Efficacy of Subcutaneous Epinephrine versus Nebulized Salbutamol in the Emergency Department Treatment of Bronchiolitis

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Abstract

Background: By age 2 years, 50% of children will have been infected with bronchiolitis, with severe disease more common among infants aged 1–3 months. Despite wide spread use of nebulized B_2-agonists in infants with bronchiolitis since the late 1950s, the efficacy of these drugs remains unproven. Statistical improvement in clinical scoring systems seen with the use of beta agonists is not always clinically significant, and desaturations have been reported after salbutamol nebulization. Epinephrine hydrochloride is being used with increasing frequency in bronchiolitis. Subcutaneous administration of it may produce its effects within 10 minutes and maximal effects in about 30 minutes.

Aim of the study: To determine the efficacy of S.C Epi. versus Neb. salbutamol in the Emergency Department treatment of patients (age 2 years or less) with bronchiolitis.

Patients and method: Two hundreds patients less than 2 years of age with a clinical diagnosis of bronchiolitis were enrolled in a prospective, randomized and controlled study to receive either subcutaneous epinephrine (n=100) or nebulized 0.5% salbutamol sulfate (n=100). This study was done in the Emergency Department of Babylon maternity and children teaching hospital. Study enrollment occurred in sequential winter season from the first of September 2007 to the first of March 2008.

Results: There is high significant improvement in O_2 saturation at 30 and 60 min., in respiratory rate at 60 and 90 min., heart rate improvement at 60 min. and better improvement in the wheeze, chest retraction, nasal flaring, and reduced rate of admission to the wards in patient who were treated with subcutaneous epinephrine than those who were treated with nebulized salbutamol.

Conclusions: The response to subcutaneous epinephrine in patients younger than 12 months was better than older patients. Subcutaneous epinephrine improves the clinical manifestation and parameters of respiratory distress with maximum effectiveness at 30-60 min. Subcutaneous epinephrine decreases the load of patients on E.D and reduces the rate of admission to the wards in comparison with nebulized salbutamol.

الخلاصة

خلفية الدراسة: إن مرض التهاب القصيبات الحاد يصيب50% من الأطفال تقريبا خلال السنتين الأولى من العمر، ويكون شديدا مابين عمر 1-3 شهر. على الرغم من الانتشار الواسع لاستعمال الأدوية الموسعة للقصبات عن طريق الاستنشاق والتي تعمل عن طريق تحفيز مستقبلات البيتا –2 منذ الخمسينات من القرن الماضي لعلاج هذا المرض لكن لم يتم إثبات فعالية هذه الأدوية حتى الآن. إن التحسين الإحصائي في أنظمةِ الإحراز السريريةِ باستعمال هذه الأدوية ليستْ هامّة سريرياً دائماً ، ولقد تم تسجيل العديد من حالات انخفاض مستوى الأوكسجين في الدم بعد اخذ هذه الأدوية عن طريق الاستنشاق. بدا استخدام ابنفرين هيدروكلورايد (الادرينالين) بشكل

متزايد في علاج هذا المرض. إن إعطاء الادرينالين تحت الجلد يؤدي إلى توسيع القصبات خلال عشرة دقائق ويصل أقصى مفعول له بعد 30 دقيقة من إعطائه.

هدف البحث: لتقرير فاعلية الابنفرين(تحت الجلد) مقابل السالبيوتامول(تبخير)في علاج التهاب القصيبات الحاد في قسم الطوارئ لدى الأطفال دون عمر السنتين.

المرضى وطريقة العمل: اشتملت هذه الدراسة العشوائية المتوقعة مائتي طفل (بعمر سنتين او اقل) مصابون بالتهاب القصيبات الحاد المشخص سريريا، حيث تم علاج نصفهم بابنفرين هيدروكلورايد تحت الجلد و النصف الآخر عولجوا بسالبيوتامول عن طريق الاستنشاق. أجريت الدراسة في قسم الطوارئ لمستشفى بابل التعليمي للنسائية والأطفال للفترة من الأول من أيلول 2007 إلى الأول من آذار 2008.

النتائج: إن هنالك تحسن معنوي عالي لدى الأطفال الذين تم علاجهم بابنفرين هيدروكلورايد تحت الجلد من حيث تشبع الدم بالأوكسجين بعد 30 و60 دقيقة من بدء العلاج وتحسن معدل التنفس بعد 60 و90 دقيقة وتحسن معدل ضربات القلب بعد 60 من بدء العلاج وكذلك تحسن في علامات المرض السريرية كالأزيز, إعادة جر الصدر, الاندلاع الأنفي ومعدل دخول المرضى إلى ردهات المستشفى بالمقارنة مع المرضى الذين تم علاجهم بالسالبيوتامول عن طريق الاستنشاق .

الاستنتاجات: إن استجابة المرضى الذين تقل أعمارهم عن السنة للابنفرين تحت الجلد كانت أفضل من أولئك الذين تزيد أعمارهم عن ذلك. يؤدي الابنفرين تحت الجلد إلى تحسن أفضل في العلامات السريرية وعلامات عسر التنفس بتأثير أقصى عند الدقيقة الثلاثون والستون. يقلل استخدام الابنفرين تحت الجلد الحمل على قسم الطوارئ وكذلك معدلات الدخول إلى ردهات المستشفى مقارنة بالسالبيوتامول تبخير.

