doi: 10.13241/j.cnki.pmb.2019.23.019

奥美拉唑不同给药方式治疗新生儿应激性溃疡的效果分析 *

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摘要 目的:探讨奥美拉唑不同给药方式治疗新生儿应激性溃疡的临床效果及安全性。**方法:**选取 2014 年 1 月~2018 年 6 月我院收治的应激性溃疡新生儿 61 例,根据随机数字表法分为两组,对照组患儿给予奥美拉唑 0.6 mg/kg 胃管注入治疗,观察组患儿给予奥美拉唑 2 mg/kg 持续 24 h 微泵静脉滴注。比较两组患儿的临床治疗效果、临床症状缓解时间、止血时间、胃肠喂养开始时间、pH 值和不良反应的发生情况。**结果:**治疗后,两组患儿的临床总有效率比较无统计学差异($P>0.05$);观察组患儿临床症状消失时间和止血时间均显著短于对照组($P<0.05$),喂养开始时间≤ 24 h 的患儿比例高于对照组,喂养开始时间≥ 72 h 的患儿比例显著低于对照组($P<0.05$),pH 值显著高于对照组($P<0.05$)。两组患儿治疗期间均未发生恶心、呕吐、便秘、皮疹等不良反应,且肝肾功能未受明显影响。**结论:**2 mg/kg 奥美拉唑持续 24 h 微泵静脉滴注与 0.6 mg/kg 胃管注入治疗的临床总有效率相当,但微泵静脉滴注可显著提高患儿的 pH 值,缩短临床症状恢复时间、止血时间和胃肠喂养开始时间,且安全性高。

关键词:奥美拉唑;不同给药方式;新生儿;应激性溃疡;效果

中图分类号:R722.1;R725.7 **文献标识码:**A **文章编号:**1673-6273(2019)23-4483-04

Analysis of the Effect of Omeprazole on the Stress Ulcer in Neonates*

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ABSTRACT Objective: To investigate the clinical effect and safety of omeprazole on stress ulcer in neonates. **Methods:** 61 cases of neonates with stress ulcer admitted to our hospital from January 2014 to June 2018 were selected and divided into two groups according to the random number table method. Neonates in the control group were given omeprazole 0.6 mg/kg gastric tube injection therapy, while neonates in the observation group were given omeprazole 2 mg/kg continuous micropump intravenous infusion for 24 h. The clinical treatment effect, clinical symptom remission time, hemostasis time, gastrointestinal feeding start time, pH value and adverse reactions were compared between the two groups. **Results:** After treatment, there was no statistically significant difference in the total clinical effective rate between the two groups ($P>0.05$). The clinical symptom remission time and hemostasis time in the observation group were significantly shorter than those in the control group ($P<0.05$). In the observation group, the proportion of children with feeding time ≤ 24 h was significantly higher than that of the control group, the proportion of children with feeding time ≥ 72 h was significantly lower than that of the control group ($P<0.05$), and the pH value was significantly higher than that of the control group ($P<0.05$). There were no adverse reactions such as nausea, vomiting, constipation and rash in the two groups of neonates during the treatment, and the liver and kidney function had not been significantly affected. **Conclusion:** The total effective rate of 2 mg/kg omeprazole for 24 h micropump intravenous infusion and 0.6 mg/kg gastric tube injection was similar, but micropump intravenous infusion significantly increased the pH value and shortened clinical symptom remission time, hemostasis time and gastrointestinal feeding start time, and its safety is higher.

Key words: Omeprazole; Different delivery methods; Neonates; Stress ulcer; Effect

Chinese Library Classification(CLC): R722.1; R725.7 Document code: A

Article ID: 1673-6273(2019)23-4483-04

前言

应激性溃疡是由于多种外源性或内源性的致病因素造成的粘膜防御机制破坏或粘膜血流量降低[1,2],临床表现为粘膜充血、溃疡及糜烂形成,累及血管后引起出血,导致胃肠功能紊乱[3-5],是新生儿重症监护室常见的并发症之一[6,7]。我国新生儿应激性溃疡的发生率显著逐年上升，尤其是早产儿发病率更高。如果不能进行及时有效的治疗,可能会引起消化道大出血,甚至休克和死亡,严重威胁新生儿的生命。

新生儿应激性溃疡的发病机制尚不完全明确[8,9],研究显示早期的病变部位多发生于胃体和胃底粘膜,进而扩展至胃窦和十二指肠等部位。目前,临床对于该病的治疗以阻止胃粘膜进

* 基金项目:江苏大学科学技术项目(JLY20160167)

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(收稿日期:2019-06-06 接受日期:2019-06-29)

一步损害为主。奥美拉唑可抑制胃酸分泌,对于应激性溃疡具有较好的临床效果[10,11],但目前临床用药方式较多,尚未形成统一的标准。为了寻找更加安全有效的治疗方法,本研究比较了奥美拉唑胃管注入和微泵静脉滴注对新生儿应激性溃疡的治疗效果及安全性,以期为临床应用提供依据。

