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<< Previous Articles | Next Articles >>

隐孢子虫感染昆明小鼠后肠道病理变化及螺旋霉素治疗效果

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Intestinal Pathological Changes of Kunming Mice Infected by Cryptosporidium and the Therapeutic Efficacy of Spiramycin on Infected Mice

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摘要目的 观察隐孢子虫感染小鼠后的症状、病程和治疗后改善情况,为隐孢子虫病的临床研究提供依据。 方法 昆明小鼠70只随机分为4组,A组(10只)为健康对照组,实验组(B、C和D组,每组20只)小鼠分别在其饮水上加入地塞米松5.0、7.5和10.0 mg/L,连续2周,制备隐孢子虫感染小鼠模型。免疫抑制后每天观察小鼠的症状,粪检计数隐孢子虫卵囊。2周后处死各组50%小鼠,取小鼠肠黏膜观察隐孢子虫的寄生部位,镜下观察病理变化并测定肠黏膜分泌型免疫球蛋白A(slgA)水平。剩余小鼠停用免疫抑制剂2周后,粪检阳性的小鼠随机分为治疗组(6只)和对照组(7只),治疗组给与螺旋霉素2 mg/d(溶于1 ml生理盐水中)灌胃治疗,连续10 d,观察小鼠治疗后表现并计数卵囊排出量的变化,对照组灌胃等量生理盐水。 结果 各实验组小鼠免疫抑制第6天粪检隐孢子虫卵囊呈阳性,B组和D组小鼠的每克粪虫卵数分别于第10 d(31.9±2.4)和第12天(70.3±4.0)达高峰,两组之间卵囊排出数量差异有统计学意义(P<0.05),各实验组均有小鼠出现明显的消化道症状。该虫主要寄生在小肠上段(27/54只)。病理结果显示,D组病变较重,肠黏膜充血、水肿,伴局灶性出血,B和C组仅见少量炎细胞浸润。各实验组肠黏膜肠液slgA含量均下降,D组[(2.7±0.6)μg/ml]、C组[(3.2±0.8)μg/ml]、B组[(4.9±1.3)μg/ml]与A组[(6.1±1.2)μg/ml]之间差异均有统计学意义(P<0.05)。免疫抑制剂停止应用后,小鼠腹泻、稀便等症状减轻56.7%(17/30只)。免疫抑制剂停用2周后,粪检阳性的小鼠经螺旋霉素治疗后症状改善,治疗组(0)和对照组(11.3±8.1)小鼠卵囊排出数量差异有统计学意义(P<0.05)。 结论 隐孢子虫感染小鼠卵囊排出数量、持续时间和对肠黏膜的损伤程度与免疫状态密切相关,螺旋霉素治疗有效。

关键词: 隐孢子虫 小鼠 病理变化 治疗

Abstract: Objective To observe the symptom, disease course of Cryptosporidium-infected mice, and the therapeutic effect of spiramycin on infected mice. Methods Seventy Kunming mice were randomly divided into normal control group (A, n=10) and 3 experimental groups (B, C, and D). Mice in groups B, C, and D (n=20) were immunosuppressed with 5, 7.5, and 10 mg/L dexamethasone in drinking water for two weeks, respectively. The mice were observed and the number of oocysts in fecal sample was counted daily after immunosuppression. Two weeks post immunosuppression, 50% of mice in each group were sacrificed, and small intestine was removed for observation of parasitic site. The pathological changes of mucous membrane were observed under microscope, and sIgA level in intestinal fluid was determined. Immunosuppression was withdrawn in the rest mice, and after two weeks unrecovered mice were divided into treatment group (n=6) and control group (n=7). Mice in treatment group were each given 2 mg/d spiramycin for 10 d. Each mouse in control group was given same amount of normal saline. The mice were observed and the oocysts shedding in fecal pellets were counted after treatment. Results On the 6th day post immunosuppression, Cryptosporidium sp. positive fecal samples were found in the experimental groups. The number of oocysts per gram of feces in groups D (70.3 ± 4.0) and B (31.9 ± 2.4) reached a peak on the 12th day and 10th day post immunosuppression, respectively (P < 0.05). The conspicuous enteron symptom was observed in each experimental group. *Cryptosporidium* parasitized mainly in upper jejunum. Pathological examination of intestinal mucous membrane showed that swollen mucous membrane and hemorrhages were observed in group D, and less inflammatory cell occurred in groups B and C. sIgA level in intestinal fluid of experiment mice descended, there was a statistical significance between groups D $[(2.7\pm0.6) \mu g/ml]$, C $[(3.2\pm0.8) \mu g/ml]$, B $[(4.9\pm1.3) \mu g/ml]$ and A $[(6.1\pm1.2) \mu g/ml]$ μ g/ml] (P<0.05). After withdrawal of immunosuppression, out of 30 positive mice, symptoms including diarrhea and loose stools improved in 17 mice. After treated with spiramycin, status of the mice got improved, and there was statistical significance in the level of oocyst shedding between treatment group (0) and control group (11.3 \pm 8.1) (P< 0.05). Conclusion The level of oocyst shedding, disease course, and pathological change of intestinal mucosa membrane are closely related to immune status of Cryptosporidium-infected mice. Spiramycin is effective in treating of Cryptosporidium infection.

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