Original Article

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Comparison of Effectiveness of Jet Nebulizer and Mesh Nebulizer in Epinephrine Inhalation Therapy of Children with Acute Bronchiolitis*

Akut Bronşiolitli Çocuklarda Epinefrin İnhalasyon Tedavisinde Jet Nebülizatör ile Mesh Nebülizatörün Etkinliğinin Karşılaştırılması

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ABSTRACT

Objective: *Inhaled bronchodilators are commonly used in the treatment of patients hospitalized with the diagnosis of acute bronchiolitis. The mesh nebulizer, developed in recent years, allows to deliver the smaller particles of drugs to the distal airways. The aim of this retrospective study is to compare the effectiveness of mesh nebulizers with jet nebulizers in terms of clinical improvement, length of hospital stay and intensive care requirement.*
Method: *The study was conducted in Haseki Research and Training Hospital. Seventy-five pediatric patients between 1-24 months of age who were hospitalized with the diagnosis of acute bronchiolitis were included in the study. Forty patients were treated with jet nebulizer and 35 patients were treated with mesh nebulizer. The responses to the treatment were evaluated with duration of hospitalization, changes in heart rates, respiratory rates and Wang respiratory scores at 24th and 48th hours of therapy and requirement of intensive care.*
Results: *Respiratory syncytial virus was the most commonly isolated viral pathogen (37.3%), followed by rhinovirus. Wang respiratory scores were significantly decreased in patients using mesh nebulizers at the 24th (p<0.001) and 48th hours (p<0.001) of treatment. Respiratory and heart rates were significantly improved at the 48th hours of therapy (p=0.026, p=0.023, respectively). The patients who were treated with jet nebulizer had longer hospital stay than those treated with mesh nebulizer (p=0.006).*
Conclusion: *It was concluded that mesh nebulizer contribute to rapid improvement in acute respiratory failure, shortened the duration of hospitalization and may decrease the requirement of intensive care in patients with acute bronchiolitis.*

Keywords: *bronchiolitis, inhalation therapy, epinephrine, nebulized bronchodilators*

ÖZ

Amaç: *Akut bronşiyolit tanısıyla hastaneye yatan hastalarda, tedavi olarak inhale bronkodilatörler sıklıkla kullanılmaktadır. Son yıllarda geliştirilen mesh nebülizatör, ilaçların daha küçük partiküller halinde distal hava yollarına iletilmesini sağlamaktadır. Bu geriye dönük çalışmanın amacı, mesh nebülizörler ile jet nebülizörlerin etkinliğini klinik düzelme, hastanede kalış süresi ve yoğun bakım ihtiyacı açısından karşılaştırmaktır.*
Yöntem: *Bu çalışma Haseki Eğitim ve Araştırma Hastanesi'nde yapıldı. Akut bronşiolit tanısı ile hastaneye yatırılan 1-24 ay arası 75 çocuk çalışmaya alındı. Kırk hasta jet nebülizatör ile 35 hasta mesh nebülizatörle tedavi edildi. Tedaviye yanıt hastanede kalış süresi, tedavinin 24 ve 48. saatlerindeki kalp, solunum sayıları ve Wang solunum skorundaki değişiklik ile yoğun bakım gereksinimi açısından değerlendirildi.*
Bulgular: *En sık izole edilen viral etken respiratuar sinsisyal virüs (%37,3) idi onu rhinovirüs takip ediyordu. Mesh nebülizatör kullanan hastalarda tedavinin 24. (p<0.001) ve 48. (p<0.001) saatlerinde Wang solunum skoru anlamlı olarak düşüktü. Tedavinin 48. saatinde solunum ve kalp hızları belirgin olarak düzeldi (p=0,026, p=0,023, sırasıyla). Jet nebülizatörle tedavi olan hastaların hastanede kalış süreleri mesh nebülizatör ile tedavi edilenlere göre daha uzundu (p=0,006).*
Sonuç: *Akut bronşiolitli hastalarda, mesh nebülizörünün akut solunum yetmezliğinde hızlı iyileşmeye katkıda bulunduğu, hastanede yatış süresini kısalttığı ve yoğun bakım gereksinimini azaltabileceği sonucuna varılmıştır.*

Anahtar kelimeler: *bronşiolit, inhalasyon tedavisi, epinefrin, nebülize bronkodilatörler*

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INTRODUCTION

Acute bronchiolitis, commonly seen in children under two years, causes obstruction of distal airways. It is the most common lower respiratory tract disease in childhood [1-3]. Viral infections mostly cause this disease and the most common pathogen is respiratory syncytial virus (RSV) [1-3]. The disease is classified as mild, moderate, and severe due to clinical signs [3]. While mild cases can be followed up on an outpatient clinics, babies with bronchiolitis lasting less than 3 months and have a moderate to severe bronchiolitis should be hospitalized [1,3]. In some periods these patients accumulate in emergency departments, lock the pediatric intensive care units and bring an economic burden to the health system [1,2].

