The Relation Between Oxygen Therapy Duration and Free Radical Generation In Infants With bronchiolitis

R.M.Hannun, A.G.Al- Goubori*, M.A.AL-Equabi*
Department of Chemistry ,College of Science ,University of Thi-Qar .
***Department of Chemistry ,College of Education**
Ibn AL-Haitham , University of Baghdad

Abstract

Oxygen therapy (OT) is considered an essential process for survival for the infants with bronchiolitis > However, it may reach the status of being harmful when using it for along beriod . We , here, attempted to shed a light on relations between oxygen therapy duration(OTD) and each of serum malondialdehyde (MDA) that is used as index for free radical generation , and serum albumin level , in infants with bronchiolitis . Our results confirmed that (OTD) from (1-48) hr. was non effective , while from 49 was very effective where a grave in crease in serum (MDA)level and a decrease in serum albumin concentration were observed during that time . The relation between age and serum albumin level proved that (OTD)plays an important role as a pathogenitic factor in infants aged (1-3)months

Introduction

Acute bronchiolitis is a common disease of the lower respiratory tract of infants(1) .Usually it results from inflammatory obstruction of the small airways . In general , approximately 50% of cases of bronchiolitis are caused by respiratory synsytial virus, para influenza virus , mycoplasma, some adenoviruses, and occasionally other viruses produce most of the remaining cases (2) .However , there is no Firm evidence that bacteria cause bronchiolitis (1).

It is well known that this disease occurs during the first two years of life . The disease causes, to a greater extent , the hospitalization of in fants . After a few hours of the onset of the

disease the infant is fighting for his breath and therefore is nursed in a tent with adequate oxygen (2).

Several studies have shown that the prolonged exposure to environmental toxins or oxygen usually leads to generation of oxygen free radicals (3,4,5,). In general , the latter have an important role in thedevelopment of most diseases such as the respiratory disease (6). It is known that these oxygen free radicals attack the tissues of the organelle to cause cell injury and tissue damage in the site of inflammation (3) . Normally , the respiratory tract lining produces fluid which incorporates many defense mechanisms against oxidative damage and toxic effects of oxygen free radicals , by a well balanced mechanism of extracellular and intracellular defense system (7,8).This fluid contains low molecular weight antioxidant such as ascorbic acid , glutathione , uric acid , and albumin (8)

It is notable that oxygen therapy can be considered an important exogenous source of oxygen free radicals(9). Usually, the increase in generation of free radicals associates with a decrease in antioxidant system contents (7) . In plasma , hypoproteinemia is always observed in patients with respiratory diseases (10). This ,indeed, is due to the fact that most plasma protein types have active antioxidant functions such as albumin, transferring , and ceruloplasmin (10). Consequently ,oxygen therapy can be regarded as a major pathogenetic factor (9).Besides the previonsly mentioned , the immaturity of infant respiratory tract may also be an important pathogenitic factor (11)

From such a serious situation , it is an essential task of the present research to study oxygen therapy and its interactions with generation of free radicals , development of disease , antioxidant system ,and age

Selection of Subjects :The study was conducted in Maternity and Children Hospital in Nassyriah City during the period from January 5,2000 to April 20,2000. Forty –nine (49) infants (2-18months) were included in this study .

They have been classified in to four groups as the following :

- **Control group**: Included fourteen (14) healthy infants , so that the normal control values for all measured parameters were obtained from them .

-**A group**: In cluded ten (10) infants suffering from bronchiolitis without oxygen therapy supplementation.

- **B group:** Included eleven (11) infants suffering from bronchiolitis with oxygen therapy supplementation from 1to 48 hours.

-C group: Included fourteen (14) infants suffering from bronchiolitis with oxygen therapy supplementation from 49 hours and on

It is notable that the clinical and characteristics data (age, sex , oxygen therapy duration , and chest x-ray)for all studied groups , were shown in Table (1)

Collection of Blood Samples : (4ml) of blood have been withdrawn from the study subjects at 10 a.m this with drawing process was jagular vien by experienced nurses . The blood then transferred into a disposable tube that did not contain (EDTA)and centrifuged (750xg,10min) within 15min . after collection , the produced serum stored at -20 C° , unless used at work directly.

