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ICU 行气管切开患者下呼吸道感染危险因素及血清 PCT、hCRP 联合检测的早期预测价值研究 *

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摘要 目的:研究 ICU 行气管切开患者下呼吸道感染危险因素及血清 PCT、hCRP 联合检测的早期预测价值。**方法:**选择 2017 年 1 月至 2019 年 12 月在我院 ICU 病房接受气管切开患者 82 例作为研究对象,按照是否下呼吸道感染分为观察组(n=41)和对照组(n=41),观察组为合并下呼吸道感染病人,对照组为无下呼吸道感染病人。对比两组病人的临床资料、特征、血清超敏 C- 蛋白(hCRP)和降钙素原(PCT)检测值、细菌性感染情况、应用 Logistic 回归分析其危险因素。**结果:**年龄、入住 ICU 时间、气道开放时间、手术时机、呼吸机的应用、侵入性操作、使用抗生素种类及使用抗生素时间等情况与 ICU 下呼吸道感染病人有关,对比差异显著($P<0.05$);观察组病人的 PCT 及 hCRP 水平明显高于对照组($P<0.05$);通过 CURB 病情高低分为:高危组 8 例、中危组 11 例和低危组 22 例,高危组病人的血清 hCRP 和 PCT 检测值明显高于低危组和中危组($P<0.05$);PCT 检测的病人灵敏度、特异度、阳性预测值和阴性预测值均高于 hCRP 的检测结果($P<0.05$);年龄、入住 ICU 时间、手术时间、呼吸机的应用、侵入性操作、气道开放时间及抗生素≥ 2 种≥ 2 周均为 ICU 行气管切开下呼吸道感染病人的独立危险因素。**结论:**ICU 行气管切开术患者合并下呼吸道感染的危险因素较多,如年龄、入住 ICU 时间、气道开放时间、手术时机、呼吸机的应用、侵入性操作、使用抗生素种类及使用抗生素时间等均为主要因素,血清 PCT 及 hCRP 水平变化可作为 ICU 下呼吸道感染病人早期诊断和病情检测的指标之一。

关键词:重症监护室病房;气管切开;下呼吸道感染;超敏 C- 蛋白;降钙素原;危险因素

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Risk Factors of Lower Respiratory Tract Infection in Patients with Tracheotomy in ICU and Early Predictive Value of Combined Detection of Serum PCT and hCRP*

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ABSTRACT Objective: To study the risk factors of lower respiratory tract infection and the early predictive value of serum PCT and hCRP in ICU patients undergoing tracheotom. **Methods:** From January 2017 to December 2019, 82 patients receiving tracheotomy in the ICU ward of our hospital were selected as the study objects. According to whether or not lower respiratory tract infection was detected, they were divided into the observation group (n=41) and the control group (n=41). The observation group was patients with lower respiratory tract infection, while the control group was patients without lower respiratory tract infection. The clinical data, characteristics, serum hypersensitive c-protein (hCRP) and procalcitonin (PCT) detection values, bacterial infection status and risk factors of the two groups were compared using Logistic regression analysis. **Results:** Age, ICU admission time, airway opening time, surgical timing, ventilator application, invasive operation, antibiotic types and duration of antibiotic use were significantly correlated with patients with subicu respiratory tract infection ($P<0.05$). PCT and hCRP levels in the observation group were significantly higher than those in the control group ($P<0.05$). The patients in the high-risk group were divided into 8 patients in the high-risk group, 11 patients in the medium-risk group and 22 patients in the low-risk group. The serum hCRP and PCT values in the high-risk group were significantly higher than those in the low-risk group and the medium-risk group ($P<0.05$). The sensitivity, specificity, positive predictive value and negative predictive value of PCT were higher than that of hCRP ($P<0.05$). Age, ICU admission time, surgical duration, ventilator use, invasive procedures, airway opening time and ≥ 2 antibiotics ≥ 2 weeks were independent risk factors for lower respiratory tract infection in patients undergoing tracheotomy in ICU. **Conclusion:** Line ICU patients with tracheotomy with lower respiratory infection risk factors, such as age, ICU admission time, airway open time, operation time, the application of the breathing machine, invasive operation, types of antibiotics, and use of antibiotics are the main factors such as time, serum PCT and hCRP level changes can be used as a lower respiratory tract infections in the ICU patients early diagnosis and a test of one of the indicators.

