doi: 10.13241/j.cnki.pmb.2019.21.040

骨化三醇联合腹膜透析疗法治疗慢性肾功能衰竭的临床疗效及对患者血清 ProGRP、Cysc、Chemerin 水平的影响 *

李 丹 李 杨 丁小明△ 王 华 朱晓荣

（西安交通大学第一附属医院 肾移植科 陕西 西安 710061）

摘要 目的：探讨骨化三醇联合腹膜透析疗法治疗慢性肾功能衰竭的临床疗效及对患者血清 Pro-Gastrin-Releasing Peptide (Pro-GRP)、CystatinC(Cysc)、Chemerin 水平的影响。**方法：**选取我院 2017 年 2 月至 2018 年 1 月收治的 98 例慢性肾功能衰竭患者，按照随机数表法将其分为观察组(n=51)和对照组(n=47)。对照组采用腹膜透析疗法治疗，观察组采用骨化三醇联合腹膜透析疗法治疗。观察和比较两组治疗前后肾功能指标尿素氮(blood urea nitrogen，BUN)、血清肌酐(Serum creatinine Cr)、24 小时尿蛋白(24 h urinary protein，24 h UP)，生化指标白蛋白(albumin，Alb)、血红蛋白(hemoglobin，Hb)及红细胞(red blood cell，RBC)，胃泌素释放肽前体(ProGRP)、血清胱抑素(CysC)、趋化素(Chemerin)水平的变化，6 个月、1 年生存率及不良反应的发生情况。**结果：**治疗后，观察组 BUN、SCr、24hUP 水平均显著低于对照组[(13.95± 3.06)mmol/L vs. (21.10± 3.85)mmol/L，(260.12± 40.32)μmol/L vs. (354.93± 51.06)μmol/L，(1.75± 0.45)g/24 h vs. (2.67± 0.80)g/24 h](P＜0.05)；Alb 水平显著低于对照组[(27.85± 3.58)g/L vs. (33.06± 4.27)g/L](P＜0.05)；Hb、RBC 显著高于对照组 [(91.72± 13.46)g/L vs. (82.36± 10.15)g/L，(379.47± 92.08)× 10^{12}/L vs. (315.70± 73.24)× 10^{12}/L](P＜0.05)；ProGRP、Chemerin 水平显著低于对照组 [(49.23± 4.72)pg/mL vs. (63.87± 7.30)pg/mL，(37.02± 6.15)μg/L vs. (30.63± 4.81)μg/L](P＜0.05)；Cysc 水平显著高于对照组[(80.75± 16.08)mL/min vs. (98.81± 18.07)mL/min](P＜0.05)；6 个月、1 年生存率均显著高于对照组[96.08%(49/51) vs. 91.49%(43/47)，90.20%(46/51) vs. 74.47%(35/47)](P＜0.05)；不良反应总发生率显著低于对照组[17.65%(9/51) vs. 44.68%(21/47)](P＜0.05)。**结论：**骨化三醇联合腹膜透析疗法治疗慢性肾功能衰竭的临床效果显著优于单用，其可有效减轻患者的临床症状，纠正电解质紊乱，改善肾功能和预后，可能与降低血清 ProGRP、Chemerin 水平及提高血清 Cysc 水平有关。

关键词：骨化三醇；腹膜透析疗法；慢性肾功能衰竭；肾功能

中图分类号：R459.5；R692.5 **文献标识码：**A **文章编号：**1673-6273(2019)21-4176-04

Clinical Efficacy of Calcitriol Combined with Peritoneal Dialysis in the treatment of Chronic Renal Failure and its Effects on the Serum ProGRP, Cysc and Chemerin Levels*

LI Dan, LI Yang, DING Xiao-ming△, WANG Hua, ZHU Xiao-rong

(Department of Kidney Transplantation, First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi, 710061, China)

