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RESEARCH ARTICLE

Cluster Analysis to Characterize the Patterns of Complementary and Alternative Medicines Usage in Asthma Controls

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Abstract:

Background:

Clinicians and physicians need to be aware of the high prevalence of complementary and alternative medicines use in patients with asthma, as it is found to be associated with lack of asthma control, though the degree to which associations exist is still not clear.

Methods:

We have performed a cluster analysis to characterize patterns defining different asthma control levels and the extent to which the medicines have an impact in these categories.

Results and Conclusion:

We have explored the association of Complementary and Alternative medicines utilization with asthma control and the effect of asthma controller medications, with the conclusion that the usage of complementary and alternative medicines does not have a significant impact on partially and uncontrolled asthmatics.

Keywords: CAM, Control, Cluster analysis, Patterns, Initialization, Cluster.

Article History

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1. INTRODUCTION

Global Initiative for Asthma criteria proposed a guideline to define the different degrees of asthma control based on the symptoms during the past three months and FEV1 /FPRED ratio, where FPRED is the False Positive Reduction which is computed based on the NHANES(National Health and Nutrition Examination Survey)-III standards and FEV1 is the Forced Expiratory Volume of air one can force from the lungs in one second.

Asthma medications, including LABA (long-acting beta-agonists), SABA(short-acting beta-agonists), and ICS (Inhaled corticosteroids) usage are the commonly preferred options depending on the degree of asthma control. Complementary and Alternative medicines (CAM) for asthma treatment in the recent days is of utmost concern in patient care because the chronicity of the disease necessitates long-term medications involving the use of inhaled corticosteroids, which could possi-

bly prove to be toxic if taken over a long period of time [1, 2]. The usage of the CAM is even more in work-related asthmatics when compared to their counterparts [3]. However, physicians' involvement in the usage of the same is not demonstrated well in most of the population studies [4]. Of the wide variety of complementary and alternative asthma treatments seen to be associated with asthma control, CAM usage is one that has drawn widespread attention, especially in the pediatric population [5 - 7].

Here, we try to assess the usage of complementary and alternative medicines (CAMs) in treating asthma and its relation to the clinical control of asthma and the possible use of conventional asthma controller therapies. Previous studies demonstrated that Controller medication use was not associated with CAM usage in general and in the subgroups defined by asthma control [2, 8]. In the dataset under consideration for our study, the usage of CAMs in the past 12 months was assessed with respect to the following options:

- (i) Osteopathy or massage apart from other manipulative techniques
- (ii) herbal treatment
- (iii) homeopathy
- (iv) acupunc-

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ture (v) exercises to ease breathing (vi) supplements including vitamins (vii) chiropractic (viii) naturopathy (ix) diet programs. Wherever other CAMs were used apart from those specified, it was considered to be under the category “others”.

2. MATERIALS AND METHODS

2.1. Data Description

The data used for the validation of cluster analysis were collected in a prospective population-based, cross-sectional study setting. The population involved the residents of census areas in the province of Canada and British Columbia. 486 patients with self-reported/physician-diagnosed asthma were involved in the data collection. Primary and secondary outcome measures included assessment of CAM usage over the past year, asthma control level as defined by the Global Initiative for Asthma, along with self-reported intake of controller medications. A total of 179 (36.8%) of the sample reported CAM usage in the past 12 months. Breathing exercises (17.7%), herbal medicines (10.1%), and vitamins (9.7%) were the most popular CAMs reported. After adjustment, female sex (OR: 1.66; 95% CI: 1.09-2.52) and uncontrolled asthma (*vs.* controlled asthma, OR: 2.25, 95% CI: 1.30-3.89) were associated with a higher likelihood of using any CAMs in the past 12 months. Controller medication use was not associated with CAM usage in general and in the subgroups defined by asthma control [6].

The data file, as made available by BMJ (British Medical Journal) Publishing Group from an electronic file supplied by the authors, has been used for the study and has not been edited for content [2].

2.2. Cluster Analysis and Initialization Methods (IMs)

Cluster analysis aims at grouping individual entities into groups such that objects within the group tend to exhibit a high degree of similarity while objects of different groups seem to demonstrate a low similarity. Clustering techniques are widely used in the process of asthma phenotyping [8, 9].

The categorical attributes were treated as numerical attributes while applying the K-Means algorithm and different initialization methods have experimented.

2.3. Random Initialization

The steps involved in the selection of the seeds using random initialization areas follows:

Step 1: Choose ‘K’, representing the number of clusters

Step 2: Randomly choose ‘K’ centroids from the input data-set

Step 3: Allocate each data point to its nearest centroid

Step 4: Place the new centroid for each cluster by re-computing the new centroid

Step 5: Check if any data points in the dataset can be reassigned to a different cluster based on the new centroid

2.4. K-Means++

K-means++ is designed to improve the centroid initialization for k-means. The basic idea is that the initial

centroid should be far away from each other. The algorithm starts by randomly selecting a centroid c_0 from all data points. For centroid c_i , it is interpreted that the probability of a data point, x , been chosen as a centroid is proportional to the squares of the distance of x to its nearest centroid.

