doi: 10.13241/j.cnki.pmb.2017.12.019

肝细胞生长因子和基质金属蛋白酶 -9 在过敏性紫癜中表达的意义 *

阿迪力江·喀日[1] 阿曼姑·阿不都沙拉木[2] 郭艳芳[1] 朱洪涛[1] 阿布来提·阿布都卡德尔[1△]

（1 新疆医科大学第一附属医院儿科小儿重症监护室 新疆 乌鲁木齐 830054；
2 喀什地区第一人民医院冠心病二科 新疆 喀什 844000）

摘要 目的：探讨肝细胞生长因子（HGF）和基质金属蛋白酶 -9（MMP-9）在儿童过敏性紫癜（HSP）中表达的意义，探寻肾脏损害预测的敏感指标。**方法**：选取 HSP 与过敏性紫癜肾炎（HSPN）患儿各 30 例，并选取同期体检的健康儿童 30 名作为对照组，采用酶联免疫吸附试验法（ELISA）检测 3 组血清和尿液中的 HGF 及血清 MMP-9 含量，并采用比浊法检测 24 h 尿蛋白，分析 HGF、MMP-9 与 24 h 尿蛋白的相关性。**结果**：HSP 组、HSPN 组血清、尿液 HGF，血清 MMP-9 及尿蛋白定量均高于对照组（P＜0.05）；HSPN 组中Ⅱ~Ⅳ期患者血清 HGF 及Ⅰ~Ⅳ期尿液 HGF、Ⅲ~Ⅳ期 MMP-9 及Ⅰ~Ⅳ期尿蛋白定量均高于 HSP 组（P＜0.05）；血清及尿液 HGF 与血清 MMP-9 无明显相关性（r＝0.014，0.027，P＞0.05）；血清 HGF 与尿蛋白定量无明显相关性（r＝0.032，P＞0.05）；尿液 HGF、血清 MMP-9 与尿蛋白定量均呈正相关（r＝0.412、0.302，P＜0.05）。**结论**：尿液 HGF、MMP-9 均参与 HSP、HSPN 病情的发展，尿液 HGF、MMP-9 水平的监测有助于评估 HSPN 的病情及预后，但 HGF 与 MMP-9 之间无明显相关性。

关键词：过敏性紫癜 / 过敏性紫癜肾炎；肝细胞生长因子；基质金属蛋白酶 -9；尿蛋白定量
中图分类号：R692.34 **文献标识码**：A **文章编号**：1673-6273(2017)12-2279-03

Expressions of Hepatocyte Growth Factor and Matrix Metalloproteinases -9 in Henoch-Schonlein Purpura*

Adilijiang·Kari[1], Amangu·Abudushalamu[2], GUO Yan-fang[1], ZHU Hong-tao[1], Abulaiti·Abudukadeer[1△]

*(1 Department of paediatrics, the First Affiliated Hospital of Xinjiang Medical University, Urumqi, Xinjiang, 830054, China;
2 Department of Coronary heart disease, the First People's Hospital of Kashi, Kashi, Xinjiang, 844000, China)*

ABSTRACT Objective: To investigate expressions of hepatocyte growth factor (HGF) and matrix metalloproteinases-9 (MMP-9) in henoch-schonlein purpura (HSP), and to explore the sensitive indicators of nephritis. **Methods:** 30 children with henoch schonlein purpura nephritis (HSPN) were selected as the (HSPN group, and another 30 healthy children were selected as the control group. The enzyme-linked immunosorbent assay (ELISA) was applied to detect the HGF levels in serum and urine and serum contents of MMP-9, and turbidimetric method was used to detect the 24 h urine protein. Analyze the correlation of MMP-9 and HGF with 24 h urine protein. **Results:** The levels of urine and serum HGF, serum MMP-9 and urinary protein were higher in HSP and HSPN group than in control group (P<0.05). The levels of serum HGF of Ⅱ ~ Ⅳ stage patients, the urine levels of HGF of Ⅰ ~ Ⅳ stage patients, the serum levels of MMP-9 of Ⅲ~ Ⅳ stage patients and the urinary protein levels of Ⅰ ~ Ⅳ stage patients were higher in HSPN group than in HSP group (P<0.05). Serum and urine HGF levels had no significant correlation with MMP-9 serum levels (r=0.014, 0.027, P>0.05). Serum HGF had no significant correlation with urine protein quantitative (r=0.032, P>0.032). HGF urine level and MMP-9 serum level both had a positive correlation with urine protein quantitative (r=0.412, 0.302, P<0.05). **Conclusion:** The urine HGF and MMP-9 participates in the development of HSP and HSPN. The monitoring on the levels of urine HGF and MMP-9 may help to assess the state and prognosis of HSPN. But there was no significant correlation between HGF and MMP-9.