ABSTRACT Objective: To explore the clinical efficacy of calcitriol combined with peritoneal dialysis in the treatment of chronic renal failure and its effects on the serum ProGRP, Cysc and Chemerin levels. **Methods:** 98 patients with chronic renal failure who were treated from February 2017 to January 2018 in our hospital were selected as the research objects. According to the random number table, those patients were divided into the observation group (n=47) and the control group (n=51). The control group was treated with peritoneal dialysis, while the observation group treated with Calcitriol combined with peritoneal dialysis. The changes of blood urea nitrogen (BUN), serum creatinine (Cr), 24-hour urinary protein (24-hour UP), albumin (Alb), hemoglobin (Hb), red blood cell (RBC), gastrin-releasing peptide precursor (ProGRP), serum CysC and Chemerin levels before and after treatment, 6-month and 1-year survival rates as well as the incidence of adverse reactions were compared between two groups. **Results:** After treatment, the BUN, SCr and 24hUP levels in the observation group were significantly lower than those in the control group [(13.95± 3.06)mmol/L vs. (21.10± 3.85)mmol/L, (260.12± 40.32) μmol/L vs. (354.93± 51.06) μmol/L, (1.75± 0.45)g/24 h vs. (2.67± 0.80)g/24 h](P<0.05). The Alb level was significantly lower than that of the control group [(27.85± 3.58)g/L vs. (33.06± 4.27)g/L](P＜0.05). The Hb and RBC were significantly higher than those in the control group[(91.72± 13.46)g/L vs. (82.36± 10.15)g/L, (379.47± 92.08)× 10^{12}/L vs(315.70± 73.24)× 10^{12}/L](P<0.05). ProGRP and Chemerin levels were significantly lower than those in the control group [(49.23± 4.72) pg/mL vs. (63.87± 7.30) pg/mL,

* 基金项目：陕西省自然科学基金项目(20140127)

作者简介：李丹(1981-)，女，本科，主治医师，研究方向：肾脏移植，电话：18991232347，E-mail：fengshunyiyi@21cn.com

△ 通讯作者：丁小明(1970-)，男，博士，主任医师，博士生导师，主要从事肾脏移植工作

(收稿日期：2019-07-11 接受日期：2019-08-05)

(37.02± 6.15)μg/L vs. (30.63± 4.81)μg/L](*P*<0.05). The Cysc level was significantly higher than that of control group [(80.75± 16.08) ml/min vs. (98.81± 18.07)ml/min](*P*<0.05). The 6-month and 1-year survival rates were significantly higher than those in the control group[96.08%(49/51) vs.91.49%(43/47), 90.20%(46/51) vs.74.47%(35/47)](*P*<0.05). The total incidence of adverse reactions was significantly lower than that in the control group [17.65%(9/51) vs.44.68%(21/47)](*P*<0.05). **Conclusion:** Calcitriol combined with peritoneal dialysis has a better clinical effect on chronic renal failure than single use. It can effectively alleviate the clinical symptoms, correct the electrolyte disturbance, improve the renal function and prognosis. It may be related to lower the serum levels of ProGRP, Cysc, Chemerin and increase the serum levels of Cysc.

Key words: Ossification three alcohol, peritoneal dialysis, Chronic renal failure, renal function

Chinese Library Classification(CLC): R459.5; R692.5 Document code: A

Article ID: 1673-6273(2019)21-4176-04

前言

慢性肾功能肾衰竭是临床上常见的慢性肾脏系统疾病，具有进展缓慢、病情难以逆转的特点[1]，临床表现为厌食、恶心、呕吐、腹胀、口舌溃疡、上消化道出血等症状，可伴有心血管疾病及肾性骨病等并发症，给患者的日常生活及生命健康均带来了严重的威胁[2]。临床研究表明[3]该病主要是因相关肾脏疾病引发肾功能损伤，导致肾小球滤过功能出现异常，肾脏细胞出现紊乱，酸碱平衡被破坏，使大量的代谢物堆积[4]。