Introduction

Acute bronchiolitis is the commonest cause of lower respiratory tract illness in infants resulting in inflammatory obstruction of the small airways. By age 2 years 50% of children have been infected, with severe disease more common among infants aged 1–3 months. Bronchiolitis is seasonal, with peak activity during winter and early spring [(1)]. Acute bronchiolitis is predominantly a viral disease; Respiratory Syncitial Virus (RSV) is responsible in around 75% of cases, other agents include metapneumovirus, parainfluenza, adenovirus, Mycoplasma, and occasionally other viruses [(2)]. Estimates suggest that 50,000–80,000 of hospitalizations annually among children younger than 1 year around the world are attributable to RSV infection, representing an increase over the past decade [(3)]. Bronchiolitis occurs more often and earlier in life in lower socioeconomic groups, in those who have not been breast-fed, and in those who live in crowded conditions; older family members are a common source of infection but may experience only minor respiratory symptoms [(4)]. The peak age of infants hospitalized with RSV bronchiolitis is around 3 months [(5)]. The diagnosis is clinical, particularly in a previously healthy infant, presenting with a first-time wheezing episode during a community outbreak [(6)]. Definitive diagnosis of RSV infection is based on the detection of virus or viral components in respiratory secretions and rapid identification of RSV infection can be confirmed by immunofluorescence on nasopharyngeal aspirate samples, which gives a result within hours, or by viral culture but the utility of viral testing (rapid immunofluorescence, polymerase chain reaction, or viral culture) is debatable [(2)]. Infants with respiratory distress should be hospitalized; the mainstay of treatment is supportive, involving maintenance of hydration and oxygen status [(1)]. Beta agonists produce modest short-term improvement in clinical features, but the statistical improvement in clinical scoring systems seen with them is not always clinically significant, and desaturations have been reported after salbutamol nebulization. Salbutamol stimulates β -adrenergic receptors and has little or no effect on α -adrenergic

receptors; the drug also has some vasodilating effect on peripheral vasculature and may decrease diastolic blood pressure to a small extent [7]. Beta-agonists stimulate the production of cAMP by activation of the enzyme adenyl cyclase; cAMP appears to mediate numerous cellular responses[8]. Following administration of salbutamol via nebulization, the peak plasma salbutamol concentrations were reached within 0.5 hour, bronchodilation usually begins within 5 minutes; the effect usually last approximately 1-2 hours [7]. Epinephrine is an endogenous catecholamine. It acts directly on both alpha- and beta-adrenergic receptors of tissues innervated by sympathetic nerves except the sweat glands and arteries of the face; the main effects of therapeutic parenteral doses of Epinephrine are relaxation of smooth muscle of the bronchial tree, cardiac stimulation, and dilation of skeletal muscle vasculature. In patients with bronchiolitis, the drug reduces congestion and edema, increases tidal volume and vital capacity, inhibits histamine release and antagonizes the effect of the mediator on end organs; as a result, the drug may reverse bronchiolar constriction, vasodilatation, and edema produced by this mediator [7].

Aim of study

To determine the efficacy of subcutaneous epinephrine versus nebulized salbutamol in the Emergency Department treatment of patients (age 2 years or less) with bronchiolitis.

Patients and method

In this study, we choose salbutamol as a control for subcutaneous epinephrine because it was the local standard of care at the time our trial was designed. Two hundreds patients less than 2 years of age attending the Emergency Department of Babylon maternity and children teaching hospital (with a clinical diagnosis of bronchiolitis) were enrolled in a prospective, randomized and controlled study to receive either subcutaneous epinephrine (n=100) or nebulized 0.5% salbutamol sulfate (n=100) with continuous flow of 100% oxygen at 0.5 L/min. Table (1) shows the numbers of patients enrolled in this study according to their ages and modes of treatment.

Table 1. distribution of the patients according to their ages and modes of treatment

Ages of patients	Modes of treatment	Numbers of patients
Less than 6 mo.	Neb. salbutamol	58
	S.C Epi.	57
7-12 mo.	Neb. salbutamol	25
	S.C Epi.	29
13-18 mo.	Neb. salbutamol	5
	S.C Epi.	9
19-24 mo.	Neb. salbutamol	12
	S.C Epi.	5
Total	Neb. salbutamol	100
	S.C Epi.	100

Study enrollment occurred in sequential winter season from the first of September 2007 to the first of March 2008. Children were not eligible for enrollment if they had any one of the following: (previous diagnosis of asthma, critically ill patient, and chronic pulmonary or

cardiac disease, presence of tachycardia exceeding 200 beats per minute, use of glucocorticoids or sympathomimetic amines). The patients were subjected to detailed history concerning the age, duration of illness, concomitant medications, other illnesses and associated symptoms. Treatment allocation was determined by randomization. Study drugs were administered at the time of admission at the request of the attending physician and informed consent was taken from the parent before giving subcutaneous epinephrine. The wheezing, chest retractions, flaring of ala nasi, heart rate, respiratory rate and O_2 saturation were measured before administration and every 30 minutes up to 90 minutes after administration of the drugs with observation for the appearance of side effects of the drugs. Oxygen saturation was measured using a pulse oximeter (Nellcor Pulse Oximeter, Nellcor Puritan Bennet Inc., Pleasanton, CA). Proper aseptic technique was used when salbutamol is administered via nebulization. The concentration of salbutamol respirator solution (made by Glaxo Wellcome Operations, Greenford, Middlesex, UK) is 0.5% (5 mg/mL). The dose of Neb. solution was 0.15 mg\kg. The appropriate amount of 0.9% sodium chloride solution is then added to the reservoir to provide a total diluted volume of 3 mL. The patient then breathes through the face mask as calmly, deeply, and evenly as possible until the nebulizer stops producing mist. The flow rate of the nebulizer was adjusted so that salbutamol is delivered over a period of approximately 5 minutes. The nebulizer was cleaned after use. Epinephrine (made by MISR CO-Egypt) was used by S.C route in the upper third of the arm, and the absorption was hastened by massaging the injection site. The dose of subcutaneous epinephrine was 0.01 mg/kg (0.01 mL/kg of a 1:1000) not exceeding 0.5 mg.

Statistical analysis:
The data were analyzed statistically by using computerized *t*-test (SPSS, version 10) and Chi-square (X^2) test, which was carried out to measure the relative importance of various variables. *P*-value less than 0.05 were considered as statistically significant, and value less than 0.01 was considered to be highly significant.

