

ASTHMA QUALITY OF LIFE AS A MARKER OF DISEASE SEVERITY AND TREATMENT EVALUATION IN SCHOOL CHILDREN

Svetlana S. Pljaskić-Kamenov¹, Dragoslav V. Djordjević², Stojan S. Radić³, Borislav A. Kamenov⁴

¹Health Center, Niš

²Clinic of Pulmology, Clinical Center, Niš

³Department of Pathophysiology, Medical Faculty, Niš

⁴Clinic of Pediatrics, Clinical Center, Niš, Yugoslavia

Summary. *The parameters of the quality of life in school age asthma afflicted children were analyzed and correlated to clinical, inflammatory parameters and pulmonary function disorders during 3 month inhalatory corticosteroid treatment. The testing has included 125 asthma patients 7 to 17 years old who were symptomatic. Out of this number there were 40 female subjects and 85 male ones, mean age 12.14. Criteria for severity of asthma included the following: daily symptoms; exacerbations affecting activity and/or sleep; nighttime asthma symptoms experienced more than once per week; daily use of a β_2 -agonist; and PEF and FEV1. Diagnosis of asthma has been given on the basis of the following: anamnesis, eosinophils in periphery blood and running nose, allergy test with inhalatory allergens according to "prick method", total and specific IgE, spirometric parameters, data from the symptoms list, estimate of the degree of dyspnea according to Borg's scale, answers from the quality of life questionnaire according to Juniper. T-test has established no significant difference in the changes of quality of life scores and the age of the children ($p>126$). Statistically significant difference has been found in the changes of the quality of life scores and sex of the children. Better results have been obtained with the male sex. The difference in relative changes of the scores of the quality of life and the severity of the disease ($p>125$) has been not found statistically significant. Results of T-test changes in AQLQ score before and after therapy show statistical significance in all categories. The greatest changes in the domain of symptoms have been obtained within the categories of wheezing and chest tightness. The best results in the domain of emotions have been obtained within the categories of embarrassment, anger, frustration and worry. The best results in the domain of activity are obtained in the category of physical activities and activities with friends and family. The score of the total quality of life showed statistically significant improvements after the use of beclomethasone dipropionate.*

Key words: *Asthma, quality of life, corticosteroids*

Introduction

Quality of life is an individual's satisfaction or happiness with life in domains he or she considers important. (1). Historically it is known as life satisfaction or subjective well being. It is now sometimes referred to as overall quality of life or global quality of life to distinguish it from health related quality of life (HRQL). It is the broadest of all dimensions of life that contribute to its richness and reward, pleasure and pain. These dimensions include, but are not limited to health.

In the past, it was assumed that clinicians could obtain a good estimate of a child's asthma specific quality of life from the conventional measures of asthma severity, using measurements such as spirometry, medication requirements, and from discussion with the parents and patients.

There is now clear evidence that the clinical indices only weakly correlate with how the child feels and how the child functions in everyday life. In addition, a num-

ber of investigators have shown that parents may not perceive accurately their child's asthma quality of life (2,3).

Because one of the aims of treating pediatric asthma is to ensure that the child's problems are addressed and because these problems correlate poorly with clinical indices and parental reporting, assessment of HRQL should be an essential component of all clinical evaluations.

Valid disease specific instruments for children with asthma now exist that allow quick and simple assessment to be incorporated into both clinical trials and clinical practice.

Children are distressed by the symptoms themselves, such as cough, shortness of breath, wheezing, and chest tightness. Children are disturbed by any limitations in the activities that they like doing, such as sports, playing with their friends and/or pets, and going to their friend's homes. Older children are distressed because their asthma interferes with schoolwork. Children with

asthma also have to deal with emotional problems such as being frightened by an asthma attack, frustrated at not being able to do the things they wish to do, feeling different and left out, and not being able to keep up with their peers, and they say that their asthma makes them feel irritable, grumpy, grouchy. Younger children often express anger at having asthma, although in older children this usually alters into frustration (4,5,6,7,8).

There is a broad consensus that assessments of life quality encompass three major domains: physical, psychological, and social functioning. (9). Physical functioning refers to symptoms, such as chest pain, fatigue, or chest tightness, as well as to functional status. Functional status covers a broad range of activities; the main categories include instrumental activities of daily living (for example, play), mobility (for example, walking, climbing stairs), and basic activities in daily functioning (for example, dressing, feeding). Psychological functioning refers to wellbeing, psychological distress, and mental abilities. Related measures focus on anxiety, depression, and cognitive functioning. Social functioning represents the performance of social roles, and is defined in terms of interpersonal relationships, family functioning, sexual functioning, and social participation.