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前言

下呼吸道感染是重症加强护理病房(ICU)的常见疾病,被世界列为疾病死亡的首要原因之一[1]。相关研究证明[2],气道切开术后下呼吸道感染的发生不仅延长了病人的住院时间和治疗费用,同时增加了病人的病死率。因此,对 ICU 行切管切开术后下呼吸道感染的相关进行了综合分析,掌握医院下呼吸道感染的危险,便于临床采取有效的防治措施[3,4]。近年来,随着医疗技术的不断发展,大量医学设备等的引进,是我国的诊断和治疗技术不断进步。相关文献显示[5,6],随着 PCT 和 hCRP 等检测的广泛应用,可对病人感染的发生及发展进行准确预测,早期合理治疗,避免滥用抗生素而产生的耐药性,有效改善 ICU 病人的预后效果,为临床提供一个参考依据。本文旨在探讨 ICU 行气管切开患者下呼吸道感染危险因素及血清 PCT、hCRP 联合检测的早期预测价值研究。现报道如下。

1 材料与方法

1.1 一般资料

选择 2017 年 1 月至 2019 年 12 月在我院 ICU 病房接受气管切开患者 82 例作为研究对象,纳入标准[7]:(1)血白细胞升高或降低,且发热者(T>37.5℃);(2)术前服用糖皮质激素者;(3)均入住 ICU 病房者。排除标准:(1)在研究期死亡者;(2)对氨溴索等药物过敏者。将入选病人按照是否下呼吸道感染分为观察组(n=41)和对照组(n=41),观察组为合并下呼吸道感染病人,对照组为无下呼吸道感染病人。其中观察组男 26 例,女 15 例,平均年龄(55.23±6.18)岁;对照组男 24 例,女 17 例,平均年龄(43.28±5.82)岁,两组患者上述基线资料相比具有可比性。本次研究经伦理委员会批准同意且患者知情并签署同意书。

1.2 方法

对照组:在患者入院后,接受氧疗、口腔护理、气道护理等治疗措施。观察组:在患者确诊下呼吸道感染后,及时送检病原标本,根据病人基础病情,给予抗感染治疗,加强痰液引流、气道护理、营养支持等。可给予沐舒坦(勃林格英格翰公司,15 mg/支,20180112)30 mg/ 次,静脉注射,每 8 小时一次,以及联合沐舒坦给予气道雾化使用,15/ 次,每 8 小时一次。

1.3 观察指标

所有病人均于住院后次日清晨取静脉血 4 mL,经 3000 r/min 离心后,置入 -20℃待检。hCRP:采用免疫透射比浊法检测,使用日立 7600 仪器,参考范围 0 到 2 ng/mL。PCT:采用 ELISA 法检测,使用罗氏 ES2012 仪器测试,试剂为德国 BRAHMS,正常值为 0 到 6 mmol/L。以上操作严格按照试剂盒说明进行。观察并记录病人的临床资料及特征。

1.4 统计学分析

本研究数据采用 spss19 软件包进行统计学处理,计量资料使用平均值±标准差表示,组间采用独立样本 t 检验进行比较,计数资料使用百分比表示,采用 χ^2 检验进行比较,等级资料使用致和检验,应用 Logistic 回归分析多因素,当 $P<0.05$ 时表示其差异在统计学上有意义。

2 结果

2.1 临床特征结果对比

两组病人性别对比无明显差异($P>0.05$);而在年龄、入住 ICU 时间、气道开放时间、手术时机、呼吸机的应用、侵入性操作、使用抗生素种类及使用抗生素时间等情况对比差异显著,($P<0.05$)。详见表 1。

表 1 两组病人临床特征结果对比[n(%)]

Table 1 Comparison of clinical characteristics between the two groups [n(%)]

Clinical features		Observation group(n=41)	Control group(n=41)
Age (years)		55.23±6.18a	43.28±5.82
Gender (ex)	male	26(63.41)	24(58.54)
	Female	15(36.59)	17(41.46)
ICU admission time(d)		19.73±3.52[a]	12.89±2.84
Airway opening time(d)		24.23±3.63[a]	11.27±2.16
Operation time(n)	Early	9(21.95)	14(34.15)
	initiative	15(36.59)[a]	23(92.68)
	passive	17(41.46)	4(9.77)
Use a ventilator(n)	Yes	30(73.17)[a]	21(51.22)
	No	11(26.83)	20(48.78)
Invasive operation(n)	Yes	29(70.73)[a]	9(21.95)
	No	12(29.27)	32(78.05)

续表 1 两组病人临床特征结果对比[n(%)]

Table 1 Comparison of clinical characteristics between the two groups [n(%)]

Clinical features		Observation group(n=41)	Control group(n=41)
Types of antibiotics used(n)	≥ 2 species	33(80.49)[a]	16(39.02)
	<2 species	8(19.51)	25(60.98)
Duration of antibiotic use (n)	≥ 2 weeks	10(24.39)[a]	19(46.34)
	<2 weeks	31(75.61)	22(53.66)

Note: compared with the control group, [a]$P < 0.05$.