Results

The difference in O_2 saturation between patients (less than 2 years of age) treated with subcutaneous epinephrine and those who have been treated with nebulized salbutamol was shown in table (2), where significant difference regarding increment of O_2 saturation at 30 and 60 min. in those treated with subcutaneous epinephrine. The difference in respiratory rate between patients(less than 2 years of age) treated with subcutaneous epinephrine and those who have been treated with nebulized salbutamol was shown in table (3) where significant difference regarding decrement of respiratory rate at 60 and 90 min. in those treated with subcutaneous epinephrine. The difference in heart rate between patients (less than 2 years of age) treated with subcutaneous epinephrine and those treated with nebulized salbutamol was shown in table (4) where significant difference regarding decrement of heart rate at 60 min. in those who have been treated with subcutaneous epinephrine.
The response of wheezing in patients treated with subcutaneous epinephrine and those who have been treated with nebulized salbutamol was shown in figure 1 where the number of patients

with wheezing decreased from 61 before treatment with subcutaneous epinephrine to 13 after 30 min., 6 after 60 min. and 90 min. while the number of patients with wheezes decreased from 59 before treatment with nebulized salbutamol to 33 after 30 min., 29 after 60 min., and 30 after 90 min. The *P*-values at 30, 60 and 90 min. were < 0.01 which means that there was better improvement in patients who were treated with subcutaneous epinephrine than those who were treated with nebulized salbutamol.

Table 2. Effects of S.C Epi. and Neb. salbutamol on oxygen saturation in patients below 2 years with bronchioliti

Time(min.)	Mode of treatment	Oxygen saturation(oximetry)Mean± Std.dev.	*P*. value
0	Neb. salbutamol	90.78±3.8	> 0.05
	S.C Epi.	90.32±3	
30	Neb. salbutamol	89.43±5.25	< 0.01
	S.C Epi.	92.21±3.38	
60	Neb. salbutamol	90.12±4.27	< 0.05
	S.C Epi.	91.54±4.31	
90	Neb. salbutamol	91.11±4.36	> 0.05
	S.C Epi.	92±3.92	

Table 3 Effects of S.C Epi. and Neb. salbutamol on respiratory rate in patients below 2 years with bronchiolitis

Time(min.)	Mode of treatment	Respiratory rate Mean± Std.dev.	*P*. value
0	Neb. salbutamol	56±18.61	> 0.05
	S.C Epi.	55±14.61	
30	Neb. salbutamol	46±16.14	> 0.05
	S.C Epi.	42±13.65	
60	Neb. salbutamol	43±15.2	< 0.05
	S.C Epi.	38±13.64	
90	Neb. salbutamol	47±17.63	< 0.01
	S.C Epi.	38±13.54	

Table 4. Effects of S.C Epi. and Neb. salbutamol on heart rate in patients below 2 years with bronchiolitis

Time(mi.)	Mode of treatment	Heart rate Mean± Std.dev.	*P*. value
0	Neb. salbutamol	119.16±30.19	> 0.05
	S.C Epi.	117±30.71	
30	Neb. salbutamol	122.6±29.79	> 0.05
	S.C Epi.	119.95±33.36	
60	Neb. salbutamol	122.78±27.9	< 0.01
	S.C Epi.	111.81±32.94	
90	Neb. salbutamol	112.99±27.44	> 0.05
	S.C Epi.	106.94±31.75	

The response of chest retractions in patients treated with subcutaneous epinephrine and those who were treated with nebulized salbutamol was shown in figure (2) where the number of patients with chest retractions

decreased from 46 before treatment with subcutaneous epinephrine to 33 after 30 min., 18 after 60 min., and 16 after 90 min. while the number of patients with chest retractions decreased from 40 before treatment with nebulized salbutamol to 32 after 30 min., 20 after 60 min., and 23 after 90 min.. The *P*-value was < 0.01 only at 90 min. which means that there was better improvement in patient who treated with subcutaneous epinephrine than those who treated with nebulized salbutamol. The response of nasal flaring in patients treated with subcutaneous epinephrine and those treated with nebulized salbutamol was shown in figure (3) where the number of patients with nasal flaring decreased from 45 before treatment with S.C Epi. to 13 after 30 min., 4 after 60 min., and 7 after 90 min. while the number of patients with nasal flaring decreased from 52 before treatment with nebulized salbutamol to 33 after 30 min., 28 after 60 min., and became 32 after 90 min.. The P-values at 30, 60 and 90 min were < 0.01; this means that there is better improvement in patients who treated with subcutaneous epinephrine than those who treated with nebulized salbutamol.