Key words: Henoch-schonlein purpura/Henoch-schonlein purpura nephritis; Hepatocyte growth factor; Matrix metalloproteinases -9; Urine protein quantitative

Chinese Library Classification(CLC): R692.34 Document code: A

Article ID:1673-6273(2017)12-2279-03

前言

过敏性紫癜（Henoch-schonlein purpura，HSP）是儿童继发肾脏损害的常见疾病，常因弥漫性小血管炎和免疫球蛋白复合

* 基金项目：新疆维吾尔自治区自然科学基金项目（2014211C097）
作者简介：阿迪力江·喀日（1983-），男，硕士研究生，主治医师，主要从事小儿危重症监护及肾脏保护，
电话：0991-4362930，E-mail: 2382990359@qq.com
△ 通讯作者：阿布来提·阿布都卡德尔（1975-），男，主任医师，主要从事小儿危重症监护及肾脏保护，
电话：0991-4362930，E-mail: 2382990359@qq.com
（收稿日期：2016-07-30 接受日期：2016-08-23）

物沉积而导致肾小球改变而发展成为过敏性紫癜肾炎(Henoch-schonlein purpura nephritis,HSPN)[1]。肾间质纤维化是的 HSPN 的主要病理特征。近年研究显示，肝细胞生长因子(Hepatocyte growth factor,HGF)参与肾间质纤维化的进程[2]。而基质金属蛋白酶 -9(Matrix metalloproteinases- 9,MMP-9)的过度表达可加强细胞外基质降解而加快肾小球硬化[3]。但临床对于 HGF 与 MMP-9 及与 HSP、HSPN 的相关性尚无报道。本研究通过检测 HSP 与 HSPN 患儿血清及尿液 HGF 及 MMP-9 含量,探讨 HGF 与 MMP-9 是否可作为预测早期肾脏损害的敏感性指标的可能性。

1 资料与方法

1.1 临床资料

选取 2011 年 7 月至 2012 年 12 月在新疆医科大学第一附属医院就诊的 HSP、HSPN 患儿各 30 例。纳入标准:① 符合《儿科学》中有关 HSP、HSPN 相关诊断标准[4];② 伴有骨关节疼痛、胃肠道疼痛、尿常规异常等症状;③ HSP 均为初次发病;④ 1 个月前未使用免疫介导或激素类药物; ⑤ 家属签署知情同意书。排除标准:① 伴有严重心、肝、血液提供疾病者;② 伴有糖尿病、肾病综合征、系统性红斑狼疮、川崎病者。同时选取同期在本院体检的健康儿童 30 名作为对照组,对照组无心、脑、肺、肝、肾、内分泌及生殖系统疾病。HSP 组男 19 例,女 11 例,年龄 2~13 岁,平均(7.34± 2.03)岁。HSPN 组男 17 例,女 13 例,年龄 3~14 岁,平均(7.69± 2.34)岁;病理分期:Ⅰ期 7 例,Ⅱ期 13 例,Ⅲ期 6 例,Ⅳ期 4 例。对照组男 17 例,女 13 例,年龄 2~14 岁,平均(7.15± 1.96)岁。三组临床基本资料无差异具有可比性。

1.2 检测方法

抽取 3 组空腹静脉血 3 mL 各 2 份,1 份进行 3000 r/min 离心 20 min,取上层血清,置于 -80℃冰箱中保存,用于检测血清 HGF;1 份静置 30 min，待其凝血后进行 3000 r/min 离心 5 min,取上层血清,置于置于 -80℃冰箱中保存,用于检测血清 MMP-9。同时留取晨尿 10 mL 各 2 份,1 份进行 1500 r/min 离心 5 min，取上清液，置于 -80℃冰箱中保存，用于检测尿液 HGF。采用 ELISA 法血清、尿液 HGF 及血清 MMP-9,试剂盒购自江苏晶美生物科技有限公司。1 份尿液采用比浊法检测尿蛋白定量，采用酶促动力学法检测尿肌酐仪器均为 Cobas MIRA plus 全自动生化分析仪(瑞士生产)。为降低人为误差增加可比性,尿液 HGF 水平以其与尿肌酐的比值表示。

