MY CONTRIBUTION TO MEDICAL SCIENCE

DR. K.K. MATHEW

MY CONTRIBUTION TO MEDICAL SCIENCE

Dr. K.K. MATHEW

Published by:

International Chavara Cancer Research Institute
Nedumangad, Thiruvananthapuram, Kerala.

MY CONTRIBUTION TO MEDICAL SCIENCE

Dr. K.K. Mathew

First Impression
May 2016

ISBN: 978-81-922116-3-3

Layout & Printing:

Good Shepherd Press
Good Shepherd Complex,
Good Shepherd Street
Kottayam-686001
Tel: 0481-2569180
Mob: 944777 9180

Typesetting

Sreedevam Graphics
Kayamkulam

Published by:

International Chavara Cancer Research Institute
Christ Hills, Panavoor P.O., Nedumangad,
Thiruvananthapuram, Kerala, India.
Ph: +91471 2310269/63, +91472 2814044, Fax: 2310634

Contents

Publisher's Desk **7**

Preface **9**

Treatment of Asthma with Alkaloids of *Tylophora-Indica*- a double blind study **13**
My research work for the post graduate studies at Maulana Azad Medical College, New Delhi; did the work at Vallabhai Patel Chest Institute, in Delhi.

Metronidazole in Primary Cholangitis **31**
Work done in 1980; working as chief Physican at St. Thomas Mission Hospital, Kattanam.

Radiological Pulmonary Opacities and Shock **37**
Study conducted on thirteen patients suffering from an interesting type of preumonia which is found in Kerala.

Micrococcus Ureae Bacteremia and Hypouraemia **47**
Study of blood infection by a very rare type of bacteria named Micrococcus Ureae.

Effect of Micrococcus Ureae on blood urea level **51**

Metronidazole in Endometriois **59**

Imipramine in persistent vomiting **63**
The patient, daughter of a former govt. secretary was treated at a major medical college and at a super speciality hospital without relief and had to stop her college studies because of persistent vomiting.

Persistent Vomiting **67**
Three patients of persistent vomiting of long duration responded very well to the drug imipramine

Essential Thrombocythaemia 71
Study done in 1984. Part of the study was done in the Department of Haematology, Coney Island Hospital, Brooklyn, New York. Two consultant doctors working there are co-authors.

Acquired Hyper High-Density Liproproteinemia 75

Alfacalcidol in Cervical Spondylosis - A clinical study 79
study of seventy five patients suffering from Cervical Spondylosis, treated with Alfacaleidol

Life after Death 89

Healing of the Soul 93
concept derived from clinical observations of forty two years.

FROM THE PUBLISHER'S DESK

We feel privileged and honoured to publish the book **My Contribution To Medical Science** written by Dr. K.K. Mathew. This book compiles the original research papers of Mathew, published mainly in national medical journals; and most of them are the first of their kind in medical science. The clinical observations of Dr. K.K. Mathew were quoted in prestigious international medical journals and were appreciated by reputed experts in western countries.

The clinical observations made by Dr. K.K. Mathew, thirty years ago were found to be identical with the observations made by the researchers of the most reputed centres in western countries.

Dr. B. Umadethan, former principal of Govt. Medical College, Trivandrum and Director of Medical Education, Kerala in a recently published article in **Keralasabdam** (10 April 2016, Book 54, Issue 35) evaluates Dr. Mathew's contributions to the field of medical science and elaborates the different circumstances which have paved the way for such wonderful findings. Mathew is not only an expert medical practitioner, but also an excellent researcher. He is also a writer of eminence whose wide range of publications, twenty five of them, includes poems, novels, short stories and essays.

This book a collection of Dr. Mathew's research papers, is also a compendium of Mathew's ideas about spirituality as medical cure which he has mastered and practised, some consciously, some unconsciously.

We believe that these essays can be read with profit by both professional biologists and medical practitioners.

Dr. K.K. Mathew is a reputed physician and scientist. His scientific observations have attracted attention and approval at the international level. He is the recipient of many awards for outstanding service. Dr. Mathew is a noted poet in English. His main works are:

- **To My Love and To My Sorrow**
- **Jasmine and Mourning of a Soul**
- **Light in Darkness**
- **Poetry My Soul**
- **Heaven on Earth**
- **The Voyage**
- **The Selected Shorter Poems of Dr. K.K. Mathew**, edited by Dr. John E. Abraham.