These domain specific measures, together with global, overall measures of perceived health and wellbeing, are seen as the pillars of the concept of health related quality of life.

The aim of the study

To analyze the parameters of the quality of life in school age, asthma inflicted children and to correlate these parameters to clinical, inflammatory parameters and pulmonary function disorders during 3 months inhalatory corticosteroid treatment.

Materials and Methods

Patients

Testing has included 125 asthma patients. Out of this number there were 40 female subjects and 85 male ones, mean age 12.14. School children 7 to 17 years old with asthma who were symptomatic were considered for participation. Patients were excluded for the following reasons: if they had any clinically significant abnormality or disease (other than asthma); if they had an acute upper or lower respiratory tract infection within 4 weeks before the start of the trial or during the run-in period; or if they were taking any other medication. Use of an inhaled (β_2 -agonist bronchodilator, however, was permitted to relieve symptoms of asthma on the "as needed" basis throughout the study.

Patients completed a 7-day run-in period to establish the presence of symptoms, lung function parameters, and bronchodilator usage consistent with the classification of light, moderate or severe asthma. Criteria for severity of asthma included the following: daily symp-

toms; exacerbations affecting activity and/or sleep; nighttime asthma symptoms experienced more than once per week; daily use of a β_2 -agonist; and PEF and FEV1. During the run-in period, patients continued to take their β_2 -agonist and previously prescribed inhaled corticosteroids. Patients were required to show evidence of active asthma during the last 5 days of the run-in to be eligible to continue in the trial. This was defined as a mean morning (AM) PEF between 50% and 85% of the predicted normal value plus one or more of the following: sleep disturbance due to asthma on 1 or more nights; asthma symptoms on 3 or more days; use of a β -agonist inhaler on average at least twice daily to relieve symptoms. During the period of 3 months patients were treated with inhalatory corticosteroids (Becotide 400-600 mcg)

Diagnoses

Diagnosis of asthma has been given on the basis of the following: anamnesis, eosinophils in periphery blood and nose, allergy test with inhalatory allergens according to "prick method", total and specific IgE, spirometric parameters, data from the symptoms list, estimate of the degree of dyspnea according to Borg's scale, answers from the quality of life questionnaire according to Juniper (10).

Pediatric Asthma Quality of Life

The PAQLQ (Pediatric Asthma Quality of Life Questionnaire by Juniper) has been developed to measure asthma-specific quality of life in children aged 7-17. Patients completed the Asthma Quality of Life Questionnaire (AQLQ) at the end of the run-in period, and after 3 months of follow up during which period the patients were receiving inhalatory corticosteroids. The questionnaire consists of 23 items that cover those problems identified by children with asthma as being most important and troublesome to them in their everyday lives because of asthma, each of which carries a 7-point series of response options (a score of 1 indicates "extremely bothered/all the time"; a score of 7 indicates "not bothered/none of the time"). A change in AQLQ score of 0.5 was considered to be clinically relevant.

The items are in three domains:

1. Symptoms (consisting of 10 items)
 - K4 cough,
 - K6 tiredness,
 - K8 asthma attacks,
 - K10 wheezing,
 - K12 tightness of chest,
 - K14 shortness of breath,
 - K16 wake up during the night,
 - K18 out of breath,
 - K20 trouble sleeping at night
 - K23 deep breath

2. Emotional function (consisting of 8 items)
 - K5 frustration,
 - K7 worried,
 - K9 angry,
 - K11 irritable,
 - K13 feeling different or left out,
 - K15 frustrated can't keep up with others,
 - K17 uncomfortable,
 - K21 frightened by asthma attack
3. Activity limitation (consisting of 5 items)
 - K1 physical activities,
 - K2 being with animals,
 - K3 activities with friends and family,
 - K19 can't keep up with others,
 - K22 bothered in activities overall

The interviewer reads the question and the child gives a response, by the card that best describes his or her experiences during the previous week.