Treatment of acute bronchiolitis consists of supportive treatments based on oxygenation and hydration in children [1-3]. Some patients need bronchodilators to reduce edema of the small airways [3]. Jet nebulizer (JN) is one of the easiest, almost effective, inexpensive device in inhalation therapy and is widely used [4]. However, it has been shown that the concentration of the nebulized drug reaching into the small airways decreases due to the increased respiratory rate [5]. A new technologic device, named mesh nebulizer (MN), has been developed to overcome this obstacle [6-9]. It is made of palladium element, and contains one thousand holes in a diameter of 5 mm that vibrate 128,000 times per second [6]. It enables to deliver drug particles into the distal airways of the lung [8]. It has been claimed that it accelerates recovery and shortens hospital stay [8,9].

The aim of this study is to compare the effectiveness of JN and MN in clinical recovery, hospital stay and intensive care requirement in patients who were diagnosed with bronchiolitis.

MATERIAL and METHOD

This retrospective study was conducted in S.B.Ü. Haseki Training and Research Hospital and was approved by the local ethical board (No:2019-18). The children under two years of age who diagnosed with acute bronchiolitis and hospitalized were included in the study. Data of patients were collected from the hospital's registration system. The severity of the disease was determined using Wang respiratory score [10]. In this scoring system there are four parameters; respiratory rate, wheezing, retraction and general condition. The total score ranges from 0 to 12. In order to design equal groups, in terms of the severity of the disease, the patients who had Wang respiratory score of 7 at admission and received only epinephrine inhalation were enrolled. All patients were scored according to the clinical records at admission, at 24th hours and 48th hours of treatment. The dose of epinephrine was determined as 0.1 ml/kg/ dose (1 mg/1 ml) (1: 1000 Adrenaline) due to the routine protocol of our department. Every child received six doses of epinephrine in a day, extra doses were not needed. The hypoxic patients were excluded from the study , only the ones who had oxygen saturations above 92% were selected. Additional oxygen therapy was not given during the treatment except for the patients who were transferred to intensive care unit. We formed the groups according to the type of nebulizer. Group 1 used JN (CGR-1002®, CGR Medical Ltd, Istanbul, Turkey) and Group 2 used MN (Aerogen Solo®, Aerogen Ltd, Galway, Ireland). Sterile masks were used for inhalation therapy in every child in the MN group. The infected materials of MN was removed with surface disinfectant containing didecyldimethylammonium chloride and left in disinfectant which contains non-corosive quarterner amonium carbonate, non-ionic surface active material and enzymatic complex.

The demographic features such as age, sex, breastfeeding in the first 6 month of life, consanguinity, history of atopy and exposure of smoke were noted. Length of hospitalization, steroid or magnesium use, fever (if body temparature above 38.5°C), presence of acute phase reactants, and results of nasal swabs were noted. Respiratory and heart rates, Wang respiratory scores at admission and after 24th-48th hours of therapy were compared according to nebulizer's type. Also nasal swabs and acute phase reactants were evaluated in groups. Since routine use of pulse oximeter was not available in all patients in pediatric wards, we could not obtained oxygen saturation values of the patients.

Exclusion criteria

Patients who had history of prematurity, and recurrent wheezing, pneumonia, chronic lung diseases

such as asthma, congenital heart disease and who received inhalation therapy other than epinephrine were excluded.

Statistical analysis: To analyze the data SPSS 15.0 for Windows was used. The categorical variables were given as frequencies and percentages for continuous variables as mean and standard deviations (SD). Comparison of the data which did not show normal distribution, were analyzed with Mann-Whitney U test. Chi- square test was used for comparing categorical variables. Statistically significant p value was accepted at <0.05.

Based on previous studies with 95% confidence intervals, the sample size was determined to be n1=n2=35, N=70. The level of statistical significance was established as 0.05 with 95% statistical power.