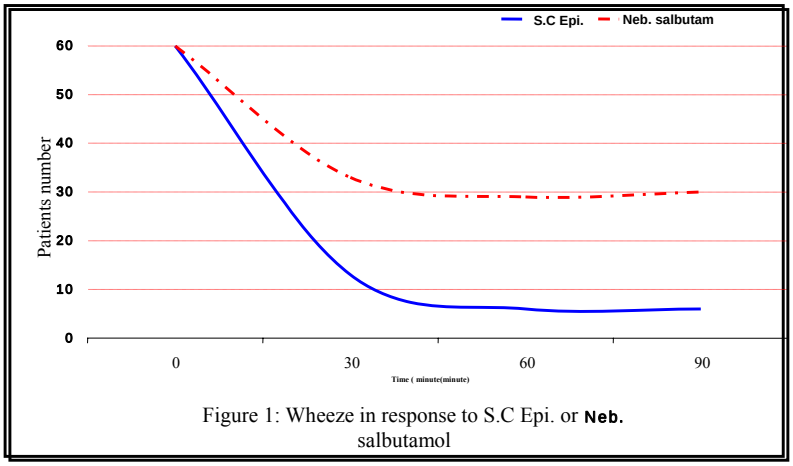

Figure 1: Wheeze in response to S.C Epi. or **Neb.** salbutamol

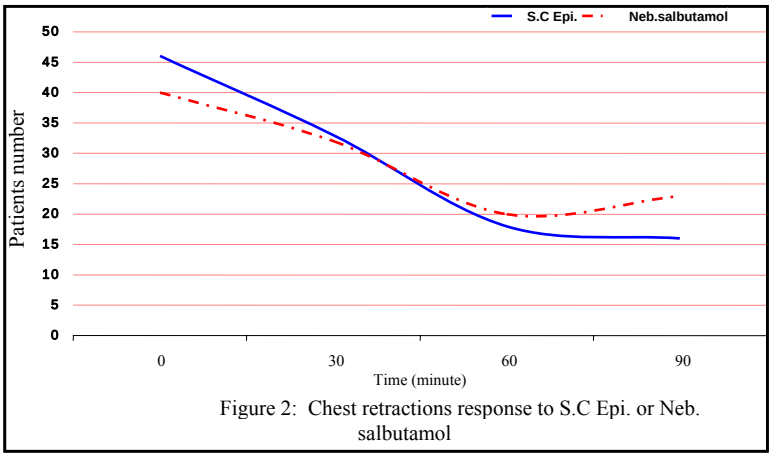

Figure 2: Chest retractions response to S.C Epi. or Neb. salbutamol

Figure 4 shows the age distribution of all 200 patients with bronchiolitis, where 115 patients (57.5%) presented in the first 6 months of their life (mostly in second month of life). There was a reduction in the rate of admission in patient treated with subcutaneous epinephrine than those treated with nebulized salbutamol; 24% of patients treated with nebulized salbutamol have been admitted to the wards, while only 13% of patients

treated with subcutaneous epinephrine need admission to the wards (P-value < 0.01) (figure 5). Significant differences have been noted regarding increment of O_2 saturation at 30 and 60 min. in those patients (less than 6 months of age) and those (7-12 months of age) who treated with subcutaneous epinephrine than those who treated with nebulized salbutamol (figure 6 and 7). Significant differences have been noted regarding increment of O_2 saturation at 30 min. in those patients (13-18 months of age) and (19-24 months of age) that treated with subcutaneous epinephrine than those who treated with nebulized salbutamol (figure 8 and 9).

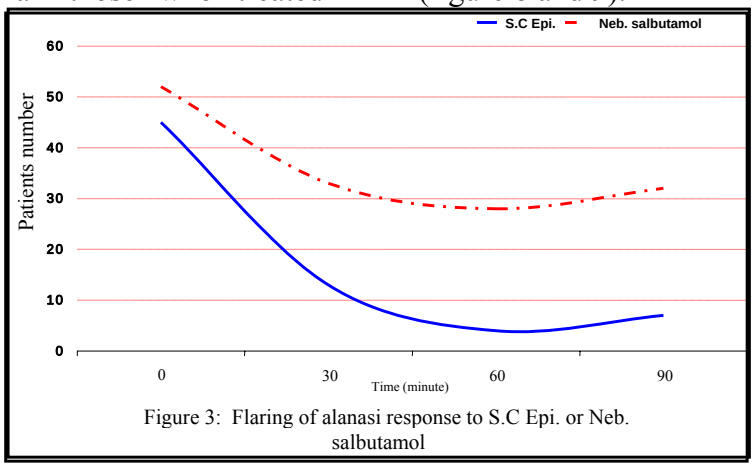

Figure 3: Flaring of alanasi response to S.C Epi. or Neb. salbutamol

The difference in respiratory rate between patients (less than 6 months of age) treated with subcutaneous epinephrine and those treated with nebulized salbutamol was shown in figure (10) where significant difference regarding decrement of respiratory rate at 60 and 90 min. in those who treated with subcutaneous epinephrine. The difference in respiratory rate between patients (7-12 months), (13-18 months) and (19-24 months) of age who treated with subcutaneous epinephrine and those who treated with nebulized salbutamol was shown in figure (11, 12 and 13 respectively) where significant difference regarding decrement of respiratory rate at 90 min. in those who treated with subcutaneous epinephrine. Figure (14) shows that no significant difference in heart rate between patients less than 6 months of age who treated with subcutaneous epinephrine and those who treated with nebulized salbutamol. The difference in heart rate between patients (7-12 months of age) who treated with subcutaneous epinephrine and those who treated with nebulized salbutamol was shown in figure (15) where significant difference at 60 and 90 min. in those who treated with subcutaneous epinephrine. The difference in heart rate between patients (13-18 months of age) who treated with subcutaneous epinephrine and those who treated with nebulized salbutamol was shown in figure (16) where significant difference at 60 min. in those who treated with subcutaneous epinephrine.

The difference in heart rate between patients (19-24 months of age) who treated with subcutaneous epinephrine and those who treated with nebulized salbutamol was shown in figure (17) where significant difference at 60 and 90 min. in those who treated with subcutaneous epinephrine.

Discussion

Transplacentally transmitted anti-RSV antibody, when present in high concentration, has some protective

effect, this probably accounts for the low frequency of severe infections in the first month of life, except in infants born prematurely who are receiving less than a full complement of maternal immunoglobulin (IgG); nevertheless, serum antibody is not fully protective, and the age at which an infant undergoes first infection depends also on the opportunities for exposure[2]. Physiological studies carried out on wheezy infants have failed to show any useful response to nebulized β-adrenergic agents in reduction of the overall respiratory resistance or work of breathing [9].