K means ++ aims at choosing the initial centroids in such a way that the initial centroids are far as possible from each other.

2.5. Method: Farthest First

The issue of k-center clustering is also called the min-max radius clustering problem, whose goal is to minimize any cluster's peak diameter on some set of points. Gonzales, using a farthest-point clustering heuristic, proposes a straightforward 2-approximation algorithm for the k-center clustering issue.

The heuristic of farthest point begins with an arbitrary point s_1 . Select a point s_2 as far as possible from s_1 . Preference of s_i is done so as to maximize the distance selected so far to the nearest of all centroids. This means maximizing $\min \{ \text{dist}(s_i, s_1), \text{dist}(s_i, s_2), \dots \}$. The partition of D after all k representatives have been selected, may be defined as: cluster C_j comprises of all points nearer to s_j than any other representative. The maximum radius of these k clusters should be π , and then the maximum radius, even in the ideal k-clustering, should be at least $\pi/2$. This is most preferred for minimizing any cluster's maximum radius.

2.6. Method: Canopy

To group objects into clusters, Canopy Clustering is a very easy, quick, and amazingly precise technique. All items in the multidimensional feature space are depicted as a point. For processing, the algorithm utilizes a rapid approximate range metric and two range thresholds $T_1 > T_2$. The fundamental algorithm is to start with a set of points and randomly remove one. As the algorithm utilizes distance features and needs distance threshold specification, the curse of dimensionality limits its applicability to high-dimensional information. The produced canopies will only maintain the clusters generated by K-means when an inexpensive and approximate-low-dimensional-distance function is accessible.

3. RESULTS AND DISCUSSION

K-Means clustering was adopted to perform clustering of the subjects into three clusters, as we had three distinct groups of asthma control. The results obtained by applying various initialization techniques for k-means clustering are shown below: Table 1-4 depict final cluster centroids with respect to KMeans++, random initialization, farthest first and canopy initialization methods, respectively.

Type: Kmeans++

Number of iterations: 5

Within cluster sum of squared errors: 470.27

Type: Random

Number of iterations: 7

Within cluster sum of squared errors: 470.27

Type: Farthest first

Number of iterations: 11

Within cluster sum of squared errors: 504.86

Type: Canopy

Number of iterations: 8

Within cluster sum of squared errors: 496.60

Table 1. Results of final cluster centroids using KMeans++ IM.

Attribute	Full data	0	1	2
-	486	142	165	179
Asthma_ER_or_Hospitalization	no	no	no	no
fev1_to_fvc	69.291	67.2921	71.468	68.87
Fvc	3.6232	3.3575	3.9961	3.4904
fev1	2.6144	2.3288	2.9675	2.5155
predicted_fev1	3.0304	2.8227	3.3531	2.8978
fev1_over_pred	0.8494	0.8255	0.8856	0.835
cam_acupuncture	0.0453	0	0	0.1229
cam_breathingexercises	0.177	0	0	0.4804
cam_chiropractic	0.0536	0	0.0003	0.1453
cam_dieting	0.0825	0	0.0005	0.0005
cam_herbal	0.1008	0	0	0.2737
cam_homeopathy	0.0329	0	0	0.0894
cam_massage	0.0784	0	0	0.2127
cam_naturopathy	0.0351	0	0.0002	0.095
cam_vitamins	0.0967	0	0	0.2626
cam_other	0.1629	0.1127	0.0737	0.2849
cam_use	N0	N0	N0	Yes
cam_types	0.7016	0	0	1.905
controller_medicine_use	1.0082	1.8873	0.1636	1.0894
resuse	92.4604	110.6992	46.5723	120.2906
Age	52.2132	58.0414	47.0514	52.3477

Table 2. Results of final cluster centroids –Random IM.

Attribute	Full data	0	1	2
-	486	142	165	179
Asthma_ER_or_Hospitalization	no	no	no	no
fev1_to_fvc	69.291	67.2921	71.468	68.87
Fvc	3.6232	3.3575	3.9961	3.4904
fev1	2.6144	2.3288	2.9675	2.5155
predicted_fev1	3.0304	2.8227	3.3531	2.8978
fev1_over_pred	0.8494	0.8255	0.8856	0.835
cam_acupuncture	0.0453	0	0	0.1229
cam_breathingexercises	0.177	0	0	0.4804
cam_chiropractic	0.0536	0	0.0003	0.1453
cam_dieting	0.0825	0	0.0005	0.0005
cam_herbal	0.1008	0	0	0.2737
cam_homeopathy	0.0329	0	0	0.0894
cam_massage	0.0784	0	0	0.2127
cam_naturopathy	0.0351	0	0.0002	0.095
cam_vitamins	0.0967	0	0	0.2626
cam_other	0.1629	0.1127	0.0737	0.2849
cam_use	N0	N0	N0	Yes
cam_types	0.7016	0	0	1.905

(Table 2) *contd....*

Attribute	Full data	0	1	2
controller_medicine_use	1.0082	1.8873	0.1636	1.0894
resuse	92.4604	110.6992	46.5723	120.2906
age	52.2132	58.0414	47.0514	52.3477

Table 3. Results of final cluster centroids -Farthest First IM.