RESULTS

The study was performed on 75 patients diagnosed with acute bronchiolitis including 42 (56%) girls and 33 (44%) boys, whose ages ranged from 1 to 23 months. The inhalation therapy with epinephrine was given to 40 patients with a JN, and 35 patients with a MN. The characteristic features of the groups were detailed in Table 1. There was no statistically significant difference between the age and sex of the children in groups (p>0.05). The history of breastfeeding, consanguinity, exposure to smoking and the presence of atopic individuals in the family showed no statistically significant difference between groups (p>0.05). There was no statistically significant difference in the number of febrile episodes and the use of steroid and magnesium therapy during hospitalization between groups (Table 2). RSV was observed in nasal swabs of 37.3% of the patients who participated in the study. Rhinovirus, one of the most common viruses after RSV, was detected in 25.3% of patients. There was no statistically significant difference in the comparative respiratory panel results examined for the control of the homogeneity of the groups (p>0.05) (Table 3). There were no significant differences between the groups in terms of the presence of viral agents, acute phase reactants and blood counts (p>0.05).

Table 2. Viral etiologies of the study groups.

	Nebulizer type	
Virus n (%)	**Jet nebulizer**	**Mesh nebulizer**
Rhinovirus	9 (22.5)	10 (28.6)
Parainfluenza	3 (7.5)	4 (11,4)
Coronavirus	0 (0.0)	1 (2.9)
Respiratory syncytial virus	15 (37.5)	13 (37.1)
Human metapneumovirus	1 (2.5)	3 (8.6)
Human bocavirus	2 (5.0)	0 (0.0)
Adenovirus	2 (5.0)	2 (5.7)
Influenza A	1 (2.5)	1 (2.9)
Influenza B	1 (2.5)	0 (0.0)
Negative	6 (15.0)	1 (2.9)

Table 3. Comparison of receiving magnesium and steroid in study groups.

	Nebulizer type		
	Jet nebulizer	**Mesh nebulizer**	**p value**
Magnesium (i.v) n (%)	9 (22.5)	13 (37.1)	0.785
Systemic steroid n (%)	12 (30.0)	10 (28.6)	0.892

p<0.05 accepted statistically significant

We did not find any statistically significant difference in the mean respiratory rates at admission and 24th hour of the treatment (p>0.05). The respiratory rate was significantly lower at 48th hour after treatment in MN group than JN group (p=0.026). The children's

Table 1. Characteristic features of the groups.

	Nebulizer type		
	Jet nebulizer	**Mesh nebulizer**	**p value**
Age (month) Median (IQR)	6.0 (7.0)	5.0 (8.0)	0.970
Sex (male) n (%)	19 (47.5)	14 (40.0)	0.514
Breastfeeding first 6 months n (%)	25 (62.5)	24 (68.6)	0.582
Consanguinity n (%)	13 (32.5)	5 (14.3)	0.065
Exposure to smoking n (%)	16 (40.0)	17 (48.6)	0.456
History of familial atopy n (%)	10 (25.0)	7 (20.0)	0.606

Standard deviation: SD, IQR: Interquartile range, p<0.05 accepted statistically significant

Table 4. Comparison of clinical variables of the groups.

	Nebulizer type		
	Jet nebulizer	**Mesh nebulizer**	**p value**
Fever n (%)	5 (12.5)	8 (22.9)	0.237
Respiratory rate (Mean±SD)			
Admission	49.9±6.5	48.1±6.3	0.271
24th hour	41.6±5.9	41.4±6.9	0.926
48th hour	38.4±5.0	35.4±5.6	0.026
Heart rate (Mean±SD)			
Admission	133.6±11.5	131.6±10.9	0.492
24th hour	125.9±12.0	123.9±10.6	0.398
48th hour	121.9±11.4	116.3±10.6	0.023
Wang scores (Mean±SD)			
Admission	7.00±0.00	7.0±0.00	1,000
24th hour	6.00±0.00	5.7±0.5	<0.001
48th hour	4.80±0.41	4.23±0.43	<0.001
Duration of hospitalization Median (IQR)	7.0 (3.0)	5.0 (4.0)	0.006

Standard deviation: SD, IQR: Interquartile range, p<0.05 accepted statistically significant

heart rates were not significantly different in two groups at admission and at 24th hour of therapy (p>0.05), otherwise heart rates decreased in MN group at the 48th hours of treatment (p=0,023). The mean Wang respiratory scores of patients using JN was statistically significantly higher than patients using MN at 24th and 48th hours (p<0.001). The mean hospitalization time of patients using JN was statistically significantly higher than patients using MN (p=0.006) (Table 4). We also detected that five children needed intensive care in JN group (12.5%) during the treatment course. However, in MN group no one was treated in the intensive care unit.