Dr. Mathew is a noted novelist, story writer, spiritual thinker and orator. His novels are:

- **Ente Sakhi, Tata, Neelaganthikal, Darshanam, Anarkham** and **Nere**.

His writings include collection of stories

- **Mazha Deyvangal, Aramindriyam**
- **Treatises Kurishinte Thanalil**
- **Athmavinte Snehagita**
- **Spiritual Medicine a Doctor's Confession**
- **Doctor's Witness to the Mystery of God**
- **Mind and Peace, Healing of the Soul**
- **Love Beyond the Stars**
- **Yesuvil Athma Sakshalkaram**
- **Manasantharathile Rasapravarthanangal**
- **His Marks on Me**

The two books published on Dr. K.K. Mathew :

1) ***Biography*** - '**Kripaude Sangeetham**' by Rev. Dr. Mathew Daniel.

(2) Study, review and criticism on shorter poems, '**World within the World**' by Dr. Nibu Thomson (Editor)

PREFACE

This book is a collection of my research papers, the result of my studies, clinical observations and experiments conducted in the last forty two years. These are original and authentic; and most of them are the first of their kind. These are my contribution to medical science.

All the research tasks, except the first one, were done in a rural area in Kerala where no proper facilities for a proper research work are available. The place has no specialised research facilities for any advanced studies.

I have some physical impediments too. In 1946, when I was a one year old child, I was stricken by poliomyelitis, and in 1983 developed post polio Syndrome, a complication of poliomyelitis, which has almost paralysed me, and my mobility is limited now. Within these drawbacks I have worked hard, for I never allow failure to be part of my life. I admire and have great regard for Stephen Hawking because I find a lot of parallels between us. I have set a goal in my life 'citus, altius and fortius' and for my unending will is set to 'strive, to seek, to find and not to yield.'

The first research paper was the results of the work done in 1973 when I was doing M.D. at Maulana Azad Medical College, New Delhi. It proved that alkaloids of Tylophora Indica is effective in the treatment of Asthmatic Bronchitis. It was quoted in 'Thorax' a British Medcial journal. In 1983, I found that Metronidazole is effective in the treatment of the dreadful disease primary cholangitis. It won international recognition when my findings were corroborated by Tabiban and team of Mayo Clinic in the US. In 2002, I proved that a combination of Aspirin and

Hydroxy Urea is effective in the treatment of the horrible disease, Essential Thrombocythaemia.

In 1985, I found out a new concept 'The Healing of the Soul' which recognizes the importance of spirituality in the treatment of ailments, that have been written off by doctors as hopeless and incurable. The mind governs the expression of the disease.

I think this age of rapid development has created more problems than it has solved. In this context I believe that we should owe our fair share of responsiblity and sincerely think about the ways by which we can solve these present maladies that confront humanity today. We must show determination and courage and not lose hope and benevolence.

I am a person who is guided entirely by Jesus Christ. Jesus lives in me and it is He who works in me. It is purely by intuition from Him, I could do great things in treatment of patients, in the field of research (innovative field), in literary composition and in spiritual work. The whole credit of my achievement goes to Jesus Christ as I am only an instrument in His hands. This book is a witness to Christ.

I am thankful to my friend Dr. John E. Abraham for his valuable suggestions. I express my deep gratitude to Mr. K.A. Abraham, the Executive Director of International Chavara Cancer Research Institute, Nedumangad, Thiruvananthapuram for undertaking the arduous task of publication of this book.

Dr. K.K. Mathew
Kayamkulam
Tel: 0479 - 2445976
14-02-2016
Email: drkkmathew@gmail.com

To
My Grand sons
Aaron, Abel and Yohan

Treatment of Asthma with Alkaloids of *Tylophora - Indica* A Double Blind Study

K.K. Mathew & D.N. Shivpuri

Tylophora indica is a tropical creeper (climber) of family Asclepidaceae. Its extraordinary therapeutic properties of providing prolonged relief in symptoms in a significant number of asthmatics have already been reported by us1-3.

The results of two double-blind studies in 305 asthmatics with 6 days treatment of one leaf of *Tylophora indica* daily, or its equivalent alcoholic extract 40 mg. daily have shown a new significant feature2,3.

At the end of one week, not only 50-100 percent relief in symptoms was seen in 56 to 62 percent patients of the *Tylophora* groups as compared with 28 to 31 percent patients of the placebo groups in different double-blind studies, but during the follow-up period of 12 weeks, the difference between the *Tylophora* and placebo groups increased and was highly significant upto 8 weeks and was just below the significance level at 12 weeks, although no *Tylophora* or *placebo* was administered after the 6th day.