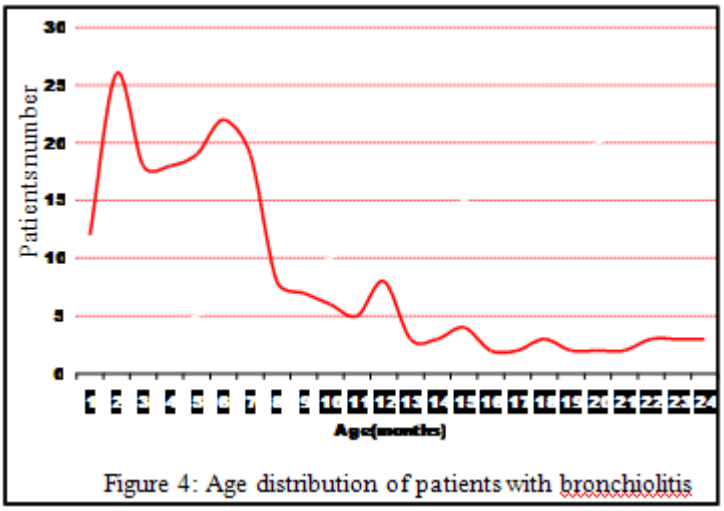

Figure 4: Age distribution of patients with bronchiolitis

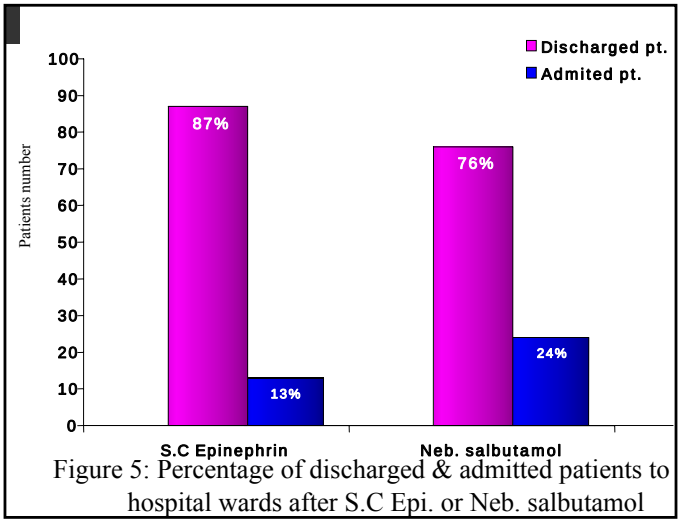

Figure 5: Percentage of discharged & admitted patients to hospital wards after S.C Epi. or Neb. salbutamol

Controversy exists surrounding the use of bronchodilators for bronchiolitis, and epinephrine hydrochloride is being used with increasing frequency in this group [10]. The results of this study favored the use of subcutaneous epinephrine in comparison with nebulized salbutamol for treating patients with bronchiolitis regarding the studied variables. Regarding all patients who are less than 2 years of age: For the O_2 saturation, it was highly significant at 30 and significant at 60 min. (table 2); these results are similar to the results of studies done in Turkey [11] and Australia [12].

For the respiratory rate it was significant at 60 and highly significant at 90 min. (table3) and is similar to the results of an Australian study [12]. For the heart rate it was highly significant at 60 min. (table4) and is similar to the

results of a study in Turkey [11], Australia [12] and Canada [13].

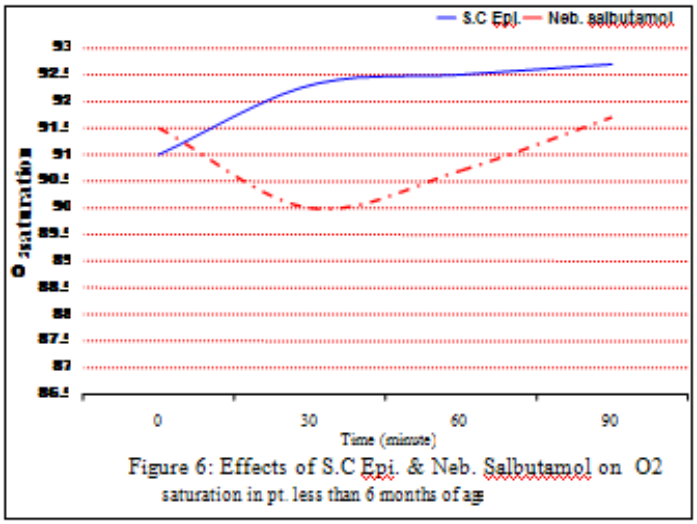

Figure 6: Effects of S.C Epi. & Neb. Salbutamol on O2 saturation in pt. less than 6 months of age

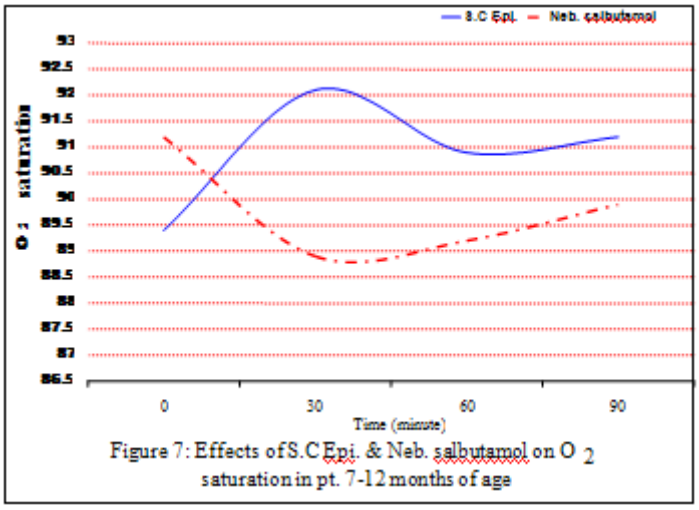

Figure 7: Effects of S.C Epi. & Neb. salbutamol on O 2 saturation in pt. 7-12 months of age

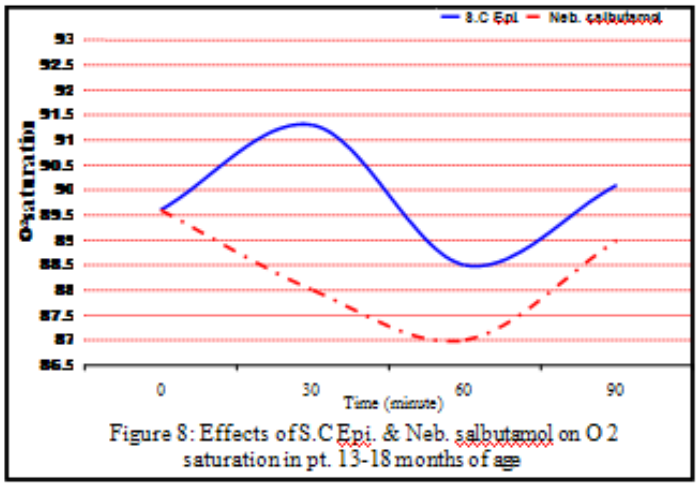

Figure 8: Effects of S.C Epi. & Neb. salbutamol on O 2 saturation in pt. 13-18 months of age