Patients were instructed to record PEF, asthma symptoms, and bronchodilator use in an asthma diary on a daily basis. PEF measurements were taken using a mini-Wright peak flowmeter before using a β -agonist or other medication, in the morning on awakening, and in the evening before sleep. Daytime asthma symptoms (wheezing, shortness of breath, chest tightness, and cough) were recorded using a 6-point assessment scale, and sleep disturbance scores were recorded using a 5-point assessment scale. Spirometry was performed in accordance with American Thoracic Society criteria to determine FEV1 and forced expiratory flow > 25 to 75% of the full FVC at the screening visit, at the end of the run-in period, and at the end of the studied period of 3 months. The percentage of predicted normal values for FEV was calculated according to the regression equation of Crapo et al (11); for PEF, the percentage of predicted normal values was calculated using the equation of Nunn and Gregg (12).

Statistical Analysis

Asthma quality of life was expressed as the mean score per item for each of the four AQLQ domains, and the overall score was derived from the mean score of all items. All patients for whom there was a postbaseline AQLQ assessment were included in the AQLQ analysis. For each of the three domains and the overall score mean changes were analyzed. Data are grouped and graphically shown. The following statistical parameters have been used: arithmetic means and standard deviation. The testing of the difference between mean values has been done by the Students T- test of difference. There has been given a correlation between parameters according to Pearson's statistical method. For statistical analysis a program SPSS 8.0 for Windows surrounding has been used.

Results

125 school children 7-17 years of age were analyzed (Table 1.)

Table 1. Basic demographic characteristics of the patients

Sex	No	Age	Height	Duration
Female	40	12.35±3.5	150.68±14.55	9.98±3.76
Male	85	12.05±2.92	154.07±16.52	9.59±3.42
Total	125	12.14±3.11	152.98±15.94	9.71±3.52

Symptoms occurring at night are shown in Table 2.

Table 2. Symptoms occurring at night

Numerical values	Symptoms occurring at night	Mean value
0	No symptoms during the night	18.6
1	Symptoms disturbing me once during the night or waking me up earlier	33.8
2	Symptoms that make me wake up twice or more often	23.8
3	Symptoms that made me awake most of the night	3.5
4	Symptoms so severe that I couldn't fall asleep during the night	0

It has been noticed that symptom no. 1 (Symptoms disturbing me once during the night or waking me up earlier) occurred with most of the children during night (Table 2).

Daily symptoms divided into 6 categories 0 -5 (Table 3).

Table 3. Daily symptoms

Numerical values	Daily symptoms	Mean value
0	No symptoms	5.8
1	Symptoms occurring for a short period of the day	26.2
2	Symptoms occurring twice or more often during the day	31.8
3	Symptoms not affecting my usual daily activities	11.6
4	Symptoms occurring most of the day affecting my usual daily activities	3.6
5	Symptoms so difficult that I couldn't do anything or have my daily activities	0

Most of the children reported symptoms marked 1 (Symptoms occurring for a short period of the day) and 2 (Symptoms occurring twice or more often during the day) during the day (Table 3.)

Age related changes in AQLQ score: overall, activity, symptoms and emotions are presented in Table 4.

Table 4. Age related changes in AQLQ score

Age	OVERALL	Activity	Symptoms	Emotions
7-10	0.60	0.62	0.76	0.46
11-14	0.66	0.65	0.91	0.48
15-18	0.56	0.55	0.73	0.47

T-test has established no significant difference in the changes of quality of life scores and the age of the children ($p>126$).

Sex related changes in AQLQ score: overall, activity, symptoms and emotions are presented in Table 5.

Table 5. Sex related changes in AQLQ score

Sex	OVERALL	Activity	Symptoms	Emotions
Female	0.49	0.47	0.65	0.36
Male	0.67	0.68	0.87	0.52
	$P=0.006$	$P=0.005$	$P=0.013$	$P=0.035$

A statistically significant difference has been found in the changes of the quality of life scores and sex of the children. Better results have been obtained with the male sex.

Changes in AQLQ score in relation to asthma type: overall, activity, symptoms and emotions are presented in Table 6.

Table 6. Changes in AQLQ score in relation to asthma type

Asthma type	OVERALL	Activity	Symptoms	Emotions
Light	0.62	0.61	0.79	0.50
Moderate	0.63	0.69	0.87	0.41
Heavy	0.57	0.54	0.76	0.45

The statistically significant difference in relative changes of the scores of the quality of life and the severity of the disease ($p>125$) has been not found.