Attribute	Full data	0	1	2
-	486	111	68	307
Asthma_ER_or_Hospitalization	no	no	no	no
fev1	2.6144	2.3583	2.7722	2.6721
predicted_fev1	3.0304	2.7931	3.0687	3.1078
fev1_over_pred	0.8494	0.7897	0.9091	0.8578
cam_acupuncture	0.0453	0.0721	0.2059	0
cam_breathingexercises	0.177	0.5315	0.3971	0
cam_chiropractic	0.0536	0.009	0.3676	0.0002
cam_dieting	0.0825	0.2072	0.25	0.0003
cam_herbal	0.1008	0.2883	0.25	0
cam_homeopathy	0.0329	0.0721	0.1176	0
cam_massage	0.0784	0.1629	0.2941	0
cam_naturopathy	0.0351	0.0631	0.1471	0.0001
cam_vitamins	0.0967	0.2613	0.2647	0
cam_other	0.1629	0.4324	0.0441	0.0917
cam_use	N0	Yes	Yes	N0
cam_types	0.7016	1.6667	2.2941	0
controller_medicine_use	1.0082	1.4775	0.4559	0.9609
resuse	92.4604	147.6414	75.6445	76.2336
age	52.2132	53.9272	49.7695	52.1347

Table 4. Results of final cluster centroids -Canopy IM.

Attribute	Full data	0	1	2
	486	307	103	76
Fvc	3.6232	3.7007	3.2572	3.8064
fev1	2.6144	2.6721	2.3012	2.806
predicted_fev1	3.0304	3.1078	2.7858	3.0495
fev1_over_pred	0.8494	0.8578	0.7692	0.9242
cam_acupuncture	0.0453	0	0.1456	0.0921
cam_breathingexercises	0.177	0	0.534	0.4079
cam_chiropractic	0.0536	0.0002	0.1262	0.1711
cam_dieting	0.0825	0.0003	0.165	0.3026
cam_herbal	0.1008	0	0.3398	0.1842
cam_homeopathy	0.0329	0	0.0971	0.0789
cam_massage	0.0784	0	0.2241	0.1974
cam_naturopathy	0.0351	0.0001	0.0777	0.1184
cam_vitamins	0.0967	0	0.2816	0.2368
cam_other	0.1629	0.0917	0.2427	0.3421
cam_use	N0	N0	Yes	Yes
cam_types	0.7016	0	1.9903	1.7895
controller_medicine_use	1.0082	0.9609	1.7961	0.1316
resuse	92.4604	76.2336	170.9191	51.6757
age	52.2132	52.1347	54.594	49.3033

4. DISCUSSION

Of the different initialization methods used with K Means clustering, K-Means ++ was able to demonstrate considerably good performance with reduced iterations while yielding a comparatively lower sum of squared error within clusters.

A significant difference is also observed in terms of the cytokine and chemokine profile found in BAL fluids within controlled and uncontrolled asthmatics [6, 10]. A summary of the following observations was made, which majorly characterize each of the three clusters, namely uncontrolled, partially controlled, and controlled asthmatics groups.

In the uncontrolled asthma category, the usage of Complementary and Alternative medicines, as well as controller medication, was high. An FEV/FVC ratio of below 0.70 characterized this group of patients predominantly. Further, fev1 over predicted ratio was also below 0.85. The average age was 52 years. Almost all types of Complementary and Alternative medicines were used.

In the partially controlled asthma category, the usage of Complementary and Alternative medicines was low with moderate usage of controller medication. An FEV/FVC ratio of below 0.70 characterized this group of patients predominantly. Further, fev1 over predicted ratio was also below 0.85. The average age was 58 years.

In the controlled asthma category, there was no usage of any of the Complementary and alternative medicines, excluding substantially lower usage of chiropractic, dieting, and naturopathy with the controller medication usage close to nil. An FEV/FVC ratio of above 0.70 characterized this group of patients predominantly. Further, fev1 over predicted ratio was also above 0.85. The average age was 47 years.

CONCLUSION

It can be clearly observed that no association exists between CAM usage and asthma control in partially controlled and uncontrolled asthma categories. This study, as confined to the application of a data-driven approach to population data available, indicates that CAM usage in itself is not a very promising approach to control asthma, thus asserting the inference drawn earlier.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

HUMAN AND ANIMAL RIGHTS

Not applicable.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

The data supporting the findings of the article is available in the Dryad repository at <https://datadryad.org/stash/dataset/doi:10.5061/dryad.8bv8p>.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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