The therapeutic efficacy of this plant was also assessed by its ability to inhibit experimentally induced attacks of asthma in different groups of patients, during their symptom-free period4'5.

In the first such study on 31 symptom-free asthmatics, who received one leaf of *Tylophora indica* daily for 6 days only, there was significant protection or increase in bronchial tolerance (ranging from 46 to 100%) to the repeat identical inhalation challenge in 71 percent of these asthmatics. There was no protection in controls4.

In another similar study on 31 symptom-free asthmatics, who received 30 mg. of alcoholic extract of leaves of *Tylophora indica,* three times a day for six days, 58 percent showed protection ranging from 31 to 100 percent to repeat identical challenge5.

In the third study on 24 symptom-free asthmatics, who received in a closed nebulizer-spirometer circuit, 2 minutes aerosol treatment by inhalation with alkaloids of *Tylophora indica,* three times a day for six days, 62 percent showed protection

ranging from 36 to 100 percent to an identical repeat challenge5.

This paper reports the results of double blind trial with oral administration of alkaloids of *Tylophora indica* in the treatment of 123 symptomatic asthmatics.

Methods and Material

The total alkaloids of Tylophora indica were extracted in our Laboratories from shade dried leaves of the plant by standard techniques. The dose of the alkaioids used was 0.5 mg in 0.5 gm glucose prepared as follows : The alkoloids was mixed well and triturated for one hour, in pestle and mortar in bulk, so as to make 500 doses. The placebo was prepared by adding a few drops of juice of fresh spinach leaves to glucose and mixed well in a pestle and mortar in a similar way so that both powders looked alike. After the Statistician, had given them code names, the powders were distributed in small packets of the same colour containing 0.5 gm of the material, by the non-clinical staff and handed over to the Health Visitor-Technician for issuing them to the patients as per table of randomization prepared by the Statistician.

One hundred twenty three patients who were getting symptoms of asthma either daily or several times a week for the past few weeks and were known from the past history to suffer from symptoms for several subsequent months were included in this study. They were selected on the basis of history of recurrent paroxysmal attacks of breathlessness with ronchi in the chest relieved by bronchodilators. They had either family history of allergy or associated allergic rhinitis. Care was taken to exclude patients with other broncho-pulmonary disorders like chronic bronchitis with or without emphysema, tropical eosinophilia, bronchial carcinoma and heart disease etc by history, physical examination routine laboratory tests and x-ray of the chest. Patients with an acute respiratory tract infection or exacerbation of infection or those who were steroid-dependent, were not included in'this study.

Administration of Code Drugs

According to the randomisation table, the patients were alloted to C or D group. Those in C group were given C powder, those in D group were given D powder. Each patient was advised to take one packet of coded powder daily at about 6 a.m. for six days. They were asked to put the powder on the tongue let it mix with saliva for a short while and then swallow it with about half an ounce of water. They were then advised to take rest in bed for an hour or two and not to take any meal for at least two hours Thereafter they could have a breakfast of milk or fruit juice or tea. The other meals were not to contain fried or heavily seasoned food. .

Follow up Study

Patients were examined daily during the first 10 days and their progress was assessed every week thereafter. A 12 week follow up study was done. Their daily proforma showing the duration of symptoms in minutes or hours and need based consumption of prescribed drugs for each 24 hours was examined and entered into physician's assessment card kept for each case. In addition, the results of examination of chest and pulmonary functions like peak expiratory flow rate (PEFR) and *FEVl* daily for the first six days, then on every visit of the patient once a week for two weeks; and thereafter PEFR at two weeks interval and FEV10 at four weeks interval were also recorded.

Methods of Assessment

Shivpuri's scoring system6 was employed for the presence and duration of symptoms and for the amount of prescribed medicines used only when needed, during each 24 hours. Patients were trained in the very beginning by giving them instructions and demonstration as how to record on the proforma very briefly every 24 hours, the duration of the daily symptoms in minutes or hours and the amount of drugs used, to relieve those symptoms. They were supplied a printed proforma on which they

were to enter the above information daily by spending about one minute each day6.

In addition, there was a physician's card for each patient for recording scores from the data of syptoms and durgs entered in patients proforma plus the scores of the amount of ronchi found on chest examination6.