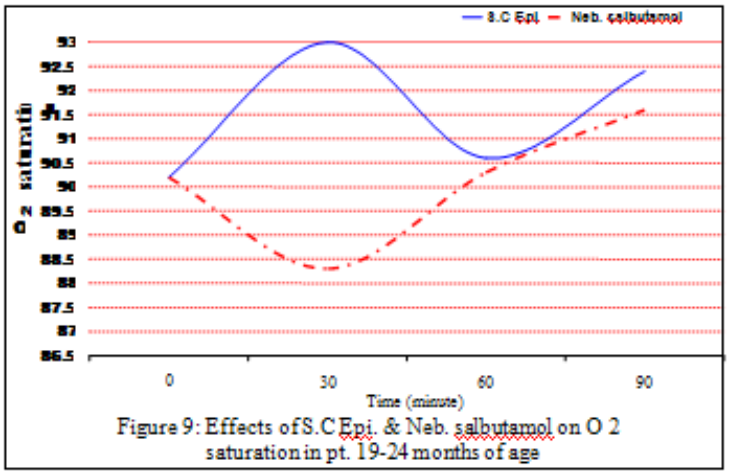

Figure 9: Effects of S.C Epi. & Neb. salbutamol on O 2 saturation in pt. 19-24 months of age

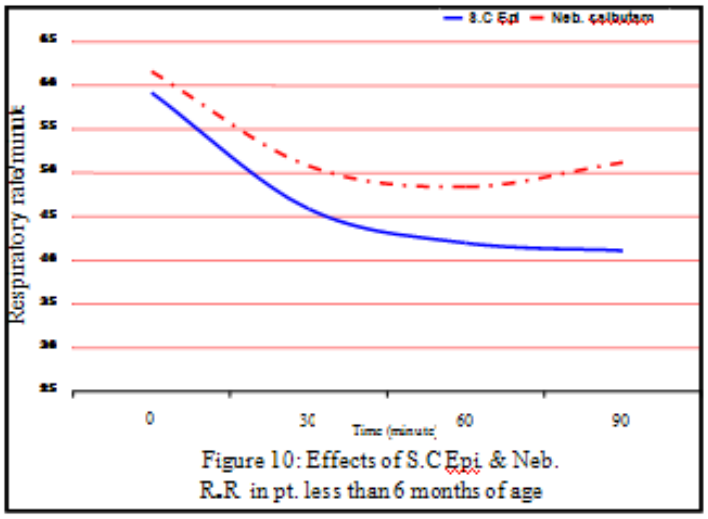

Figure 10: Effects of S.C Epi. & Neb. R.R in pt. less than 6 months of age

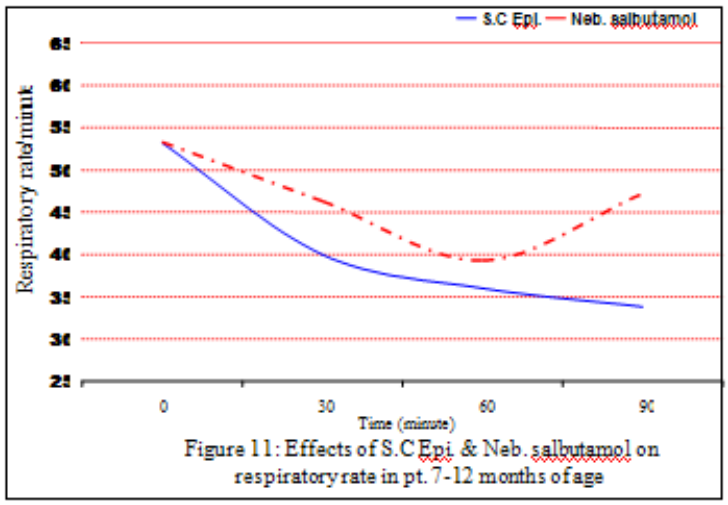

Figure 11: Effects of S.C Epi. & Neb. salbutamol on respiratory rate in pt. 7-12 months of age

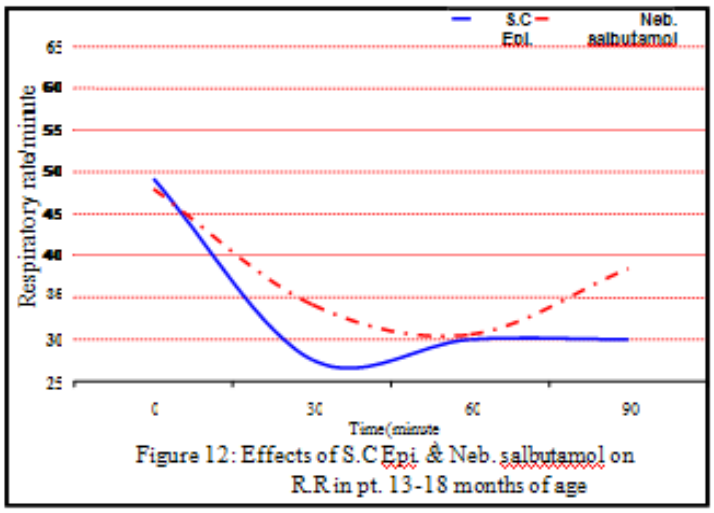

Figure 12: Effects of S.C Epi. & Neb. salbutamol on R.R in pt. 13-18 months of age