1 资料和方法

1.1 一般资料

选取 2014 年 1 月 ~2018 年 6 月我院收治的应激性溃疡新生儿 61 例, 临床主要表现为突发的反复呕血和 / 或柏油样大便,且胃管中抽出物呈咖啡样或鲜红色。根据随机数字表法分为两组,对照组 30 例,男 17 例,女 13 例;日龄 2~9 d,平均 5.86± 1.25 d;胎龄 35~40 周平均 37.89± 1.58 周;出血程度:中度 21 例,重度 9 例;其中颅内出血 8 例、败血症 2 例、缺血缺氧性脑病 10 例、坏死性肠炎 6 例,其他 4 例。观察组 31 例,男 16 例,女 15 例;日龄 1~9 d,平均 5.25± 1.13 d;胎龄 35~41 周平均 38.12± 1.64 周;出血程度:中度 20 例,重度 11 例;其中颅内出血 10 例、败血症 2 例、缺血缺氧性脑病 11 例、坏死性肠炎 5 例,其他 3 例。两组患者一般资料具有可比性(P>0.05)。

1.2 入选标准

纳入标准:① 符合中华医学会制定的应激性溃疡相关诊断标准[9];② 胃内容物和大便隐血试验阳性;③ 患儿家属知情同意并签署知情同意书。

排除标准:① 合并自然出血症者;② 先天性消化道畸形者;③ 消化道邻近器官出血进入消化道者;④ 凝血功能异常者。

1.3 方法

所有患儿均给予原发病的治疗,同时常规禁食、抗感染、胃肠减压、止血、纠正水电解质平衡、营养支持等综合治疗,并将患儿置于 33~35 ℃保温箱内。对照组患儿将口腔和鼻腔分泌物清理干净后置入新生儿胃管, 然后用 1%碳酸氢钠与 40 ml 蒸馏水混匀后洗胃,奥美拉唑 0.6 mg/kg 胃管注入,1 次 /d,连续治疗 5 d, 维持治疗至胃回抽物无咖啡样或鲜红色液体后再治疗 1 d。观察组患儿奥美拉唑 2 mg/kg 持续 24 h 微泵静脉滴注,持续治疗 3 d。

1.4 观察指标

① 比较两组患儿临床治疗效果,痊愈:临床症状消失,胃内容物颜色清亮,隐血试验阴性;有效:临床症状消失,胃内容物颜色接近清亮,隐血试验阳性;无效:临床症状未缓解甚至加重,胃内容物颜色未改变。② 比较两组患儿临床症状消失时间,包括肌张力恢复时间、循环不良消失时间、胃肠功能紊乱消失时间和意识恢复时间。③ 比较两组患儿止血时间、开始胃肠喂养时间和 pH 值。④ 比较两组患儿不良反应发生情况,治疗后采集患儿的空腹静脉血,离心后取上清液,采用 7180 全自动生化分析仪(日本日立公司生产)检测谷丙转氨酶(Alanine aminotransferase,ALT)、谷草转氨酶(Valley grass transaminase,AST)、血尿素氮(Blood urea nitrogen,BUN)和肌酐(Creatinine,Cr)水平。

1.5 统计学方法

采用 SPSS 20.0 软件进行数据分析,计量资料($\bar{x}\pm s$)行 t 检验;计数资料(%)行 x^2 检验,P<0.05 为差异有统计学意义。

2 结果

2.1 两组患儿的临床疗效比较

治疗后, 两组患儿的临床总有效率比较无统计学差异(P>0.05),见表 1。

表 1 两组患儿临床有效率比较[例(%)]

Table 1 Comparison of the clinical effective rates between the two groups of children [n(%)]

Groups	n	Cured	Valid	Invalid	Total effective rate
Control group	30	19(63.33)	8(26.67)	3(10.00)	27(90.00)
Observation group	31	23(74.19)	7(22.58)	1(3.23)	30(96.77)

Note: Compared with the control group, x^2=1.142, P=0.354, using continuous calibration chi-square test.

2.2 两组患儿的临床症状消失时间比较

观察组患儿临床症状消失时间均显著短于对照组(P<0.05),见表 2。

表 2 两组患儿临床症状消失时间比较($\bar{x}\pm s$, 天)

Table 2 Comparison of the disappearance time of clinical symptom between the two groups of children ($\bar{x}\pm s$, d)

Groups	n	Gastrointestinal dysfunction disappearance time	Muscle tension recovery time	Cycle failure time	Consciousness recovery time
Control group	30	4.97± 1.23	7.25± 2.01	3.58± 0.97	3.89± 1.01
Observation group	31	4.31± 1.02	6.21± 1.84	2.86± 0.71	3.15± 0.88
t	-	2.284	2.109	3.299	3.054
P	-	0.026	0.039	0.002*	0.003

Note: * Use t' test.