Further, the actual values of pulmonary function tests like forced expirotory volume for the first second (FEV10) and peak expiratory flow rate (PEFR) were also noted at regular intervals.

Shivpuri's scoring method[6] is reproduced below :

I. Duration of Dyspnoea at rest in 24 hours = SCORES

None		0 Point
For less than ½ hour	=	1 Point
For each additional ½ hour	=	1 Point

II Need-based drug consumption in 24 hours = SCORES **(indicates severity of symptoms also)**

i. Isorprenaline (sub-lingual) 20 mg. tablet	=	1 point for each ½ Tab.
ii. E.A.P. Packet or tablet	=	3 points for each packet or tab. but
Ephedrine 30 mg Aminophylline 100 mg Phenobarbital 30 mg	=	2 points if ephedrine about 15 mg.
iii. Adrenaline S.C. 1: 1000	=	4 points for each 0.3 to 0.5ml
iv. Aminophylline I.V.	=	6 points for each 0.25 gm.

III Ronchi (the time of Abbreviation SCORES

Chest examination to be recorded)	**sign.**		
i. Chest clear on normal deep breatnmg but a few ronchi (usually sonorous) on forced expiration only.	± plus minus	=	0 point

ii. A few scattered bilateral ronchi on normal deep breathing (patient feels alright)	+ one plus	=	1 point
iii. Ronchi in between ii and iv on normal deep breathing. (Patient is not in frank attack at rest, but feels heaviness of breathing)	2+ two plus	=	2 points
iv. Innumerable high pitched bilateral ronchi on normal deep breathing (patient is in attack of varying degree)	3+ three plus	=	4 points

Equation for measuring improvement

$\frac{a - b}{a}$ X 100 = Percentage of improvement

a = is the mean of the pre-treatment base-line scores, calculated for one day from 3 to 7 days pre-treatment data.

b=is the mean of the scores calculated for one day from each week's follow-up data.

Grading of Results (Shivpuri)

Improvement as per equation.	Clinical improvement (equivalents)
96 to 100%	Complete
76 to95%	Marked
51 to 75%	Moderate
26 to 50%	Slight
16 to 25%	Insignificant
0 to 15%	None
Minus figure	Worse

Additional Precaution in Assessment7

To make certain that degree of improvement was real and significant we did dot attach much weight to improvement which was less than 50 percent and took into account only those patients (in both code groups, whether durg or placebo group) who showed 50 to 100 percent (moderate to complete) improvement during the follow-up. That makes comparison much more reliable and eliminates the effect of any unknown influences producing slight improvements in either group7.

Improvement In Ventilatory Functions

Improvement in ventilatory functions were measured separately. Serial measurements of *FEVl* and PEFR at about the same hour of day (without any drug in the previous 12 hours) is a useful method of assessing the objective response of asthmatic patients to thereapy.

Improvement of more than 20 percent in PEFR values and more than 15 percent inFEV1 values as compared to the initial values was considered significant on the basis of our previous experience with these tests.

To summarise, the patients keep a daily record in Proforma-16 of the time and the duration of each episode of symptoms as well as the quantity of each prescribed drug taken. The physician calculates the scores for the symptoms and need-based drugs used by the patient and enters the score in his assessment card (Proforma 2)6. He also enters the score of lung signs and actual values of FEV1 and PEFR along with the date and the time.

From these scores of a week, the mean was calculated for one day and the simple equation applied to obtain the percentage of improvement. After the results were graded and improvement had been tabulated under the code names of the drug and the placebo, the key of the code was then broken by the statistician to find out the actual results of the drug under trial.

Results

There were 123 asthma patients in this study. Table shows the distribution of these patients according to the type of asthma and randomization for administration of code durgs.

TABLE 1

Distribution of 123 Asthma patients in Double-Blind study with Tylophora alkaloids

Type of asthma	Tylophora	Placebo	Total
Seasonal	10	12	22
Irregular	41	42	83
Perennial	8	10	18
Total Pts.	59	64	123

During the follow-up after six days treatment with code drugs the assessmant was done by scoring method and degree of improvement was calculated by an equation already mentioned. As a further precaution to eliminate the influences of unknown factors producing slight improvement ia bronchial asthma, only improvement above 50 percent in each group was taken into account and was considered to be significant and certain7.