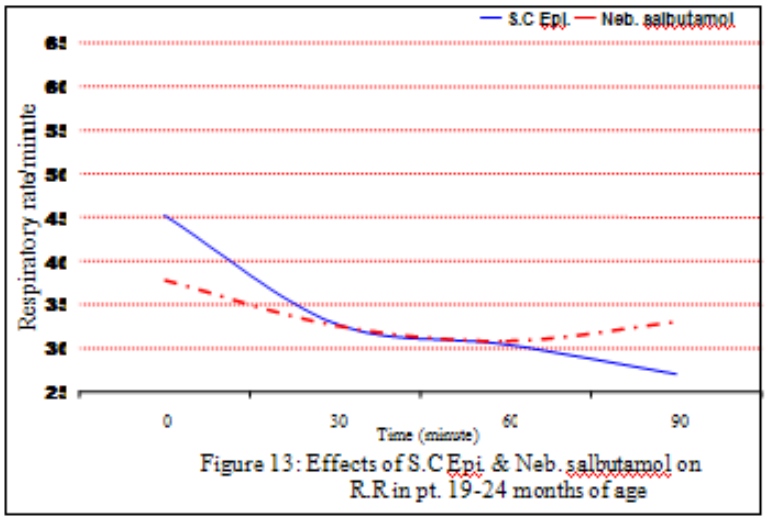

Figure 13: Effects of S.C Epi. & Neb. salbutamol on R.R in pt. 19-24 months of age

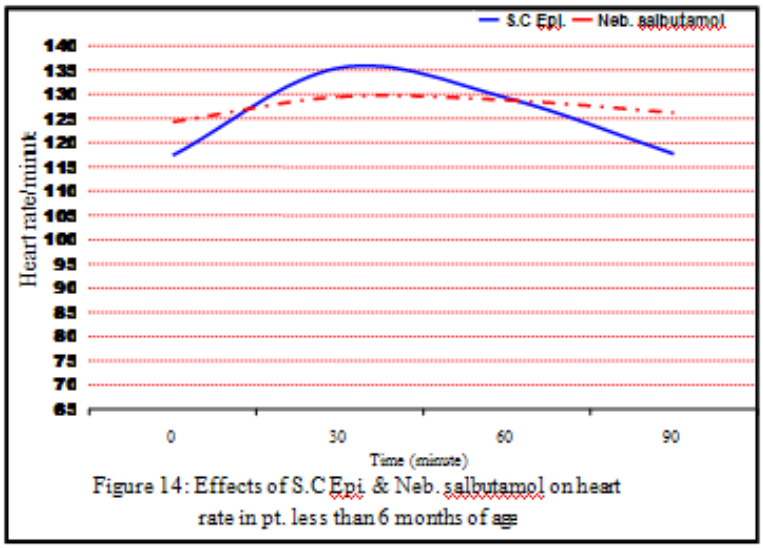

Figure 14: Effects of S.C Epi. & Neb. salbutamol on heart rate in pt. less than 6 months of age

In patients less than 6 months, the results favored subcutaneous epinephrine for O_2 saturation where it was highly significant at 30

min.[S.D,3; 95%C.I,91.5-93.1] and significant at 60 min.[S.D,3.4; 95%C.I,91.6-93.4] ,while not significant at 90 min.(figure 6).

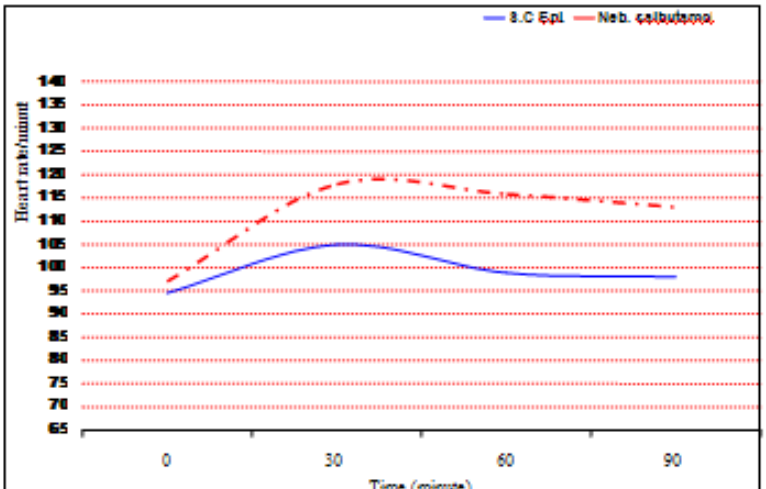

Figure 15: Effects of S.C Epi & Neb. salbutamol on heart rate in pt. 7-12 months of age

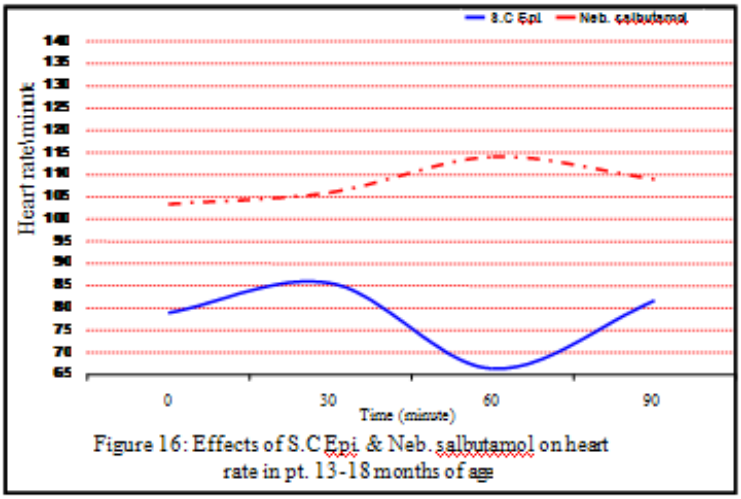

Figure 16: Effects of S.C Epi & Neb. salbutamol on heart rate in pt. 13-18 months of age

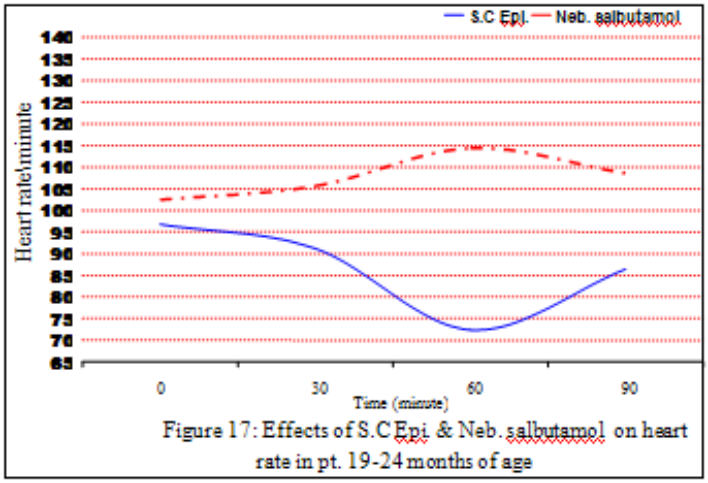

Figure 17: Effects of S.C Epi & Neb. salbutamol on heart rate in pt. 19-24 months of age