DISCUSSION

As far as we know, this is the first study that compares the efficacy of inhaled epinephrine using JN vs MN in children with acute bronchiolitis. In this study, we figured out that nebulized epinephrine treatment with a MN, significantly improved the disease severity scores at the 48th hour of management, increased the recovery rates and reduced the duration of hospitalization.

Acute bronchiolitis seems mostly in the winter period in our country and crowds emergency clinics. Many studies show that the most common factor in acute bronchiolitis is RSV [2,11,12]. RSV was found in the rate of 20-63% in infants under the age of two years in Turkey [11,13]. In the present study, RSV was the most frequently isolated viral pathogen (37.3%) followed by rhinovirus.

The main approach in the management of acute bronchiolitis is supportive therapy providing oxygenation and hydration [3,14,15]. However, beta-2 agonists, epinephrine, corticosteroid and antiviral treatments are also used in daily practice due to the severity of the disease [14]. In a meta-analysis conducted by Garrison et al. systemic and inhaled corticosteroids have been shown to have no favorable effect in the treatment of hospitalized infants with acute bronchiolitis [15]. The frequency of receiving systemic steroid was found to be 48% in the study by Offer et al. [16]. In our study, systemic corticosteroids were used in 29.3% of cases who did not respond to epinephrine. Although there was no statistically significant difference between the two groups, 54.5% of the patients were in the jet nebulizer group. Likewise, the effectiveness of intravenous magnesium has not been proven. It can be tried in patients who do not improve despite supportive treatment [17]. In our study, magnesium was used in 29.3% of the cases who did not respond to epinephrine and steroid. We found no statistically significant difference between the groups in terms of magnesium treatment.

Recently, the most popular therapy is inhalation of epinephrine [18-22]. It was reported that epinephrine is

more effective in achieving recovery compared to other bronchodilator drugs [20,23]. The mucosal edema has an important role in respiratory obstruction. The use of combined alpha and beta-adrenergic agonists instead of beta-2 agonist may be more beneficial in the treatment of acute bronchiolitis, and studies have been focused on this topic [20]. Hartling et al. reported a meta-analysis that regarded the use of inhaled epinephrine in the treatment of acute bronchiolitis to improve clinical signs and oxygenation of the patients in the emergency room [22]. The effectiveness of different agents in acute bronchiolitis is not clear, studies are ongoing in this regard.

The inhalation technique is also noteworthy to enhance the efficacy of the drugs. Different devices can be used in nebulization therapy. The nebulizer types are ultrasonic nebulizer, JN and MN [24,25]. MN creates vibration with the help of electrical energy. The drug passes through a mesh and becomes volatile [24]. MNs are more effective than the other two models of nebulizers, and the vast majority of drugs reach the distal airways in the form of microaerosels with a diameter of 0.4 to 4.4 µm [24,26,27]. However, droplet size is > 5 µm in JN [28]. The amount remaining in the chamber of MN is also very few compared to other nebulizers [24,25]. In inhalation treatments using mesh technology, the distribution of aerosol drug into the airways was found to be better when evaluated by performing lung SPECT-CT [26].

It has been suggested that the drug is nebulized faster with MN than with traditional JN, and the clinicians can precisely control drug delivery into the respiratory tract [25]. There are studies comparing different types of nebulizers on children in the literature [24,25]. Dunne et al. found a decrease in hospital stay and a significant reduction in the dose of drug in patients treated with MN in the emergency department [8]. In the present study we evaluated the clinical courses of the patients. We found that respiratory rates, heart rates and Wang severity scores improved faster in the MN group than JN group. Delivery of the drug to the distal airways and removing the obstruction in the airways rapidly may be effective in correcting tachycardia and ensuring rapid recovery in the follow-up period. The silent nature of the MN can also prevent agitation in children and cause rapid effects.

Limitations of the study: One of the limitations of our study is its retrospective nature which could not allow evaluation of the acute effects of the treatments. We could not able to compare the clinical signs at 30th, 60th and 120th minutes of the hospitalization. The second one is about its cost effectiveness. Since the MN can be used in more than one patient, prospective studies are needed to evaluate the number of MNs that are used in order to perform net cost analysis.

CONCLUSION

Delivery of epinephrine using MN in acute bronchiolitis positively contributes to the recovery of clinical signs and shortening of the hospitalization time. Further large, prospective, randomized controlled studies are needed to show the effectiveness of treatment and intensive care requirement using MN in pediatric patients with acute bronchiolitis.

Ethics Committee Approval: Approval was received from the S.B.Ü. Haseki Training and Research Hospital Clinical Research Ethics Committee (2019/18, 09.10.2019).
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