Methods

Malondialdehyde (MDA)was measured as an index of lipid peroxidation according to the method of Fong et al., 1973(12). MDA reacts with thiobarbuturic acid (TBA) toproduce a colored complex MDA $(TBA)_2$ which has the best absorbance at 532nm.

As for albumin , it was measured by a dye-binding procedure which is based on a shift in the absorption maximum of the dye when bound to albumin (13) .(Albumin kit supplied by Randox Laboratories ,England).

Statistical Analysis: Data presented werethe means and standard deviations. Analysis of students –*t*-test also made to compare between the studied groups and each others, where appropriated to test the significance of differences of means among all studied groups . Value of less than $p < 0.05$ was considered significant .Correlation coefficient (r) values was used to evaluate the relation between duration of oxygen therapy and each of MDA and albumin levels .

Results

Table (2)shows a significant elevation in serum MDA levels in both A and B groups (110%, 123%) compared to control group .

While there are no significant variations in serum MDA levels between A and B groups can be observed. Also serum MDA levels are found to be elevated significantly in C group "duration of oxygen therapy is higher than 48hr" compared to both A and B groups, and control group .

A signigicant decrease can be observed in serum albumin levels in all patient groups compared to control groups (5.4-13%) as shouwn in table (3) .However, serum albumin level in C group is found to be significantly decreased compared to both A and B groups .While no significant variation is observed between A and B groups .

Table (4) illustrates the correlation relationships between the duration of oxygen therapy , and each of serum MDA and Albumin levels (r) values show that serum MDA levels in creased with increasing duration of oxygen therapy. While serum albumin level decreased with increasing duration of oxygen therapy . Fig.(1) shows the relationship between albumin levels and patient ages . The figure has shown the grave decrease in serum albumin levels in the first three months of life of infants . However , the decreases are stable in the sixth and tenth months of age.

Discussion

Bronchiolitis can be taken as one of the inflammatory diseases . It results from infection of the respiratory tract with viruses and bacteria (2). Through such dicases the phagocytes are activated by the immune complexes and complement to perform their function in killing the bacteria and other organisms (14).If is known that these phagocytes kill bacteria by production of superoxide radical O_2 by a known mechanism (14) . The superoxide radical , in turn , undergoes further reactions to form toxic derivatives such as hydrogen peroxide (H_2O_2) , hydroxyl radical (OH) and hypochlorous acid (15), which are then used by the cell to destroy ingested organisms (14).

Through acute inflammation of bronchioles, the immune complexes usually activate the polymorphonuclear leucocyte that consumes oxygen according to the above mechanism. This process is of high rate (100-fold compared to the normal case) when oxygen is presented in high amount (14) . Accordingly , oxygen therapy use increases the rate of oxygen consumption by polymorphonuclear leucocytes. Consequently , further oxygen free radicals production takes place .

In general , oxygen toxicity plays an important role in the development of acute and chronic respiratory diseases in infants (16). A characteristic pathophysiological finding in these diseases is the pulmonary eodema. The tight junctions of the alveolar capillary

membrane show increased permeability and fluid and protein leak into the alveolar space (11,17).

Indeed when oxygen free radicals are formed , they immediately , attack the pathogensis to kill them (14) . However, these free radicals can also attack the normal cell in the site of inflammation to cause the oxidative damage of the cell contents such as membrane lipid, proteins, and DNA strand, leading to cell damage and tissue injury (14). Consequently , the use of oxygen theraby in high concentration increases the lipid peroxidation which causes an elevation in serum MDA levels. On the other hand , immaturity of the alveolar capillary membrane in infants is a fact (11), and according to the above mechanism , attack of the oxygen free radicals to the alveolar capillary membrane increases its permeability resulting in plasma protein leakage in the alveolar space (11). This, in general , explains the observed elevation in serum MDA level and the decrease in serum albumin concentration in our studied patients with the increase in oxygen therapy duration .