肾脏移植为治疗肾衰竭的有效方法，但匹配难度较高且供体较少。腹膜透析具有操作简单且安全可靠的优点，可清除患者机体代谢物，纠正水电解质紊乱[5]。骨化三醇为活化维生素D，可调节甲状旁腺激素的分泌，促进钙吸收，纠正钙磷代谢紊乱[6]。研究表明血清胃泌素释放肽前体(ProGRP)、血清胱抑素(CysC)、趋化素(Chemerin)与慢性肾功能肾衰竭存在密切的关系[7]。因此，骨化三醇联合腹膜透析疗法治疗慢性肾功能衰竭的临床疗效及对患者血清 ProGRP、Cysc、Chemerin 水平的影响。

1 资料与方法

1.1 一般资料

收集 2017 年 2 月至 2018 年 1 月我院收治的 98 例患者，均符合慢性肾功能肾衰竭诊断标准。纳入标准[8]：非终末期患者；配合研究者；对本次治疗药物不过敏者；排除标准：患有其他严重器官疾病者；妊娠期或哺乳期者；患有恶性肿瘤疾病；患有严重凝血功能障碍；患有患有精神疾病；同时参与其他研究者。

按照随机数表法将所有患者分为观察组(n=51)和对照组(n=47)。观察组中，男 28 例，女 23 例，年龄 30~75 岁，平均(48.72± 5.18)岁，病程 1~4 年，平均(1.26± 0.21)，疾病种类：慢性肾小球肾炎 32 例，糖尿病肾病 19 例；对照组中，男 25 例，女 22 例，年龄 31~75 岁，平均(47.26± 5.07)岁，病程 1~4 年，平均(1.31± 0.19)，疾病种类：慢性肾小球肾炎 29 例，糖尿病肾病 18 例。两组患者一般资料比较均无明显差异(*P*>0.05)，具有可比性。

1.2 治疗方法

两组患者均采用降糖降脂、抗感染、维持电解质、补充维生素等常规治疗。对照组在基础治疗上，采用腹膜透析疗法治疗，器械为美国 Baxter 公司，切口位于于肚脐部正中旁 1 cm，将腹膜透析管置入腹腔内膀胱直肠窝后缝合，采用间歇性腹膜透析治疗一周，后采用持续性治疗。观察组在对照组的基础上，采用骨化三醇(生产厂家：青岛正大海尔制药有限公司)于睡前口服治疗，每次 0.5 μg，每天 1 次。两组治疗疗程均为 3 个月。

1.3 观察指标

于两组治疗前后分别采集静脉血，离心分离血清，日本日立 7600 型全自动生化分析仪检测生化指标 (白蛋白(albumin，Alb)、血红蛋白(hemoglobin，Hb)及红细胞(red blood cell，RBC))水平；采用美国贝克曼全自动生化仪检测肾功能指标尿素氮(blood urea nitrogen，BUN)、血清肌酐(Cr)、24 小时尿蛋白(24 h urinary protein，24 h UP)水平；采用化学发光法检测 ProGRP 水平，采用酶联免疫吸附法检测 Cysc、Chemerin 水平。比较两组 6 个月、1 年生存率及不良反应的发生情况。

1.4 统计学分析

数据使用 SPSS18.0 软件进行统计分析，符合正态分布的计量资料以 ($\bar{x}\pm s$) 表示，组间比较采用 t 检验，计数资料以[(例)%]表示，组间比较采用 x^2 检验，以 *P*<0.05 为差异有统计学意义。

2 结果

2.1 两组治疗前后肾功能指标的对比

两组治疗前 BUN、SCr、24hUP 比较差异均无统计学意义(*P*>0.05)；治疗后，两组 BUN、SCr、24hUP 水平均较治疗前显著下降，差异存在统计学意义(*P*<0.05)，见表 1。

表 1 两组治疗前后肾功能指标对比($\bar{x}\pm s$)

Table 1 Comparison of the renal function before and after treatment between two groups($\bar{x}\pm s$)

Groups	n	BUN(mmol/L)		SCr(μmol/L)		24hUP(g/24h)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	51	26.08± 5.10	13.95± 3.06*#	460.75± 69.16	260.12± 40.32*#	5.17± 1.30	1.75± 0.45*#
Control group	47	25.79± 4.36	21.10± 3.85*	459.80± 68.92	354.93± 51.06*	5.31± 1.27	2.67± 0.80*

Note: Compared with the control group, *P<0.05; Compared with before treatment, #P<0.05.