1.3 统计学方法

本研究计量资料用 ($\bar{x}$± s)表示,采用 t 检验;血清、尿液 HGF 与血清 MMP-9 及尿蛋白定量的相关性采用 Spearman 相关性检验,P<0.05 为差异有统计学意义。

2 结果

2.1 三组血清、尿液 HGF 水平比较

HSP 组、HSPN 组血清及尿液 HGF 均显著高于对照组,差异有统计学意义(P＜0.05);HSPN 组中Ⅰ~Ⅱ期患者血清 HGF 与 HSP 组比较差异无统计学意义(P＞0.05),但Ⅲ~Ⅳ期患者血清 HGF 高于 HSP 组,差异有统计学意义(P＜0.05);HSPN 组Ⅰ~Ⅳ期尿液 HGF 均高于 HSP 组，差异有统计学意义（P＜0.05)(表 1)。

表 1 三组血清、尿液 HGF 水平比较($\bar{x}\pm s$)

Table 1 Comparison of the serum and urine HGF levels between three groups($\bar{x}$± s)

Groups	By stages	Cases(n)	Serum HGF(ng/L)	Urine HGF/urine creatinine
Control group		30	251.14± 83.21	0.74± 0.32
HSP		30	365.38± 79.35*	1.36± 0.33#
HSPN	Ⅰ	7	388.46± 85.36*	1.89± 0.31#*
	Ⅱ	13	403.21± 82.14*	2.64± 0.42#*
	Ⅲ	6	564.12± 101.24*△	2.87± 0.39#*
	Ⅳ	4	586.53± 96.53*△	3.01± 0.41#*

Note: Compared with the serum HGF levels of control group , *P＜0.05; compared with the urine HGF levels of control group, #P＜0.05; comparison of serum HGF levels between HSPN and HSP group, △ P＜0.05; comparison of urine HGF levels between HSPN and HSP group, ' P＜0.05.

2.2 三组血清 MMP-9 水平、尿蛋白定量比较

HSP 组、HSPN 组血清 MMP-9 及尿蛋白定量均显著高于对照组,差异有统计学意义(P＜0.05);HSPN 组中Ⅰ期、Ⅱ期患者 MMP-9 与 HSP 组比较差异无统计学意义(P＞0.05),但Ⅲ~Ⅳ期患者 MMP-9 高于 HSP 组,差异有统计学意义(P＜0.05);HSPN 组Ⅰ~Ⅳ期尿蛋白定量均高于 HSP 组，差异有统计学意义(P＜0.05)(表 2)。

2.3 血清、尿液与 MMP-9 及尿蛋白定量的相关性

Spearman 相关性检验显示 HSP、HSPN 患者血清及尿液 HGF 与血清 MMP-9 无明显相关性(r＝0.014,0.027,P＞0.05);HSP、HSPN 患者血清 HGF 与尿蛋白定量无明显相关性（r＝0.032,P＞0.05);尿液 HGF 与尿蛋白定量呈正相关(r＝0.412,P＜0.05);MMP-9 与尿蛋白定量呈正相关(r＝0.302,P＜0.05)。

3 讨论

过敏性紫癜肾炎是多种细胞因子共同参与及促进的结果[5]。HGF 是一种强效肾脏营养因子。研究证实 HGF 在有害刺激后,对促小管的修复及再生起关键作用[6];转化生长因子 -β(TGF-β)的过度表达与肾脏间质纤维化密切相关,而 HGF 的表达降低直接导致了 TGF-β 的升高[7,8]。研究证实过敏性紫癜

表 2 三组血清 MMP-9、尿蛋白定量比较($\bar{x}\pm s$)

Table 2 Comparison of serum MMP - 9 and urine protein quantitative between three groups($\bar{x}\pm s$)

Groups	by stages	Case number	Serum MMP-9(ng/mL)	Urine protein quantitative (g/24 h)
Control group		30	51.32± 83.21	0.08± 0.17
HSP		30	242.19± 69.22*	2.16± 0.36#
HSPN	Ⅰ	7	268.46± 75.22*	2.81± 0.30#*
	Ⅱ	13	294.21± 72.67*	3.33± 0.41#*
	Ⅲ	6	465.13± 89.14*△	3.59± 0.36#*
	Ⅳ	4	516.33± 91.06*△	4.01± 0.52#*

Note: Compared with the serum MMP-9 levels of control group , *P＜0.05; compared with the urine protein quantitative of control group, #P＜0.05; comparison of serum MMP-9 levels between HSPN and HSP group, △P＜0.05; comparison of urine protein quantitative between HSPN and HSP group, *P＜0.05.