2.2 血清 hCRP 和 PCT 检测值对比

观察组病人的 PCT 及 hCRP 水平明显高于对照组，对比差异显著（$P<0.05$）。详见表 2。

表 2 两组患者血清 hCRP 和 PCT 检测值对比（$\bar{x}\pm s$）

Table 2 Comparison of serum hCRP and PCT values between the two groups（$\bar{x}\pm s$）

Groups	n	PCT(ng/mL)	hCRP(mmol/L)
Observation group	41	6.03±0.73	55.28±6.81
Control group	41	2.78±0.36b	10.37±2.61b

Note: compared with the control group, [b]$P<0.05$.

2.3 通过 CURB 进行观察组不同程度病情的 hCRP 和 PCT 检测值对比

通过 CURB 病情高低分为：高危组 8 例、中危组 11 例和低危组 22 例，结果显示，病人在不同程度的病情下，hCRP 和 PCT 的检测数值不同，且因病情减轻数值有所下降，组间存在明显差异（$P<0.05$）。详见表 3。

表 3 不同程度病情的 hCRP 和 PCT 检测值对比（$\bar{x}\pm s$）

Table 3 Comparison of hCRP and PCT test values of different degrees of disease（$\bar{x}\pm s$）

Groups	n	PCT(ng/mL)	hCRP(mmol/L)
Low-risk group	22	20.88±3.71	2.28±0.38
Intermediate Risk Group	11	46.12±5.36	6.59±0.74
High-risk group	8	71.51±8.25[#]	15.83±2.55[#]

Note: compared with low-risk group and medium-risk group, [#]$P < 0.05$.

2.4 细菌性感染的效能评价

PCT 检测对于诊断 ICU 下呼吸道感染病人的细菌性感染的灵敏度、特异度、阳性预测值和阴性预测值均高于 hCRP 的检测结果，组间存在显著差异（$P<0.05$）。详见表 4。

表 4 hCRP、PCT 对诊断细菌性感染的效能评价(%)

Table 4 Efficacy evaluation of hCRP and PCT in the diagnosis of bacterial infection(%)

Project	Sensitivity	Specificity	Positive predictive value	Negative predictive value
PCT	87.80*	92.68*	90.24*	82.93*
hCRP	78.05	80.49	78.05	75.61

Note: compared with hCRP, *$P < 0.05$.

2.5 ICU 下呼吸道感染危险因素经 Logistic 回归分析

年龄、入住 ICU 时间、手术时间、呼吸机的应用、侵入性操作、气道开放时间及抗生素≥ 2 种≥ 2 周均为 ICU 行气管切开下呼吸道感染病人的独立危险因素，详见表 5。

3 讨论

重症加强护理病房（ICU）也称为加强监护病房综合治疗室，可为患者提供良好的隔离场所、设备、最好的综合治疗、医养结合及护理等[8,9]。ICU 对需要持续机械通气、气道保护的病人而言，都要进行气道切开，建立人工气道。对于长期需要机械通气而建立人工气道而言，气管切开术是最佳的选择[10,11]。气管切开术一般让患者取仰卧位，肩下正中垫放一小枕，这能使气管更接近皮肤，局麻后从甲状软骨下缘到胸骨上窝附近，沿着患者颈前正中线切开皮肤和皮下组织，放入准备好的气管套管[12]。这是解除患者喉源性呼吸困难、下呼吸道分泌潴留所致呼吸困难和呼吸功能失常的常见手术[13]。气管切开术能够有效减少死腔样通气容积、气道阻力，提高病人的舒适性，减少镇静镇痛药物使用剂量，利于气道分泌物得到充分引流，减少咽喉部溃疡[14]。由此可见，在一定程度上，气道切开对于改善 ICU 病人具有较大的帮助意义。但相关研究证明[15,16]，气管切开术会破