2.2 两组治疗前后生化指标的对比

两组治疗前 Alb、Hb、RBC 水平比较差异无统计学意义($P>0.05$);治疗后,两组 Alb、Hb、RBC 水平均较治疗前显著改善,观察组 Alb 明显低于对照组,而 Hb、RBC 水平显著高于对照组($P<0.05$),见表 2。

表 2 两组治疗前后生化指标的对比($\bar{x}\pm s$)

Table 2 Comparison of the biochemical indexes before and after treatment between two groups($\bar{x}\pm s$)

Groups	n	Alb(g/L)		Hb(g/L)		RBC(× 10^{12}/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	51	37.12± 6.03	27.85± 3.58*#	75.06± 9.23	91.72± 13.46*#	240.17± 59.60	379.47± 92.08*#
Control group	47	38.01± 6.15	33.06± 4.27*	74.83± 6.70	82.36± 10.15*	239.08± 58.74	315.70± 73.24*

Note: Compared with the control group, *$P<0.05$; Compared with before treatment, #$P<0.05$.

2.3 两组治疗前后血清 ProGRP、Cysc、Chemerin 水平的对比

两组治疗前血清 ProGRP、Cysc、Chemerin 水平比较差异无统计学意义($P>0.05$)。治疗后,两组血清 ProGRP、Chemerin 水平均较治疗前显著降低($P<0.05$),血清 Cysc 水平较治疗前显著上升($P<0.05$),且观察组血清 ProGRP、Chemerin 水平明显低于对照组($P<0.05$),血清 Cysc 水平显著高于对照组($P<0.05$),见表 3。

表 3 两组治疗前后血清 ProGRP、Cysc、Chemerin 水平的对比($\bar{x}\pm s$)

Table 3 Comparison of the serum ProGRP, Cysc and Chemerin levels before and after treatment between two groups($\bar{x}\pm s$)

Groups	n	ProGRP(pg/mL)		Cysc(mL/min)		Chemerin(μg/L)	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	51	191.06± 34.60	49.23± 4.72*#	22.05± 3.82	37.02± 6.15*#	119.05± 21.30	80.75± 16.08*#
Control group	47	190.86± 34.53	63.87± 7.30#	21.89± 3.79	30.63± 4.81#	120.13± 20.78	98.81± 18.07#

Note: Compared with the control group, *$P<0.05$; Compared with before treatment, #$P<0.05$.

2.4 两组生存率的对比

观察组 6 个月、1 年生存率均显著高于对照组 ($P<0.05$),见表 4。

表 4 两组生存率对比[例(%)]

Table 4 Comparison of the survival rates between two groups [n(%)]

Groups	n	6 months	1 year
Observation group	51	49(96.08)*	46(90.20)*
Control group	47	43(91.49)	35(74.47)

Note: Compared with the control group, *$P<0.05$.

2.5 两组不良反应发生情况的对比

治疗过程中,观察组不良反应总发生率显著低于对照组 ($P<0.05$),见表 5。

表 5 两组不良反应发生率的对比[例(%)]

Table 5 Comparison of the incidence of adverse reactions between the two groups[n(%)]

Groups	n	Infected	Hypoproteinemia	Nausea and vomiting	Hypercalcemia	Abdominal distention	Abdominal pain	Constipation	Total incidence
Observation group	51	1(1.96)	2(3.92)	1(1.96)	2(3.92)	1(1.96)	1(1.96)	1(1.96)	9(17.65)*
Control group	47	4(8.51)	5(10.64)	2(4.26)	3(6.38)	2(4.26)	2(4.26)	3(6.38)	21(44.68)

Note: Compared with the control group, *$P<0.05$.