Besides the above, albumin concentration decrease may be due to the fact that the albumin contributes to the chain breaking antioxidant capacity of plasma (18). In this respect considerable studies have shown that the low albumin level associates, in a greater extent , with adecrease in total peroxy radical (ROO)trapping capacity of serum (19,20). Moreover, albumin prevents formation of "free" hydroxyl radical by binding with free copper that participates as a catalyst in the reaction of OH radical production (21).

Our results , in fig.(1) , illustrate the impact of age on the development of the disease in infants This is quite conspicuously shown through the grave decrease in serum albumin levels in the first three months of life of infants . In fact , the immaturity of lung in infants and newborn plays an important role as a pathogenetic factor , in the development of the disease Consequently , oxygen free radical can attack the alveolar capillary membrane increasing the permeability of this membrane easily and instantly . This leads to leakage of plasma protein in the alveolar space leading to development of the disease during a short time.

Conclusions

Oxygen therapy can play an important role in the development of bronchiolitis in infants, simply by increasing the generation of

oxygen free radicals . The greatest importance during the first three months of the life of infants . Moreover , the effective duration of oxygen therapy occurs after 48hr . Serum albumin antioxidant capacity decreases by increasing the oxygen therapy duration .

Acknowledgements

Iwould like to thank Dr. Wafa FAL-Taie who provided me with her scientific advice. Thanks are also due to the personnel of Children and Maternity Hospital in Nassyria City for their support and help . Iwould also like to thank Mr. Raa'id Dakhil for his help in evaluating the research linguistically .

References

1.Chilmonezyk , B.A.;Salmun, L.M. and Megathlin , K.N.(1993) N.Engl. J.Med.,328: 1665.

2.Behrman, R.E. Kiegman , R.M. and Jenson , H.B.(2000) Nelson textbook of pediatrics. 16th ed., Academic Press ., London.

3.Bitterman , P.B.;Rennard , S.I., H unninghake , G.W.and Crystal , R.G.(1982)J.Clin. Invest.,70:806

4.Bitterman, P.B.; Adelberg, S. and Crystal, R.G.(1983)J. Clin. Invest .,72: 1801.

5. Davis , G.S.(1986)Chest 89:1665.

6.Dalal,N.S.;Shi, X. and Vallyathan , V.(1990) J.Toxical. Environ . Health., 29: 307.

7.Babior ,B.M.(1984)Blood .,64:959.

8. Fridovich, I.and Freeman ,B.(1986)Annu.Res Physiol 48:693

9. Inder,T.E.; Graham , P.; Sanderson, K.and Taylor, B.J.(1994) Arch. Dis . Child. 70(1):107.

10. Gutteridge, J.M.C.and Quinlan , G.J.(1993)Biochem. BIOPHYS. Acta, 1156:144.

11.Berger, H.M.;Moison , R.M.W.and Van Zocren-Grobben , D.(1994) J.R.Coll. Physicians Lond .,28:24

12.Fong, K.L.; McCay ,P.B.and Poyer, J.L.(1973) J.Biol. Che., 248:7792.

13.Doumas,B.T.;Watson, W.A.and Biggs, H.G.(1971) Clin. Chem.Acta.,31:87.

14.Laurence, A. and Boxer, (1986)Proceedings of the Nutrition Society .,45:333.