For respiratory rate it was significant at 60 min. [S.D, 15.2; 95%C.I, 38-46] and highly significant at 90 min. [S.D, 14.1; 95%C.I, 37.4-44.9], while it was

not significant at 30 min. (figure 10). For heart rate there was no significant difference at any time (figure 14) because salbutamol acts on β-adrenoceptors (which are of very low density in this age group) and the small dose of epinephrine acts on α-adrenoceptors (which are not present in the heart) [14]. In patients aged 7-12 months, the results favored subcutaneous epinephrine for O_2 saturation with high significant difference at 30 min. [S.D, 4.3; 95%C.I, 90.4-93.7] and significant at 60 min. [S.D, 4.7; 95%C.I, 91.6-94], while it was not significant at 90 min. (figure 7). For respiratory rate it was highly significant at 90 min. [S.D, 12.5; 95%C.I, 29.2-38.7], while not significant at 30 and 60 min. (figure 11). For heart rate it was highly significant at 60 min. [S.D, 28.1; 95%C.I, 88.1-109.6] and 90 min. [S.D, 31.2; 95%C.I, 86.1-109.8], while it was not significant at 30 (figure 15). In patients aged 13-18 months, there was significant difference in O_2 saturation at 30 min. [S.D, 4.7; 95%C.I, 91.8-93.8] (figure 8) and respiratory rate at 90 min. [S.D, 12.3; 95%C.I, 25.1-30.2] (fig 12) while highly significant for heart rate at 60 min. [S.D, 25.4; 95%C.I, 46.8-86] (figure 16). In patients aged 19-24 months who received subcutaneous epinephrine, there is significant difference in O_2 saturation at 30 min. [S.D, 4.4; 95%C.I, 91.8-93.8] (figure 9) and respiratory rate at 90 min. [S.D, 11.7; 95%C.I, 24.7-30] (fig 13) while it was highly significant for heart rate at 60 min.[S.D,23.5; 95%C.I 43.1-101.6] and significant at 90 min.[S.D,30; 95%C.I 85-111.3] (figure 17). The explanations of the results mentioned above, we that:

- α- adrenoceptors are present in the vascular smooth muscles and the stimulation of these receptors result in contraction of bronchial arterioles [15].
- β_2- adrenoceptors are present in the bronchial smooth muscles and the stimulation of these receptors result in relaxation of these muscles [15].
- Infants below 2 years of age (especially below 6 months) had lower β_2- adrenoceptors density than older children [14].
- β_1- adrenoceptors are present in the heart muscle and the stimulation of these receptors increase the heart rate [15].
- Small doses of epinephrine hydrochloride(0.01 mL/kg of a 1:1000) stimulates α- adrenoceptors [7].
- Large doses of epinephrine hydrochloride(more than 0.01 mL/kg of a 1:1000) stimulates β-adrenoceptors [7].
- Salbutamol stimulates β-adrenoceptors [7].

So that, for all four age groups mentioned above, the small doses of epinephrine hydrochloride stimulates α-receptors. As a result, the drug may reverse vasodilatation, congestion and edema produced by this mediator. Subsequent improvement in O_2 saturation, respiratory rate, wheeze, chest retraction and flaring of ala nasi will occur. There is no increment in the heart rate when we use a small dose of epinephrine because only large dose can stimulate β_1 receptors [7]. The improvement in heart rate after 60 min. of subcutaneous epinephrine may be attributed to the improvement in the clinical condition of the patient and relief of the distressing factors and not to the direct effect of subcutaneous epinephrine. Salbutamol stimulates β_1 adrenoceptors in the heart; therefore, increase the heart rate and also stimulates β_2 adrenoceptors resulting in relaxation of smooth muscles from the trachea to the terminal bronchial tree.

The adverse effects of salbutamol are nasal congestion increase in sputum production, dyspnea, and some vasodilating effect on peripheral vasculature (which decreases diastolic blood pressure), all decrease the O2 saturation (V/Q mismatching) [7]. Eighty seven percent of patients treated with subcutaneous epinephrine are discharged well from E.D; compared with seventy six percent of patients treated with salbutamol Neb. One patient (1%) develops central cyanosis after nebulized salbutamol. Two of four randomized clinical trials in the E.D setting using 1 to 3 doses of subcutaneous epinephrine have found a difference in admission rate [12, 16] and two have not [17, 18].

Conclusion

1. Single dose of epinephrine (0.01mg/kg) has been used across various age groups of 2 years or less (maximum dose used was 0.15 mg) and no complications were reported suggesting that the dose is safe; however the maximum safe dose cannot be interpreted from this study.
2. The response to subcutaneous epinephrine in patients younger than 12 months was significantly better than in older patients, indirectly suggesting a useful role of subcutaneous epinephrine in bronchiolitis in this age.
3. Subcutaneous epinephrine relieves clinical manifestations of respiratory distress (wheezing, chest retractions, flaring of ala nasi, cyanosis) and improves parameters of respiratory distress (oxygen saturation, respiratory rate) in infants treated for acute bronchiolitis with maximal effectiveness at 30-60 minute.
4. For subcutaneous epinephrine, every patient had his own disposable syringe; while for nebulized salbutamol, all patients share the same nebulizer. So that, subcutaneous epinephrine may decrease the likelihood of transmission of infection between the patients.
5. Subcutaneous epinephrine reduces the admission rate (13%), compared to nebulized salbutamol (24%).
6. The observation that peak action of subcutaneous epinephrine occurs 30-60 minutes after administration suggests the need for caution in repetitive administration during this period.

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