3 讨论

慢性肾功能肾衰竭为多种肾脏疾病发展的最终结局,是由各种原因导致慢性肾实质损伤,使肾功能下降及肾脏细胞组织紊乱,从而产生一系列的代谢紊乱及临床症状,临床上主要表现为尿毒症[9,10],病情严重的患者可完全丧失肾功能[11],给家庭带来了较大的负担。因此,尽早有效的治疗在延缓病情的发展具有重要的意义[12],临床以改善病情发展、保护肾脏、改善肾功能、延缓肾功损伤为主要治疗目的[13]。近年来,随着透析技术的不断研究与发展,腹膜透析疗法已在多种疾病的治疗中得到较为广泛的应用[14-16]。腹膜透析疗法利用腹膜作为半渗透膜的特性,将透析液和血液分开,可达到纠正水电解质、调节酸碱的目的[17]。此外,该法还具有保护肾脏功能、维持心血管系统稳定的作用,可有效延长患者的生存时间,提高生存率[18,19]。在本研究

中,患者采用腹膜透析疗法治疗后,临床症状、肾功能指标及生化指标均较治疗前显著改善。这可能与在透析过程中,粘附在透析器和透析管道中的血细胞大量丢失有关[20]。此外,血液透析容易造成心脑血管疾病的发生,这可能与透析过程中造成的血流动力学过大波动有关,且插入透析管容易造成患者腹腔内感染,若透析液的成分调解不及时也可使患者出现水电解质紊乱、蛋白质流失等情况[21-23]。因此,对于伴有心脑血管、具有出血倾向的患者应尽量避免采用腹膜透析疗法治疗[24]。

骨化三醇具有起效快、不需代谢活化,部分由肾脏降解的特点,口服后由小肠迅速吸收,可促进肠道对钙剂的吸收,调节骨质的钙化[25]。其主要作用机制为:直接作用于肾脏及甲状旁腺等器官,抑制甲状腺激素分泌,提高钙敏感性[26]。临床研究表明[27]骨化三醇可减轻甲状旁腺细胞的增生,有效缓解患者的临床症状。本研究显示采用联合骨化三醇治疗的患者临床症状、肾功能指标、生化指标及 6 个月、1 年生存率均显著优于采用单独腹膜透析疗法治疗的患者,说明两种方法联合治疗可有效提高治疗疗效,改善肾功能,缓解病情发展,延长患者的生存时间。且采用联合治疗的患者不良反应总发生率更低,说明了联合治疗不会增加患者的并发症,安全性高。

肾功能衰竭会引起患者体内多种物质的异常代谢,ProGRP 由胃肠道产生,可随之升高[28]。Cysc 是评价肾功能的重要指标,能自由滤过肾小球。Chemerin 由脂肪细胞分泌,可通过旁分泌途径作用于炎性反应细胞,肾功能降低可促进脂肪因子水平增高,从而加重肾功能损伤。研究表明[29]慢性肾功能肾衰竭患者血清 ProGRP、Cysc、Chemerin 水平均显著高于正常人。Trimble A [30] 等研究认为 Chemerin 的水平与肾功能的变化有关,肾功能越低,该指标水平越高。本研究显示采用两种方法联合治疗的患者血清 ProGRP、Cysc、Chemerin 水平改善更明显,说明联合治疗可更进一步减轻肾损伤,保护肾功能。

综上所述,骨化三醇联合腹膜透析疗法治疗慢性肾功能衰竭的临床效果显著优于单用,其可有效减轻患者的临床症状,纠正电解质紊乱,改善肾功能和预后,可能与降低血清 ProGRP、Chemerin 水平及提高血清 Cysc 水平有关。

参 考 文 献(References)

[1] Bai W, Wang S, An S, et al. Combination therapy of chitosan, gynostemma, and motherwort alleviates the progression of experimental rat chronic renal failure by inhibiting STAT1 activation [J]. Oncotarget, 2018, 9(21): 15498-15511

[2] Gupta R, Kumar U, Mallapragada S, et al. Comparative Evaluation of Periodontal Status of Chronic Renal Failure Patients and Systemically Healthy Individuals[J]. J Contemp Dent Pract, 2018, 19(3): 324-330