表 5 ICU 行气管切开下呼吸道感染危险因素经 Logistic 回归分析

Table 5 Risk factors of lower respiratory tract infection after tracheotomy in ICU were analyzed by Logistic regression

Risk factor	β	SE	OR	Wald	*P*	95%CI
age	1.150	0.631	3.563	5.054	0.003	1.031-12.304
Check-in time	2.160	0557	3.512	17.892	0.000	1.823-7.031
Timing of surgery	2.341	0.711	10.263	14.467	0.000	3.091-34.072
Application of ventilator	1.572	0.571	4.823	10.443	0.000	1.857-12.526
Invasive operation	0.873	0.631	3.873	14.763	0.000	0.273-3.93
Antibiotics ≥ 2 types ≥ 2 weeks	1.734	0.731	3.442	18.863	0.001	1.734-7.501
Airway opening time	1.512	0.831	6.329	13.381	0.000	1.012-4.763

坏病人气道的天然防御屏障,导致气道直接与外界相同,从而增加下呼吸道感染的风险。

下呼吸道感染病例在临床上属于较常见的感染性疾病,且具有很高的发病率[17]。相关文献显示[18,19],下呼吸道感染导致死亡的人数已达到全球总死亡人数的 4.83%,排在全球疾病死因的第四位。其传播的途径也有多种,但是在临床症状观察下发现其缺乏特异性、严重危害人类身体健康。下呼吸道感染的常见因素有人体自身免疫力降低、细菌感染、病毒感染、真菌感染及其他非典型病原体[20]。呼吸道感染发病的高发季节一般是春季和冬季,温度剧烈变化的时候,夏天有缓解的趋势[21]。一般的临床症状有流鼻涕、鼻塞、咽喉疼痛,并带有炎症;如果导致气管炎、支气管炎后,患者还会出现咳嗽;严重的会导致中耳炎,影响听力[22]。

因患者行气管切开术易导致下呼吸道感染的危险,所以临床治疗当中,医生会根据患者的血清 PCT、hCRP 检测值来判断患者是否发生感染[23,24]。其中 PCT 被称为降钙素原,是人体内的一种糖蛋白质,亦是一类无激素活性糖蛋白的降钙素前肽物质。当患者身体出现严重真菌、细菌、脓毒症、寄生虫感染、多脏器功能衰竭的时候,PCT 在血浆中的水平就会升高 [25,26]。PCT 对细菌性感染具有较高的灵敏性,主要用于细菌感染的诊断检查,可反应人体全身炎症的活跃程度[27]。hCRP 是血浆中的一种 C 反应蛋白,C- 反应蛋白是急性时的反应蛋白, 当在急性创伤和感染情况下其血浓度急剧升高,如急性炎症、手术创伤等疾病发作后 hCRP 水平会在数小时后迅速升高, 并成倍增长[28]。但病变好转时 hCRP 水平又迅速恢复正常。这种 C 反应蛋白是一种能与肺炎球菌 C 多糖体反应后形成的复合物的急性时相反应蛋白[29]。但缺点是只能提示存在有感染或炎症,并不能判断具体的部位及感染原因, 需结合其他指标联合检测诊断,因此血清 hCRP 只能用来辅助诊断一些疾病[30]。

本研究结果显示,年龄、入住 ICU 时间、气道开放时间、手术时机、呼吸机的应用、侵入性操作、使用抗生素种类及使用抗生素时间等情况与 ICU 行气管切开患者下呼吸道有关。ICU 行气管切开术后合并下呼吸道感染患者的血清 PCT 及 hCRP 水平明显高于 ICU 行气管切开术病人无下呼吸道感染患者,且合并下呼吸道感染患者在不同程度的病情下,hCRP 和 PCT 的检测数值不同,会根据病情减轻数值有所下降。此外,血清 PCT 检测对于诊断 ICU 下呼吸道感染病人的细菌性感染的灵敏度、特异度、阳性预测值和阴性预测值均高于 hCRP 的检测结果。年龄、入住 ICU 时间、手术时间、呼吸机的应用、侵入性操作、气道开放时间及抗生素≥ 2 种≥ 2 周均为 ICU 行气管切开下呼吸道感染病人的独立危险因素。针对 ICU 行气管插管合并下呼吸道感染的病人,我们认为,可从以下几点来预防,① 加强人工气道的管理;② 加强气管切开护理;③ 加强呼吸治疗器械的消毒管理;④ 缩短住院时间;⑤ 保持 ICU 的环境清洁。