Changes in AQLQ score in relation to asthma therapy: overall, activity, symptoms and emotions are presented in Table 7.

Table 7. Changes in AQLQ score in relation to asthma therapy

Category	OVERALL	Activity	Symptoms	Emotions
AQLQ score	0.53	0.53	0.69	0.39
	$p<0.001$	$p<0.001$	$p<0.001$	$p<0.006$

Results of T-test changes in AQLQ score before and after therapy show statistical significance in all categories.

The greatest changes have been obtained within the categories of wheezing (K10) and chest tightness (K12) (Figure 1).

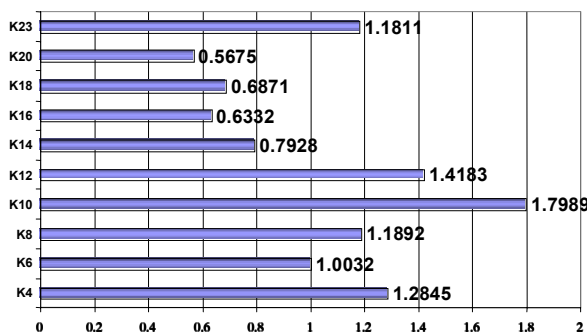


Fig. 1. Changes in AQLQ score in the domain of symptoms

The best results have been obtained within the categories of embarrassment (K11), anger (K9), frustration and worry (K5) (Figure 2).

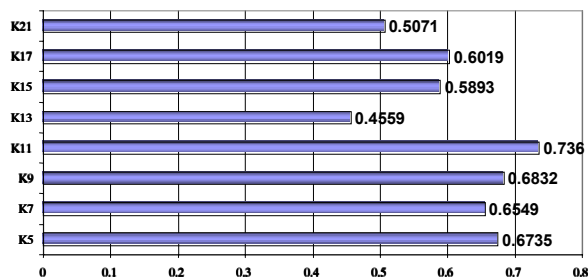


Fig. 2. Changes in AQLQ score in the domain of emotions

The best results are obtained in the category of physical activities (K1) and activities with friends and family (K3) (Figure 3.).

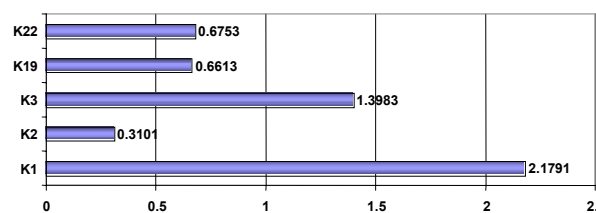


Fig. 3. Changes in AQLQ score in the domain of activity

No correlation has been found between the changes of FEV1, PEFr and Salbutamol use to activity, symptoms and emotions (Table 8.).

Table 8. Correlations between FEV, PEF, Salbutamol and the quality of life score changes

Parameters	Activity	Symptoms	Emotions
FEV1	0.158	0.158	0.158
PEFR	0.046	0.046	0.046
Salbutamol	0.118	0.118	0.118

Discussion

Development and testing of a health-related quality of life measure for children with asthma has a number of strengths. The instrument is generated on the basis of a comprehensive list of possible items and corrected on the basis of patient preferences, ensuring the content validity and sensibility of a new instrument. The administration of all measures used as patient ratings, parent ratings, clinical and physiological measures to explore the validity of the questionnaire were standardized. The approach bears an ability of the instrument to evaluate the extent of improvement or deterioration in quality of life over time, and to discriminate between children with minor and more serious impairment of quality of life (13).

The Paediatric Asthma Quality of Life Questionnaire showed excellent responsiveness with respect to its evaluative properties. It was able to detect change in patients who improved or deteriorated, and to distinguish such patients from those who remained stable and showed a high index of responsiveness.

There was no correlation between changes in questionnaire score and changes in peak expiratory flow rate and β_2 -agonist use, as well as with the correlations with changes in clinical asthma control. We found no correlation with clinic FEV1 per cent predicted. The highest correlations were between changes in questionnaire score and changes in a measure of overall quality of life, the feeling thermometer, and global ratings of change in symptoms, activities and emotions.

No correlations were found with either peak flow rates or FEV1 per cent predicted.

The validation correlations between quality of life and daily peak flow measurements are exactly as it may be predicted, namely, that there would be no correlation between absolute values of peak flow and quality of life in the cross-sectional analysis. Some level of correlation would be expected between changes in peak flow and changes in quality of life in the longitudinal analysis. Even here a lack of correlation is not unexpected since there is an individual difference in the validation of each patient regarding different areas that are questioned in PAQLQ.