及过敏性紫癜肾炎患者急性期血清 HGF 水平明显升高[9,10]。本研究中,HSP 组、HSPN 组血清及尿液 HGF 均显著高于对照组,差异有统计学意义(P＜0.05),与文献报道基本一致。过敏性紫癜及过敏性紫癜肾炎患者急性期 HGF 水平升高反映了内皮细胞的损伤和功能障碍。Jacobi 等[11]研究报道,HGF 参与了过敏性紫癜肾炎的发生、发展过程,在病理分期为Ⅰ~Ⅱ期时,随着肾脏损害的加重,HGF 的浓度呈上升趋势,而在Ⅲ~Ⅳ期时 HGF 则呈下降趋势。本研究中 HSPN 组中Ⅰ~Ⅱ期患者血清 HGF 与 HSP 组比较差异无统计学意义(P＞0.05),但Ⅲ~Ⅳ期患者血清 HGF 高于 HSP 组,差异有统计学意义(P＜0.05),与 Jacobi 等[11]等研究不符。笔者认为,过敏性紫癜肾炎Ⅰ~Ⅱ期患者肾损害与过敏性紫癜患者无明显差异,血清中的 HGF 未发生较大变化,而到了Ⅲ~Ⅳ期,随着肾损害的加重,肾脏受累,机体分泌 HGF 增多,以期实现机体自我保护作用。当肾脏受到损伤时,可诱导肾组织局部细胞因子的增加,这些细胞因子经尿液排出,因此尿液可反映肾组织局部细胞因子的状况及肾脏病变程度。HGF 分子量较大,在正常情况下不能经过肾小球滤过,70%以上的 HGF 需经肝脏代谢。而当肾脏受损时,HGF 可经肾小球滤过[12]。因此在肾脏受损情况下,尿液 HGF 的变化较血清 HGF 变化敏感。本研究中,HSPN 组Ⅰ~Ⅳ期尿液 HGF 均高于 HSP 组,差异有统计学意义(P＜0.05)。Spearman 相关性分析显示,HSP、HSPN 患者血清 HGF 与尿蛋白定量无明显相关性(r＝0.032,P＞0.05);尿液 HGF 与尿蛋白定量呈正相关(r＝0.412,P＜0.05)。由此提示,尿液 HGF 水平比血清 HGF 更能反映肾脏损害程度。

过敏性紫癜肾炎的主要病理特征是细胞外基质在肾小球基底膜和系膜区沉积导致系膜膨胀和肾小球基底膜增厚。大量研究证实,MMP-9 可促进细胞外间质降解而参与动脉粥样硬化斑块的形成、破裂,川崎病及巨细胞动脉炎等多种血管炎性疾病的发病机制[13,14]。研究发现小儿过敏性紫癜血清中 MMP-9 浓度显著高于健康儿童(P＜0.05)[15];过敏性紫癜与过敏性紫癜肾炎患儿血清、尿液中 MMP-9 的水平显著高于健康儿童(P＜0.05)[16]。本研究中,HSP 组、HSPN 组血清 MMP-9 显著高于对照组,差异有统计学意义(P＜0.05),HSPN 组中Ⅰ期、Ⅱ期患者 MMP-9 与 HSP 组比较差异无统计学意义(P＞0.05),但Ⅲ~Ⅳ期患者 MMP-9 高于 HSP 组,差异有统计学意义(P＜0.05)。Spearman 相关性分析显示,MMP-9 与尿蛋白定量呈正相关(r＝0.302,P＜0.05)。由此提示,MMP-9 与过敏性紫癜及过敏性紫癜肾炎的发生、发展密切相关。我们认为,MMP-9 作为细胞外基质降解的主要成分,其表达增加必然会对血管内皮屏障产生直接破坏作用,进而使肾脏发生损害。而血管内皮屏障的破坏可激活并释放多种细胞因子及炎性介质,进一步诱导血管内皮合成更多的 MMP-9。