[3] Akyã¼Z Ã A, Erdal R, Haberal M. Factors Predisposing to the Use of Complementary Therapies in Patients With Chronic Renal Failure[J]. Experimental & Clinical Transplantation, 2018, 16(Suppl 1): 64-69

[4] Pugh D, Gallacher P J, Dhaun N. Management of Hypertension in Chronic Kidney Disease[J]. Drugs, 2019, 79(4): 365-379

[5] Cole N I, Suckling R J, Desilva V, et al. Serum sodium concentration and the progression of established chronic kidney disease [J]. Journal of Nephrology, 2019, 32(2): 259-264

[6] Wang I K, Tsai T H, Hung Y C, et al. Increased risk of new-onset type 2 diabetes in people with chronic kidney disease [J]. International Urology and Nephrology, 2019(1): 1-6

[7] Kuro-O M. Klotho and endocrine fibroblast growth factors: markers of chronic kidney disease progression and cardiovascular complications? [J].Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association, 2019, 34(1): 15

[8] Hyun Y Y, Lee K B, Chung W, et al. Body Mass Index, waist circumference, and health-related quality of life in adults with chronic kidney disease[J]. Quality of Life Research, 2019, 28(4): 1075-1083

[9] Evans M, Palaka E, Furuland H, et al. The value of maintaining normokalaemia and enabling RAASi therapy in chronic kidney disease[J]. BMC Nephrology, 2019, 20(1): 31

[10] Schweitzer M L, Stengel B, Legrand K, et al. Obesity phenotype and patient-reported outcomes in moderate and severe chronic kidney disease: a cross-sectional study from the CKD-REIN cohort study[J].Quality of Life Research, 2019(5): 1-11

[11] Uribarri J. Nutritional Management of Chronic Kidney Disease[J]. New England Journal of Medicine, 2018, 378(6): 583

[12] Selewski D T, Hyatt D M, Bennett K M, et al. Is acute kidney injury a harbinger for chronic kidney disease?[J]. Current Opinion in Pediatrics, 2018, 30(2): 1

[13] Bischoff S C, Basrai M. Diet in Chronic Kidney Disease - A Practical Guide[J]. Deutsche Medizinische Wochenschrift, 2018, 143(12): 871

[14] Covic A, Voroneanu L. Chronic kidney disease and stroke: more observations but no trials [J]. Nephrology, dialysis, transplantation: official publication of the European Dialysis and Transplant Association - European Renal Association, 2018, 33(3): 367

[15] Connelly K, Collister D, Tangri N. Fracture risk and treatment in chronic kidney disease[J]. Curr Opin Nephrol Hypertens, 2018, 27(3): 1

[16] Kiuchi M G. Atrial fibrillation and chronic kidney disease: A bad combination [J]. Kidney Research & Clinical Practice, 2018, 37(2): 103-105

[17] Wheeler D, Turakhia M, Blankestijn P, et al. Chronic kidney disease and arrhythmias: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference[J]. European Heart Journal, 2018, 39(24): 2314-2325

[18] Gupta R, Kumar U, Mallapragada S, et al. Comparative Evaluation of Periodontal Status of Chronic Renal Failure Patients and Systemically Healthy Individuals [J]. J Contemp Dent Pract, 2018, 19(3): 324-330

[19] Zhenglin B, Ortiz A. Lipid Management in Chronic Kidney Disease: Systematic Review of PCSK9 Targeting [J]. Drugs, 2018, 78(6): 1-15

[20] Tabriziani H, Lipkowitz M S, Vuong N. Chronic kidney disease, kidney transplantation and oxidative stress: a new look to successful kidney transplantation [J]. Clinical Kidney Journal, 2018, 11(1): 130-135

[21] Aksoy G K, Koyun M, Ichida K, et al. Renal stone and chronic kidney failure associated with hypouricemia: Questions [J]. Pediatric Nephrology, 2018(6): 1-2