综上所述,ICU 行气管切开术发生下呼吸道感染的危险因素较多,血清 PCT 及 hCRP 的检测对下呼吸道感染病人的早期诊断具有较高的临床应用价值, 且 PCT 测定值特异性高于 hCRP。

参 考 文 献(References)

[1] Martin-Loeches I, Torres A, Povoa P, et al. The association of cardiovascular failure with treatment for ventilator-associated lowerrespiratory tract infection [J]. Intensive care medicine, 2019, 45 (12): 1753-1762

[2] Ferrero F, Abrutzky R, Ossorio MF, et al. Effects of contamination and climate in the Pediatric Emergency Department visits for acute respiratory infection in the City of Buenos Aires [J]. Archivos argentinos de pediatria, 2019, 117(6): 368-374

[3] Creamer AW, Kent AE, Albur. Procalcitonin in respiratory disease: use as a biomarker for diagnosis and guiding antibiotic therapy [J]. Breathe (Sheffield, England), 2019, 15(4): 296-304

[4] Giersing BK, Karron RA, Vekemans J, et al. Meeting report: WHO consultation on Respiratory Syncytial Virus (RSV) vaccine development, Geneva, 25-26 April 2016 [J]. Vaccine, 2019, 37(50): 7355-7362

[5] Shengchen D, Gu X, Fan G, et al. Evaluation of a molecular point-of-care testing for viral and atypical pathogens on intravenous antibiotic duration in hospitalized adults with lower respiratory tract infection: a randomized clinical trial [J]. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases, 2019, 25(11): 1415-1421

[6] Kapur N, Deegan S, Parakh A, et al. Relationship between respiratory function and need for NIV in childhood SMA [J]. Pediatric pulmonology, 2019, 54(11): 1774-1780

[7] Shiga H, Okuda K, Taki J, et al. Nasal thallium-201 uptake in patients with parosmia with and without hyposmia after upper respiratory tract infection[J]. International forum of allergy & rhinology, 2019, 9 (11): 1252-1256

[8] Rech JS, Arnulf B, de Margerie-Mellon C, et al. Lower

respiratory tract amyloidosis: Presentation, survival and prognostic factors. A multicenter consecutive case series [J]. American journal of hematology, 2019, 94(11): 1214-1226

[9] Vos LM, Oosterheert JJ. Testing for viral infections in severe lower respiratory tract infections; the unpredictable effects of diagnostic certainty [J]. Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases, 2019, 25(11): 1302-1303

[10] Jalink MB, Langley JM, Dodds L, et al. Severe Respiratory Syncytial Virus Infection in Preterm Infants and Later Onset of Asthma [J]. The Pediatric infectious disease journal, 2019, 38(11): 1121-1125

[11] Nowakowska M, van Staa T, Mölter A, et al. Antibiotic choice in UK general practice: rates and drivers of potentially inappropriate antibiotic prescribing[J]. The Journal of antimicrobial chemotherapy , 2019, 74(11): 3371-3378

[12] Giannini O, Del Giorno R, Zasa A, et al. Comparative Impact of C-Reactive Protein Testing in Hospitalized Patients with Acute Respiratory Tract Infection: A Retrospective Cohort Study [J]. Advances in therapy, 2019, 36(11): 3186-3195

[13] Katz SE, Sartori LF, Williams DJ. Cinical Progress Note: Procalcitonin in the Management of Pediatric Lower Respiratory TractInfection[J]. Journal of hospital medicine, 2019, 14(10): 688-690

[14] Zhou P, Wu H, Chen S, et al . MOMP and MIP DNA-loaded bacterial ghosts reduce the severity of lung lesions in mice after Chlamydia psittaci respiratory tract infection[J]. Immunobiology, 2019, 224(6): 739-746

[15] Schlechter Salinas AK, Hains DS, Jones T, et al. Testing for Urinary Tract Infection in the Influenza/Respiratory Syncytial Virus-Positive Febrile Infant Aged 2 to 12 Months[J]. Pediatric emergency care, 2019, 35 (10): 666-670

[16] Mammas IN, Spandidos DA. Paediatric Virology and respiratory syncytial virus: An interview with Honorary Senior Lecturer in Paediatric Infectious Diseases Dr Simon B. Drysdale (St. George's, University of London, UK) [J]. Experimental and therapeutic medicine, 2019, 18(4): 3226-3230