综上可知,HGF 与 MMP-9 均参与过敏性紫癜与过敏性紫癜肾炎的发生及发展,二者之间是否具有相关性呢? Danilewicz 等[17]研究发现,HGF 可显著增加诸如 MMP-9 等胶原酶的表达、降低 TIMP-1 和 TIMP-2 的表达而促进基质降解。Libetta 等[18]研究则发现,HGF 可促进 MMP-9 的表达,而加强细胞外基质的降解而促进肾纤维化。我国学者对于过敏性紫癜、过敏性紫癜肾炎患儿 HGF 与 MMP-9 之间的关系尚无研究报道。本研究中,Spearman 相关性检验显示 HSP、HSPN 患者血清及尿液 HGF 与血清 MMP-9 无明显相关性(r＝0.014,0.027,P＞0.05),与 Danilewicz[19]及 Libetta 等[20]报道不符,其原因有待进一步研究,也许 HGF 与 MMP-9 通过不同的途径参与肾损害进程。

综上所述,尿液 HGF、MMP-9 均参与 HSP、HSPN 病情的发展,尿液 HGF、MMP-9 水平的监测有助于评估 HSPN 的病情及预后,但 HGF 与 MMP-9 之间无明显相关性。

参 考 文 献(References)

[1] Mao, Song, Huang, Song-ming. Association of AGT M235T gene polymorphism with HSP/HSPN risk [J]. Renal Failure, 2015, 37(1): 16-21

[2] Holland WS, Chinn DC, Lara PN Jr, et al. Effects of AKT inhibition on HGF-mediated erlotinib resistance in non-small cell lung cancer cell lines[J]. Journal of Cancer Research and Clinical Oncology, 2015, 141(4): 615-626

[3] Ishida Y, Kuninaka Y, Nosaka M, et al. Immunohistochemical analysis on MMP-2 and MMP-9 for wound age determination[J]. International journal of legal medicine,2015, 129(5): 1043-1048

[4] 王卫平.儿科学[M].第 8 版.北京:人民卫生出版社, 2013: 112-113
Wang Wei-ping. Pediatrics [M]. The 8th edition. Beijing: people's medical publishing house, 2013: 112-113

(下转第 2293 页)

[8] Ribeiro OD, Canedo NH, Pannain VL. Immunohistochemical angiogenic biomarkers in hepatocellular carcinoma and cirrhosis: correlation with pathological features [J]. Clinics (Sao Paulo), 2016, 71(11): 639-643

[9] Lanza E, Donadon M, Poretti D, et al. Transarterial Therapies for Hepatocellular Carcinoma[J]. Liver Cancer, 2016, 6(1): 27-33

[10] Zhang Y, Tang W, Peng L, et al. Identification and validation of microRNAs as endogenous controls for quantitative polymerase chain reaction in plasma for stable coronary artery disease [J]. Cardiol J, 2016, 23(6): 694-703

[11] Shin VY, Chu KM.MiRNA as potential biomarkers and therapeutic targets for gastric cancer [J]. World J Gastroenterol, 2014, 20(30): 10432-10439

[12] Huang T, Wang-Johanning F, Zhou F, et al. MicroRNAs serve as a bridge between oxidative stress and gastric cancer (Review)[J]. Int J Oncol, 2016, 49(5): 1791-1800

[13] da Silva Oliveira KC, Thomaz Araú jo TM, Albuquerque CI, et al. Role of miRNAs and their potential to be useful as diagnostic and prognostic biomarkers in gastric cancer [J]. World J Gastroenterol, 2016, 22(35): 7951-7962

[14] El-Garem H, Ammer A, Shehab H, et al. Circulating microRNA, miR-122 and miR-221 signature in Egyptian patients with chronic hepatitis C related hepatocellular carcinoma [J]. World J Hepatol, 2014, 6(11): 818-824

[15] Zeng K, Zheng W, Mo X, et al. Dysregulated microRNAs involved in the progression of cervical neoplasm [J]. Arch Gynecol Obstet, 2015, 292(4): 905-913

[16] Jikuzono T, Kawamoto M, Yoshitake H, et al. The miR-221/222 cluster, miR-10b and miR-92a are highly upregulated in metastatic minimally invasive follicular?thyroid?carcinoma [J]. Int J Oncol, 2013, 42(6): 1858-1868

[17] Huang N, Wu Z, Lin L, et al. MiR-338-3p inhibits epithelial-mesenchymal transition in gastric cancer cells by targeting ZEB2 and MACC1/Met/Akt signaling [J]. Oncotarget, 2015, 6(17): 15222-15234