2.3 两组患儿止血时间、胃肠喂养开始时间和 PH 值比较

观察组患儿的止血时间显著短于对照组(P<0.05),喂养开始时间≤ 24 h 的患儿比例显著高于对照组,喂养开始时间≥ 72 h 的患儿比例显著低于对照组 (P<0.05),pH 值观察组显著高于对照组(P<0.05),见表 3。

表 3 两组患儿止血时间、胃肠喂养时间及 pH 值比较

Table 3 Comparison of the hemostasis time, gastrointestinal feeding time and pH between the two groups of children

Groups	n	Hemostasis time (d)	Gastrointestinal feeding start time			pH	
			≤ 24 h	24~72 h	≥ 72 h	Before treatment	After treatment
Control group	30	2.03± 0.54	14	3	13	3.85± 0.89	5.46± 1.57
Observation group	31	1.12± 0.33	27	2	2	3.92± 1.03	6.78± 1.86
t/x^2	-	7.911	13.309	0.255	11.184	-0.284	-2.990
P	-	＜0.001	0.001	0.671*	0.001	0.777	0.004

Note: *Continuous calibration chi-square test.

2.4 两组患儿不良反应发生情况比较

两组患儿治疗期间均未发生恶心、呕吐、便秘、皮疹等不良反应，且肝肾功能未受明显影响，见表 4。

表 4 两组患儿治疗后肝肾功能相关指标比较($\bar{x}\pm s$)

Table 4 Comparison of the liver and kidney function after treatment in between the two groups of children($\bar{x}\pm s$)

Groups	n	ALT(U/L)	AST(U/L)	BUN(mmol/L)	Cr(mmol/L)
Control group	30	10.23± 3.02	43.58± 11.25	3.64± 0.98	45.88± 12.23
Observation group	31	11.05± 3.11	45.33± 12.16	3.31± 0.84	46.87± 13.48
t	-	-1.044	-0.583	1.414	-0.300
P	-	0.301	0.562	0.163	0.765

3 讨论

胃是机体对应激反应比较敏感的器官，新生儿的胃粘膜屏障功能尚未发育完全，且受到母体促胃液素的影响，出生后 24 h 内的胃液分泌达到最大，且持续至 10 d。当发生颅内出血、败血症、缺血缺氧性脑病或坏死性肠炎等外界刺激时，机体产生应激反应，体内儿茶酚胺水平升高，胃液和胃酸分泌增加，引起胃粘膜自身消化而导致溃疡的发生[12-14]。研究显示新生儿应激性溃疡的发生与机体应激反应后交感神经兴奋，儿茶酚胺分泌增加，引起胃血管缺血、微循环障碍、胃粘膜血容量减少而增加粘膜对各种有害因子的敏感性，最终形成胃粘膜坏死、糜烂而发生溃疡[15-17]。当溃疡发生后，胃粘膜屏障遭到破坏，导致急性糜烂和溃疡性出血，从而出现恶心、呕吐、胃内容物咖啡色或鲜红色等症状。研究表明在尽量去除应激源的同时联合使用抑酸药物对于应激溃疡的出血和粘膜修复具有较好的临床效果[18-20]。

研究显示 pH 较低时血小板凝集发生异常，血块容易溶解，溃疡止血最适宜的环境为 pH=7，所以 PH 值的调节对于溃疡止血十分重要。H^+-K^+-ATP 酶是胃酸分泌的通道[21,22]，奥美拉唑是一种可高度浓缩于胃壁细胞内并转化为次硫磺胺的 H^+-K^+-ATP 酶抑制剂，因 H^+-K^+-ATP 酶与次硫磺胺的巯基结合失活，可抑制各种因素引起的胃酸分泌，使胃内 pH 值升高，通过增加粘膜的血流量来达到修复胃粘膜和止血的作用[23]。ALT 和 AST 是在进行肝功能检测时血清酶检测的常用指标[24-26]，正常肝脏含有 ALT 和 AST，当肝脏中细胞膜发生损伤或者细胞坏死时，这 2 种酶进入血液中的含量会增加，通过测定其活性可以得出肝细胞受损程度。在各种药物、酒精或者肝炎引起的急性肝细胞损伤中，血清 ALT 和 AST 都是比较敏感的指标。临床上根据 BUN 和 Cr 的变化情况来判断机体肾功能受损的程度和肾功能正常情况[27-29]。本研究结果显示观察组患儿治疗后的 pH 值显著高于对照组，说明奥美拉唑持续微泵静脉滴注可显著提高患儿胃 pH 值，可能是由于胃管分次注入不能维持稳定的血药浓度，而研究证明持续稳定的血药浓度与抑酸效果成正相关[30]。此外，两组患儿的临床治疗效果相当，但奥美拉唑持续微泵静脉滴注患儿的临床症状消失时间、止血时间和胃肠喂养时间显著短于胃管注入组。可能与持续微泵静脉滴注可显著改善患儿的胃内 pH 有关。由于新生儿各项功能尚未发育完全，药物治疗的安全性至关重要。本研究中，两组患儿在用药期间均未出现恶心、呕吐、便秘、皮疹等不良反应，肝肾功能均未发生明显异常，说明两种给药方式对新生儿均较安全。

综上所述，2 mg/kg 奥美拉唑持续 24 h 微泵静脉滴注与 0.6 mg/kg 胃管注入治疗的临床总有效率相当，但微泵静脉滴注可显著提高患儿的 PH 值，缩短临床症状恢复时间、止血时间和胃肠喂养开始时间，且安全性高。

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