[22] Hasan M, Sutradhar I, Gupta R D, et al. Prevalence of chronic kidney disease in South Asia: a systematic review [J]. BMC Nephrology, 2018, 19(1): 291

[23] London G M. Arterial Stiffness in Chronic Kidney Disease and End-Stage Renal Disease[J]. Blood Purification, 2018, 45(1-3): 154

[24] Moody E C, Coca S G, Sanders A P. Toxic Metals and Chronic Kidney Disease: a Systematic Review of Recent Literature [J]. Current Environmental Health Reports, 2018, 5(4): 453-463

(下转第 4187 页)

[6] Clark S M, Dunn H E, Hankins G D. A review of oral labetalol and nifedipine in mild to moderate hypertension in pregnancy [J]. Seminars in Perinatology, 2015, 39(7): 548-555

[7] Shi Q, Leng W, Yao Q, et al. Oral nifedipine versus intravenous labetalol for the treatment of severe hypertension in pregnancy[J]. International Journal of Cardiology, 2014, 32(17): 162-164

[8] Sharma K J, Greene N, Kilpatrick S J. Oral labetalol compared to oral nifedipine for postpartum hypertension: A randomized controlled trial [J]. Hypertension in Pregnancy, 2017, 1(6): 1372-1377

[9] Steiner T, Juvela S, Unterberg A, et al.European Stroke Organization Guidelines for the Management of Intracranial Aneurysms and Subarachnoid Haemorrhage [J]. Cerebrovascular Diseases, 2013, 35(2): 93-99

[10] Koren G. Systematic review of the effects of maternal hypertension in pregnancy and antihypertensive therapies on child neurocognitive development[J]. Reproductive Toxicology, 2013, 39(4): 1-5

[11] Morris R, Sunesara I, Darby M, et al. Impedance cardiography assessed treatment of acute severe pregnancy hypertension: a randomized trial[J]. Journal of Applied Ecology, 2014, 29(2): 1-22

[12] Webb T N, Shatat I F, Miyashita Y. Therapy of acute hypertension in hospitalized children and adolescents [J]. Current Hypertension Reports, 2014, 16(4): 1-9

[13] Cannon C M, Levy P, Baumann B M, et al. Intravenous nicardipine and labetalol use in hypertensive patients with signs or symptoms suggestive of end-organ damage in the emergency department: a subgroup analysis of the CLUE trial[J]. Bmj Open, 2013, 3(3): 737-743

[14] Ostrye J, Hailpern S M, Jones J, et al. The efficacy and safety of intravenous hydralazine for the treatment of hypertension in the hospitalized child[J]. Pediatric Nephrology, 2014, 29(8): 1403-1410

[15] Vesoulis Z A, Attarian S J, Zeller B, et al. Minoxidil Associated Anorexia in an Infant with Refractory Hypertension[J]. Pharmacotherapy, 2014, 34(12): 341-344

[16] Vadhera R B, Simon M. Hypertensive emergencies in pregnancy[J]. Critical Care Clinics, 2016, 32(1): 29-35

[17] Brehaut S S, Roche A M. Abstract W P65: Clevidipine Outperforms Other Agents in Emergent Acute Hypertension Treatment in Ischemic Stroke Pre-rt-PA [J]. Journal of the Peripheral Nervous System,2015, 18(1): 64-71

[18] Shawkat E, Myers J E. PMM.76 The effect of ethnicity and different antihypertensives on the 24-hour blood pressure profile during pregnancy[J]. Archives of Disease in Childhood - Fetal and Neonatal Edition, 2014, 39(16): 147-153

[19] Jung Sun K, Eun Joo K, Ok Hee W, et al. The relationship between preeclampsia, pregnancy-induced hypertension and maternal risk of breast cancer: A meta-analysis [J]. Acta Oncologica, 2013, 52(8): 1643-1648

[20] Gordin D, Kaaja R, Forsblom C, et al. Pre-eclampsia and pregnancy-induced hypertension are associated with severe diabetic retinopathy in type 1 diabetes later in life [J]. Acta Diabetologica, 2013, 50(5): 781-787