[18] Sun K, Deng HJ, Lei ST, et al. miRNA-338-3p suppresses cell growth of human colorectal carcinoma by targeting smoothened [J]. World J Gastroenterol, 2013, 19(14): 2197-2207

[19] Nie H,Li J, Yang XM, et al. Mineralocorticoid receptor suppresses cancer progression and the Warburg effect by modulating themiR-338-3p-PKLR axis in hepatocellular carcinoma[J]. Hepatology, 2015, 62(4): 1145-1159

[20] Guo B, Liu L,Yao J, et al. miR-338-3p suppresses gastric cancer progression through a PTEN-AKT axis by targeting P-REX2a[J]. Mol Cancer Res, 2014, 12(3): 313-321

（上接第 2281 页）

[5] Calvo RV, Hernández JL, Ortiz SF, et al. Relapses in patients with Henoch-Schönlein purpura:Analysis of 417 patients from a single center[J]. Medicine(Baltimore), 2016, 95(28): 217-223

[6] Iorio N, Bernstein GR, Malik Z, et al. Acute Esophageal Necrosis Presenting With Henoch-Schönlein Purpura [J]. ACG Case Rep J, 2015, 3(1): 17-19

[7] Mohtat D, Thomas R, Du Z, et al. Urinary transforming growth factor beta-1 as a marker of renal dysfunction in sickle cell disease [J]. Pediatr Nephrol, 2011, 26(2): 275-280

[8] Iekushi K, Taniyama Y, Azuma J, et al. Hepatocyte growth factor attenuates renal fibrosis through TGF-β1 suppression by apoptosis of myofibroblasts[J]. Hypertens, 2010, 28(12): 2454-2461

[9] Zhao Hui-juan, Sun Li-dong, Zhang Lin-xia. Adult allergic purpura nephritis patients serum levels of hepatocyte growth factor and the study of blood in the urine of connective tissue growth factor [J]. Journal of cellular and molecular immunology journal, 2011, 27 (3): 309-310

[10] Baum E, Pawlaczyk K, Maćkowiak B, et al. Levels of hepatocyte growth factor in serum correlate with quality of life in hemodialysis patients[J]. Int J Clin Exp Pathol, 2015, 8(10): 3477-3482

[11] Jacobi A, Pedersen JS, Morth JP, et al. Crystal structure of a two-domain fragment of hepatocyte growth factor activator inhibitor-1: funtional interactions between the kunitz-type inhibitor domain-1 and the neigboring polycystic kidney disease-like domain [J]. J Biol Chem, 2016, 291(27): 1434-1455

[12] Mizerska WM, Skrzypczyk P, Kisiel A, et al. Abdominal symptoms necessitating surgical intervention as the initial presentation of Henoch-Schönlein purpura in children-case reports [J]. Pol Merkur Lekarski, 2016, 40(240): 377-379

[13] Tripathi YB, Shukla R, Pandey N, et al. Pueraria tuberose (PTY-2) attenuates diabetic nephropathy by up-regulating the MMP-9 expression in the kidney of diabetic rats [J]. J Diabetes, 2016, 29(2): 1132-1136

[14] Pulido OH, Garcí a CF, Álvarez LG, et al. Role of matrix metalloproteinase-9 in chronic kidney disease:a new biomarker of resistant albuminuria[J]. Clin Sci(Lond), 2016, 130(7): 525-538

[15] Shi Jian, Teng Hua. Serum leukotriene B4, thrombosis, regulatory proteins, matrix metalloproteinases 9, interleukin 4 and the incidence of pediatric allergic purpura relationship [J]. Chinese journal of clinical physicians (electronic), 2015, 9(23): 4344-4347

[16] Li Cui-cui, Chen Qu-bo, Zhang Yun-jiao, et al. Children with allergic purpura matrix metalloproteinases 9 levels of change and clinical significance[J]. Guangdong medicine, 2011, 32(22): 2945-2946

[17] Danilewicz M, Wagrowska DM. Differential glomerular immunoexpression of matrix metalloproteinases MMP-2 and MMP-9 in idiopathic IgA nephropathy and Schoenlein-Henoch nephritis [J]. Folia Histochem Cytobiol, 2010, 48(1): 63-67

[18] Libetta C, Esposito P, Martinelli C, et al. Hepatocyte growth factor (HGF)and hemodialysis: physiopathology and clinical impli cations [J]. Clin Exp Nephrol, 2016, 20(3): 371-378