[17] Kumar S, Chakravarti A, Kumar S, et al. Detection of respiratory syncytial virus & in paediatric lower respiratory tract infections [J]. The Indian journal of medical research, 2019, 150(3): 306-309

[18] Von Saint André-Von Arnim AO, Okeyo B, Cook N, et al. Feasibility of high-flow nasal cannula implementation for children with acute lower respiratorytract disease in rural Kenya [J]. Paediatrics and international child health, 2019, 39(3): 177-183

[19] Salmanov A, Vozianov S, Kryzhevsky V, et al. Prevalence of healthcare-associated infections and antimicrobial resistance in acute care hospitals in Kyiv, Ukraine [J]. The Journal of hospital infection , 2019, 102(4): 431-437

[20] Oladele DM, Oladele DP, Ibraheem RM, et al. Reappraisal of respiratory syncytial virus as an aetiology of severe acute lower respiratory tractinfections in children younger than 5 years in Nigeria [J]. Transactions of the Royal Society of Tropical Medicine and Hygiene, 2019, 113(8): 446-452

[21] Wen S, Lv F, Chen X, et al. Application of a nucleic acid-based multiplex kit to identify viral and atypical bacterial aetiology of lower respiratory tract infection in hospitalized children [J]. Journal of medical microbiology, 2019, 68(8): 1211-1218

[22] San-Juan-Vergara H, Peeples ME. Importance of Virus Characteristics in Respiratory Syncytial Virus-Induced Disease [J]. Immunology and allergy clinics of North America, 2019, 39(3): 321-334

[23] González-Ortiz AM, Bernal-Silva S, Comas-García A, et al. Severe Respiratory Syncytial Virus Infection in Hospitalized Children [J]. Archives of medical research, 2019, 50(6): 377-383

[24] Manuel B, Hackbusch M, Tabatabai J, et al. RSVpredict: An Online Tool to Calculate the Likelihood of Respiratory Syncytial Virus Infection in Children Hospitalized With Acute Respiratory Disease[J]. The Pediatric infectious disease journal, 2019, 38(7): 678-681

[25] Soudani N, Caniza MA, Assaf-Casals A, et al. Prevalence and characteristics of acute respiratory virus infections in pediatric cancer patients[J]. Journal of medical virology, 2019, 91(7): 1191-1201

[26] Nascimento-Carvalho AC, Ruuskanen O, Nascimento-Carvalho CM. Wheezing independently predicts viral infection in children with community-acquired pneumonia[J]. Pediatric pulmonology, 2019, 54 (7): 1022-1028

[27] Shilovskiy IP, Andreev SM, Kozhikhova KV, et al. Prospects For the Use of Peptides against Respiratory Syncytial Virus[J]. Molekuliarnaia biologiia , 2019, 53(4): 541-560

[28] Toivonen L, Hasegawa K, Waris M, et al. Early nasal microbiota and acute respiratory infections during the first years of life [J]. Thorax, 2019, 74(6): 592-599

[29] Zhong P, Zhang H, Chen X, et al. Clinical characteristics of the lower respiratory tract infection caused by a single infection or coinfection of the human parainfluenza virus in children [J]. Journal of medical virology, 2019, 91(9): 1625-1632

[30] Keske Ş, Gümüş T, Köymen T, et al. Human metapneumovirus infection: Diagnostic impact of radiologic imaging [J]. Journal of medical virology, 2019, 91(6): 958-962

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[27] Y N Wang, H T Wang. Experimental study on nasal mucosa injury and repair induced by nasal decongestants in guinea pigs [J]. Zhonghua er bi yan hou tou jing wai ke za zhi = Chinese journal of otorhinolaryngology head and neck surgery, 2018, 53(6): 432-439

[28] Kullgren J T, Segel J E, Peterson T A, et al. Availability and variation of publicly reported prescription drug prices [J]. american journal of managed care, 2017, 23(7): 444-448

[29] Bernstein D I, Gillespie M, Song S, et al. Safety, efficacy, and dose response of fluticasone propionate delivered via the novel MDPI in patients with severe asthma: a randomized, controlled, dose-ranging study[J]. Allergy & Asthma Proceedings, 2017, 54(6): 559-569

[30] Bernstein D, Andersen L, Forth R, et al. Once-daily fluticasone furoate/vilanterol versus twice-daily fluticasone propionate/salmeterol in patients with asthma well controlled on ICS/LABA [J]. Journal of Asthma, 2017, 55(4): 27