[21] Leañosmiranda A, Méndezaguilar F, Ramírezvalenzuela K L, et al. Circulating angiogenic factors are related to the severity of gestational hypertension and preeclampsia, and their adverse outcomes [J]. Medicine, 2017, 96(4): e6005

[22] Sonnaville C D, Mol B W, Groen H, et al. 6: The impact of the HYPITAT I trial on obstetric management and outcome for gestational hypertension and preeclampsia in the Netherlands[J]. American Journal of Obstetrics & Gynecology, 2018, 218(1): S5-S6

[23] Kim S J, Ahn H J, Park J Y, et al. The clinical significance of D-dimer concentrations in patients with gestational hypertensive disorders according to the severity[J]. Obstetrics & Gynecology Science, 2017, 60(6): 542-548

[24] Malhotra A S, Goel P, Chaudhary A, et al. Serial profile of flow-mediated dilatation in primigravida for prediction of preeclampsia and gestational hypertension[J]. Hypertension in Pregnancy, 2018, 37(11): 1-8

[25] Jirakittidul P, Sirichotiyakul S, Ruengorn C, et al. Effect of iron supplementation during early pregnancy on the development of gestational hypertension and pre-eclampsia[J]. Archives of Gynecology & Obstetrics, 2018, 298(3): 545-550

[26] Breatnach C R, Monteith C, Mcsweeney L, et al. The Impact of Maternal Gestational Hypertension and the Use of Anti-Hypertensives on Neonatal Myocardial Performance [J]. Neonatology, 2017, 113(1): 21-26

[27] Jeon Y, Lee W I, Kang S Y, et al. Modified Complete Blood Count Indices as Predicting Markers of Preeclampsia from Gestational Hypertension: Neutrophil to Lymphocyte Ratio, Platelet to Lymphocyte Ratio[J]. Clinical Laboratory, 2017, 63(11): 1897-1902

[28] Dasgupta K, Pace R. Dasgupta and Pace Respond to "Gestational Hypertension and Diabetes" [J]. American Journal of Epidemiology, 2017, 186(10): 1129-1130

[29] Eche S, Mackraj I, Moodley J. Circulating fetal and total cell-free DNA, and sHLA-G in black South African women with gestational hypertension and pre-eclampsia[J]. Hypertension in Pregnancy, 2017, 36(2): 1-7

[30] Khaskheli M N, Baloch S, Sheeba A, et al. Labour induction with gestational hypertension: A great obstetric challenge [J]. Pakistan Journal of Medical Sciences, 2017, 33(1): 151-155

（上接第 4179 页）

[25] Gomaa A M S, Abdelhafez A T, Aamer H A. Garlic (Allium sativum) exhibits a cardioprotective effect in experimental chronic renal failure rat model by reducing oxidative stress and controlling cardiac Na^+/K^+-ATPase activity and Ca^{2+} levels[J]. Cell Stress & Chaperones, 2018(Suppl 1): 1-8

[26] Clifforde E L. Chronic renal disease in dogs and cats: anaesthesia considerations[J]. Veterinary Nursing Journal, 2018, 33(5): 131-137

[27] Kobusiakprokopowicz M, Krzysztofik J, Kaaz K, et al. MMP-2 and TIMP-2 in Patients with Heart Failure and Chronic Kidney Disease [J]. Open Medicine, 2018, 13(1): 237-246

[28] Hawkins C L. Protein carbamylation: a key driver of vascular calcification during chronic kidney disease [J]. Kidney International, 2018, 94(1): 12-14

[29] Hu H, Xu S, Hu S, et al. The clinical characteristics of posterior reversible encephalopathy syndrome in patients with chronic renal failure[J]. Experimental & Therapeutic Medicine, 2017, 14(1): 881

[30] Trimble A, Partridge R. Smoke on the water: A case report of chronic renal failure resulting from the ingestion of smoke machine fluid[J]. Journal of the Intensive Care Society, 2017, 18(1): 57-58