Poor correlation between daily peak flows and a single occasion FEV1 has been observed by other investigators (14,15,16,17). In aggregating scores within domains, it is assumed that each question is weighted equally. Patients almost certainly value different items differently but there are, at least, two justifications for the equal weighting of items. The difference between item weights probably is not large and there is considerable evidence that differential weighting seldom changes bottom line conclusions (18). When we calculate an overall score, we assume not only equal weights per item but that each domain is appropriately weighted in proportion to the number of items in that domain. This additional assumption and the likelihood that values between items will vary more between than within domains, makes the aggregation across the whole instrument more risky than aggregation within domains. Because of this we should consider the issue when deciding whether to report domain scores or overall scores for both the Paediatric Asthma Quality of Life Questionnaire and other similar questionnaires.

Since The Paediatric Asthma Quality of Life Questionnaire was developed to be applicable to all children

with asthma between the ages of 7 and 17, with this wide age span, validity of the instrument in all age groups is obviously a concern. Since the validity in each group was addressed in the development process by the authors of this instrument and only the items understood by each group were included and if they were frequently identified as important by a wide range of patients this concern is minimised. In the activity domain, the domain most likely to show heterogeneity across age, three of the items are individualized. Since the reliability and responsiveness across three age groups have been examined by the authors, the consistent results between these groups provide evidence that the Paediatric Asthma Quality of Life Questionnaire has good measurement properties for all children between 7 and 17 (19).

It may be proposed that the Paediatric Asthma Quality of Life Questionnaire can be used to establish differences between patients in the way asthma affects their lives and to establish important treatment effects. The questionnaire is simple and easy to use and is applicable to children as young as seven years of age and should provide a new dimension for investigations of children with asthma (20).

Conclusions

Asthma causes damages to the respiratory system, brings about dyspnea, disturbance of the parameters of the pulmonary function (FVC, FEV1, FEF25-75, PEF) and enhances disturbed quality of life of such patients.

Preventive anti-inflammatory therapy with inhaled glyocorticoides significantly reduces the inflammatory process, improves the score of daily and nightly asthma symptoms, daily variations of PEF and improves spirometry parameters.

In our research the score of the total quality of life showed statistically significant improvements after the use of beclomethasone dipropionate (52%).

Estimation of the quality of life represents a new aspect and can be defined as a marker in diagnosis and estimation of the type of the disease and final success of the total therapy as well.

References

- Oleson M. Subjectively perceived quality of life. *Image* 1990; 22: 187-190.
- Guyatt GH, Juniper EF, Feeny DH, Griffith LE. Children and adult perceptions of childhood asthma. *Pediatrics*. 1997; 99: 165-168.
- Woods PR, Hidalgo HA, Prihoda TJ, Kromer ME. Comparison of Hispanic children's and parents' responses to questions about the child's asthma. *Arch Pediatr Adolesc Med*. 1994; 148: P43.
- Townsend M, Feeny DH, Guyatt GH, Furlong WJ, Seip AE, Dolovich J. Evaluation of the burden of illness for pediatric asthmatic patients and their parents. *Ann Allergy*. 1991; 67: 403-408.
- Christie MJ, French D, Sowden A, West A. Development of childcentred disease-specific questionnaires for living with asthma. *Psychosom Med*. 1993; 55:541-548.
- Nocon A. Social and emotional impact of childhood asthma. *Arch Dis Child*. 1991; 66:458-460.
- Usherwood TP, Scrimgeour A, Barber JH. Questionnaire to measure perceived symptoms and disability in asthma. *Arch Dis Child*. 1990; 65:779-781.
- Creer TL, Wigal JK, Kotses H, Hatala JC, McConaughy K, Winder JA. A life activities questionnaire for childhood asthma. *J Asthma*. 1993; 30:467-473.
- Bowling A. *Measuring health: a review of quality of life measurement scales*. Buckingham/Philadelphia: Open University Press, 1997.

