Original Articles

Effect of Lead on Function of Endocrine Glands in Workers Occupationally Exposed to Lead

Cui Jinshan, et al

In this paper, we studied effect of lead on function of some endocrine glands in workers occupationally exposed to lead. The results showed that the levels of FT_3 , FT_4 and cortisol in serum were significantly lower in the group of lead poisoning and group of lead absorption than in of the control group ($P < 0.01$) and showed negative correlation with levels of urinary lead and δ -ALA. The levels of TSH in serum was significantly higher in the group of lead poisoning than in the control group ($P < 0.01$) and showed positive correlation with levels of urinary lead and δ -ALA. The results suggested that lead might impair the function of thyroid gland and adrenal cortex in lead over absorption workers without symptoms of lead poisoning. It showed that some endocrine glands are sensitive to toxic effects of lead and impairment of some endocrine glands by lead may be one of the important mechanisms of lead poisoning.

Key words, free triiodothyronine (FT_3), free tetraiodothyronine (FT_4), cortisol, lead absorption, lead poisoning

Study on Relationship Between Oxygen Free Radical and Injury of Rabbit Renal Epithelial Cells During Exposure to Cadmium

Jiang Tang, et al

To study the effect of oxygen free radical on the proximal tubular epithelial cells, a injury proximal tubular cells model was established by incubation with cadmium. It was found that the level of products of lipid peroxidation was significantly increased, and the

activities of SOD, CAT were inhibited at the same time. A series of ultrastructural damage was found by electronic microscopy. The use of vitamin E successfully prevented proximal tubular cells from injury. The studies revealed that proximal tubular epithelial cells would produce oxygen free radical in increasing amounts during exposure to cadmium, and oxygen free radical could play an important role in the proximal tubular cells injury.

Key words, cadmium, free radical, renal epithelial cells

Effect of Fluoride on the Activity of NK Cell and IL-2 and Antagonistic Effect of Boron to Fluoride in Rats

Xu Zhengguang, et al

This paper explored the effect of fluoride on the activity of natural killer(NK) cells and interleukin-2(IL-2) in the rats' spleen, as well as the antagonistic effect of boron to fluoride. Drinking water contained NaF(110mg F^- /L) and NaF + Borax(110mg F^- + 44mg B^{3+} /L) were administered in two groups of rats, respectively, for 4 months, the control was given tap water. The results showed that fluoride could obviously reduce the activity of NK cells and IL-2, and that boron, mixed with fluoride, could antagonise the effect of fluoride on the activity of NK cells and IL-2, and increase the excretion of fluoride in urine, and reduce the content of fluoride in bone. The study suggests that boron may antagonise the toxicity of fluoride.

Key words, fluoride, boron, antagonism, natural-killer cell, interleukin-2

The Feature of High Kilo-voltage Radiographs Taken by Reconstructed 200 mA X-ray Unit

Sun Chenye, et al

High kV radiographs taken by reconstru-