

長庚大學醫學院臨床醫學研究所

畢業生研究成果

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畢業論文題目（中文）：運用混和模型評估中西醫治療氣喘合併過敏性鼻炎孩童之效果研究

畢業論文題目（英文）：Treating allergic rhinitis with traditional Chinese medicine in children with comorbid asthma: An application of mixture modelling approach

Background

Asthma and allergic rhinitis (AR) were two common allergic diseases that frequently coexist in children. The presence of AR in asthmatic patients made them have a higher risk of poor asthma control. Moreover, researches had found that treating AR with western medicine could alleviate asthma symptoms and asthma-related outcomes. On the other hand, traditional Chinese medicines were popular in Asian countries and were usually used as a treatment of respiratory system diseases especially AR. Nevertheless, research on the influence of treating AR with TCM in asthmatic children was lacked. In addition, the severity of AR would have its impact on asthma control, thus it was important to make the severity of AR a covariate for adjustment in regression while estimating the treatment effect of TCM. However, it could have some difficulties to obtain information of AR severity and to classify patients with different severities precisely while using the National Health Insurance Research Database (NHIRD). The aim of the study was to estimate the treatment effect of TCM on asthmatic children with concomitant AR while taking AR severity into account.

Methods

Using 2004 to 2015 National Health Insurance Research Database (NHIRD), we identified 31,428 asthmatic children with comorbid AR aged 2-18 years old based on the inclusion and exclusion criteria in the present study. The risk factors of asthma hospitalization and ER visit were evaluated using multiple Cox proportional hazards regression analysis. Moreover, in order to address population heterogeneity, mixture Cox regression was introduced.

Results

Of the total of 31,428 patients, 3499 (11.13%) were included in TCM group. In TCM group, there were 246 (7.03%) children encountered with asthma hospitalization or ER visit. After adjustment of gender, age, number of asthma and AR medications, and comorbidities, TCM users had a lower risk of asthma hospitalization or ER visit than non-TCM users (aHR: 0.466; 95% CI: 0.400-0.542). After dealing with the confounding of AR severity with mixture Cox regression, TCM exhibited a greater degree of treatment effect (aHR: 0.402).

Conclusion

Children aged 2-18 years old with asthma and comorbid AR would reduce the risk of consequent asthma hospitalization or ER visit after treating AR with adjunctive TCM. Moreover, mixture Cox regression provided a more precise evaluation of TCM treatment effect after dealing with the heterogeneity in the study population. The influences of different levels of AR severity on the treatment effect required future researches. Moreover, the applications of mixture Cox regression on different scenarios and domains were expected.

Table 7. Mixture Cox regression analysis of risk factors

Variables	Component 1 (p=0.643)			Component 2 (p=0.357)		
	aHR	95% CI	p value	aHR	95% CI	p value
Gender	0.967	0.805-1.162	0.723	1.031	0.813 -1.309	0.801
Age at diagnosis	1.963e-09	0.000-Inf	0.986	8.016	6.191-10.380	<0.001
Number of asthma medications	1.645	1.360-1.989	<0.001	2.383	1.845-3.077	<0.001
Number of AR medications	0.611	0.504-0.741	<0.001	0.479	0.375-0.613	<0.001
Comorbidity						
Acute sinusitis	0.273	0.229-0.325	<0.001	0.403	0.318-0.509	<0.001
Atopic dermatitis	2.891e-09	0.000-Inf	0.988	7.568	5.866-9.764	<0.001
GERD	0.789	0.111-5.630	0.814	1.803e-07	0.000-Inf	0.986
URI	0.307	0.255-0.368	<0.001	0.420	0.329-0.537	<0.001
TCM usage	0.423	0.349-0.512	<0.001	0.370	0.288-0.476	<0.001

Table 1. Demographic characteristics study population

Characteristics	Total, N (%)	TCM, N (%)	Non-TCM, N (%)	p value
No.	31,428 (100)	3,499 (11.13)	27,929 (88.87)	
Gender				
Male	19,026 (60.54)	2,216 (63.33)	16,810 (60.19)	<0.001
Female	12,402 (39.46)	1,283 (36.67)	11,119 (39.81)	
Age at diagnosis				
2-5 y/o	24,555 (78.13)	2,537 (72.51)	22,018 (78.84)	<0.001
6-18 y/o	6,873 (21.87)	962 (27.49)	5,911 (21.16)	
Number of asthma medications				
1	12,667 (40.30)	1,389 (39.70)	11,278 (40.38)	0.215
2	9,931 (31.60)	1,110 (31.72)	8,821 (31.58)	
3	5,427 (17.27)	584 (16.69)	4,843 (17.34)	
4	2,270 (7.22)	284 (8.12)	1,986 (7.11)	
≥5	1,133 (3.61)	132 (3.77)	1,001 (3.58)	
Number of AR medications				
1	17,828 (56.73)	1,822 (52.07)	16,006 (57.31)	<0.001
2	13,600 (43.27)	1,677 (47.93)	11,923 (42.69)	
Comorbidity				
Acute sinusitis	21,543 (68.55)	2,627 (75.08)	18,916 (67.73)	<0.001
Atopic dermatitis	7,540 (23.99)	850 (24.29)	6,690 (23.95)	0.658
GERD	116 (0.37)	13 (0.37)	103 (0.37)	0.979
URI	25,008 (79.57)	2,920 (83.45)	22,088 (79.09)	<0.001
Number of events	4,711 (14.99)	246 (7.03)	4,465 (15.99)	<0.001

Table 5. Cox regression analysis of risk factors

Variables	Adjusted HR	95% CI	p value
Gender			
Male	Reference		
Female	0.996	0.862-1.152	0.961
Age at diagnosis			
2-5 y/o	Reference		
6-18 y/o	0.558	0.469-0.665	<0.001
Number of asthma medications			
1	Reference		
≥2	1.764	1.515-2.054	<0.001
Number of AR medications			
1	Reference		
2	0.406	0.350-0.470	<0.001
Comorbidity			
Acute sinusitis	0.370	0.321-0.426	<0.001
Atopic dermatitis	0.678	0.563-0.817	<0.001
GERD	0.327	0.046-2.320	0.264
URI	0.406	0.350-0.470	<0.001
TCM usage			
No	Reference		
Yes	0.466	0.400-0.542	<0.001