15. Bendich, A.(1990)Adv. Exp.Med. Biol., 262:1.
16. Frank, L.and Sosenko, I.R.S. (1987)J.Pediatr.,110:9.
17. Jefferies,A.L.;Coates, G.and O'Brodovich, H.(1984) N.Engl.J.Med.,311:1075
18. Halliwell,B.(1988) Biochem Pharmcol 37:569
19.Lindeman ,J.H.N.;Lentjes, E.Q.and Berger,H.M.(1995)J.Pareuter. Enteral .Nutr.,19:373
20.Moison,R.M.; Adrian, A ;Haasnoot,D. and Howard, M.(1998)Rad.Biol.Med.,25:321
21.Halliwell,B.(1978)Febs Lett., 92:321

Table(1):The Clinical and Characteristics Data For All Studied Groups

Groups	N	Sex Males Females	Age(Months)	Chest x- ray	Duration of oxygen therapy(n)
Control	14	6	7.5±2.3	(-)	-
A	10	5	8.2±3.1	(+)	-
B	11	4 7	6.3±3.3	(+)	35+12
C	14	5 9	6.5±3.5	(+)	67+20

Table(2):Serum MDA Levels In All Studied Groups

Group	n	MDA(nmol/L
Control	14	18.2±2.1
A	10	38.3±3.4*
B	11	40.7±3.2*
C	14	65.5±5.2**

Table(3):Serum Albumin levels In All Studied Groups

Group	n	A
Control		38.3±o.7
A		36.2±0.3*
B		35.05±0.5*
C		33.3±0.7**

Table (4):Correlation Coefficients For The Relations Between Oxygen Therapy Duration and Each Of Serum (MDA)andAlbumin Levels

Parameters	Groups	
	B	C
MDA	0.45	0.81*
Albumin	-0.62	-0.91*

***P<0.5Compared with control.**

****P<0.05Compared with control and*.**

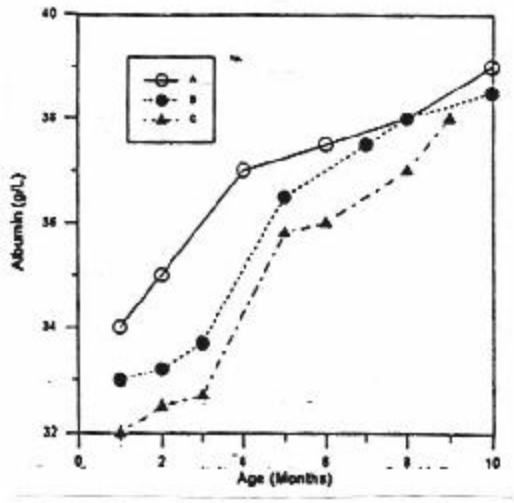

Fig.(1): The relation between age and serum albumin levels in all patient groups

العلاقة بين مدة العلاج بالاوكسجين وتوليد الجذور الحرة في الرضع المصابين بمرض التهاب القصيبات الهوائية

رائد معلك حنون ، علياء غازي الجبوري* ، منتهى عباس العقابي*
قسم الكيمياء، كلية العلوم ، جامعة ذي قار
*قسم الكيمياء ، كلية التربية أبن الهيثم ،جامعة بغداد

الخلاصة

يعتبر العلاج بالأوكسجين عملية ضرورية جدا للبقاء على قيد الحياة للرضع المصابين بمرض التهاب القصيبات الهوائية ، الا انه يصل الى حد يجعله ضارا عندما يستخدم لمدة طويلة . حاولنا في هذا البحث تسليط الضوء على العلاقات بين مدة العلاج بالأوكسجين (OTD) وكل من المالون داي الدهايد (MDA) الذي يستخدم كدليل عن توليد الجذور الحرة ، والالبومين ، في مصل دم الرضع المصابين بهذا المرض.

أثبتت نتائجنا ان (OTD) من (1–48) ساعة غير مؤثرة بينما أدى استخدام الاوكسجين لاكثر من 49 ساعة الى تزايد مضطرد في مستوى (MDA) في مصل الدم وتناقص في تركيز الالبومين في مصل الدم ، اثبتت العلاقة بين العمر والالبومين ان مدة العلاج بالاوكسجين يمكن ان تلعب دورا مهما كمسبب مرضي في الرضع الذين تتراوح اعمارهم بين 1–3 اشهر .