10. Juniper EF, Guyatt GH, Willan A, et al. Determining a minimal important change in a disease-specific quality of life questionnaire. *J Clin Epidemiol* 1994; 47:81-87.
11. Crapo RO, Morris AH, Gardner RM. Reference spirometric values using techniques and equipment that meet ATS recommendations. *Am Rev Respir Dis* 1981; 123:659-664.
12. Nunn AJ, Gregg I. New regression equations for predicting peak expiratory flow in adults. *BMJ* 1989; 298:1068-1070
13. Juniper EF, Guyatt GH, Feeney DH, et al. Measuring quality of life in children with asthma. *Qual Life Res* 1996; 5:35-46.
14. Juniper EF, Guyatt GH, Ferrie PJ, et al. Measuring quality of life in asthma. *Am Rev Respir Dis* 1993; 147:832-838.
15. Juniper E, Guyatt GH, Epstein RS, et al. Evaluation of impairment of health-related quality of life in asthma: development of a questionnaire for use in clinical trials. *Thorax* 1992; 47:76-83.
16. Rutten-van Molken MP, Clusters F, Van Doorslaer EK, et al. Comparison of performance of four instruments in evaluating the effects of salmeterol on asthma quality of life. *Eur Respir J* 1995; 8:888-898.
17. Guyatt GH, Juniper EF, Walter SD, et al. Interpreting treatment effects in randomised trials. *BMJ* 1998; 316:690-693.
18. Leidy NK, Coughlin C. Psychometric performance of the Asthma Quality of Life Questionnaire in a US sample. *Qual Life Res* 1998; 7:127-134.
19. Juniper EF, Johnston PR, Borkhoff CM, et al. Quality of life in asthma clinical trials: comparison of salmeterol and salbutamol. *Am J Respir Crit Care Med* 1995; 151:66-70.
20. Juniper EF. Quality of life in adults and children with asthma and rhinitis. *Allergy* 1997; 52:971-977.

PROCENA KVALITETA ŽIVOTA KOD ASTME KAO MARKER TEŽINE BOLESTI I USPEHA LEČENJA U ŠKOLSKE DECE

Svetlana S. Pljaskić-Kamenov¹, Dragoslav V. Djordjević², Stojan S. Radić³, Borislav A. Kamenov⁴

¹Dom zdravlja, Niš

²Klinika za plućne bolesti, Klinički centar, Niš

³Institut za patofiziologiju Medicinskog fakulteta u Nišu

⁴Dečja klinika, Klinički centar, Niš

Kratak sadržaj: Analizirani su parametri kvaliteta života kod školske dece obolele od astme i korelisani sa kliničkim, inflamatornim parametrima, poremećajima plućne funkcije u periodu od tri meseca u toku kog vremena je primenjivana inhalatorna terapija kortikosteroidima. Testiranjem je obuhvaćeno 125 dece uzrasta 7 do 17 godina sa simptomima bolesti. Bilo je 40 devojčica i 85 dečaka srednje vrednosti uzrasta 12,14. Kriterijumi za procenu težine astme su bili: dnevni i noćni simptomi koji su se javljali više puta nedeljno, dnevno korišćenje β_2 agonista i promene PEF i FEV1. Dijagnoza astme je postavljana na bazi sledećih elemenata: anamneza, eozinofilija u perifernoj krvi i nosnom sekretu, alergološkom ispitivanju "prick" metodom, ukupnom i specifičnom IgE, spirometrijskim parametrima, podacima iz liste simptoma, procene stepena dispneje po Borgu, odgovora na pitanja o kvalitetu života po Juniperu. T test pokazuje da nema značajne razlike u promeni kvaliteta života u zavisnosti od uzrasta dece ($p > 125$). Postoji statistički značajna razlika u promeni kvaliteta života vezano za pol dece. Bolji su rezultati kod muške dece. Ne postoji statistički značajna razlika promene kvaliteta života u odnosu na težinu bolesti. Rezultati promene kvaliteta života u toku primene terapije inhalatornim kortikosteroidima pokazuju statistički značajne promene u svim kategorijama. Najveće promene u domenu simptoma pokazuju se u kategoriji zviždanja i stezanja u grudima. Najbolji rezultati u domenu emocija su neudobnost, ljutnja, frustracija i zabrinutost. Najbolji rezultati u domenu aktivnosti su dobivene u kategorijama fizičke aktivnosti i aktivnosti sa prijateljima i porodicom. Ukupni skor kvaliteta života pokazuje statistički značajno poboljšanje posle upotrebe beclomethasone dipropionate-a.

Ključne reči: Astma, kvalitet života, kortikosteroidi