Table 2 shows the degree of improvement based on symptom scores in these 123 patients. It was found that at the end of first week, the number of patients who got 50 to 100 percent relief in symptoms were 57.6 percent in the *Tylophora group* against 23.5 percent in the placebo group. The respective figures for the two groups at the end of second week were 48.3 percent against 20.3 percent; at 4th week, 38.2 percent against 14.7 percent at the end of 8th week, 33.4 percent against 11.6 percent and at 12th week, 26.8 percent against 8.3 percent.

TABLE 2

Results of Double Blind Study in 123 Bronchial Asthma Patients Treated with Alkaloids of *Tylophora Indica* or Placebo

Improvement based on *symptom-scores*

Period	1st week		2nd week		4th week		8th week		12th week	
Drug	T	P	T	P	T	P	T	P	T	P
Total pts. followed	59	54	58	64	57	62	57	61	55	61
Degree of Improvement as per equation	Percent of patients showing improvement.									
96-100%	37.3	12.5	29.3	9.4	10.1	3.2	5.3	0	3.7	0
>75%	3.4	4.7	12.1	3.1	21.1	6.5	21.1	6.6	13	3.3
>50%	16.9	6.3	6.9	7.8	7	5	7	5	10.1	5
>30%	1.7	3.1	8.6	3.1	3.5	1.6	3.5	0	3.7	0
<30%***	40.7	73.4	43.1	76.6	57.9	83.9	63.1	88.5	69.1	91.8
% of pts. showing >50% improvement	57.6**	23.5	48.3**	20.3	38.2**	14.7	33.4**	11.6	26.8**	8.3

T.A. Alkaloids of *Tylophora indica* P = Placebo

**=Highly significant; ($p<0.01$);

***Less than 30 percent improvement has been shown together to save space, since only patients who experienced 50 to 100 percent improvement in the Tylophora and placebo groups are compared.

Table 3 shows the degree of improvement based on scores for need-based daily durg consumption. It was found that number

of patients who got 50 to 100 percent relief of symptoms at the end of first week were 61.3 percent in the *Tylophora* group against 23.5 percent in the placebo group. The corresponding figures at the end of second weeks, were 58.7 percent against 23.3 percent; at four weeks, 43.9 percent against 16.2 percent; at eight weeks, 38.1 percent against 11.5 percent and at twelve weeks, 32.8 percent against 9.9 percent.

TABLE 3

Results of Double Blind study in 123 Bronchial Asthma Patients Treated with Alkaloids of *Tylophora-Indica* or Placebo.

Improvement with respect to *need-based drug consumption scores*

Period	1st week		2nd week		4th week		8th week		12th week	
Drug	T	P	T	P	T	P	T	P	T	P
Total pts. followed	59	64	58	64	57	62	57	61	55	61
Degree of Improvement as per equation	Percent of patients showing improvement.									
96-100%	52.8	18.8	34.5	10.9	22.8	6.5	10.1	1.6	5.2	1.6
>75%	1.7	3.1	12.1	6.2	8.8	6.5	14	6.6	14.6	5
>50%	6.8	1.6	12.1	6.2	12.3	3.2	14	3.3	13	3.3
>30%	0	0	34	0	3.5	1.3	3.5	0	1.9	0
<30%*	39	76.6	38	76.6	62.7	82.3	58.9	88.5	65.4	90.1
% of pts. showing >50% improvement	61.3**	23.5	58.7**	23.3	43.9**	16.2	38.1**	11.5	32.8**	9.9

T.A. Alkaloids of *Tylophora indica* P = Placebo

**=Highly significant; ($p<0.01$);

*Less than 30 percent improvement has been shown together to save space, since only patients who experienced 50 to 100 percent improvement in the Tylophora and placebo groups are compared.

Table 4 shows the degree of improvement based on scores of physical signs i.e. ronchi in the chest. The number of patients who showed 50 to 100 percent improvement at the end of first week were 52.2 percent in the *Tylophora group* against 28.1 percent in the placebo group. The respective figures at the end of two weeks were 55.2 percent against 25 percent; at four weeks, 47.4 percent against 14.6 percent; at eight weeks, 36.9 percent against 11.5 percent at twelve weeks 32.6 percent 8.3 percent.

TABLE 4

Results of Double Blind Study in 123 Bronchial Asthma Patients Treated with Alkaloids of *Tylophora-indica* or Placebo

Improvement based on physical sign-scores, (ronchi)

Period	1st week		2nd week		4th week		8th week		12th week	
Drug	TA	P	TA	P	TA	P	TA	P	TA	P
Total pts. followed	59	64	58	64	57	62	57	61	55	61
Degree of Improvement as per equation	Percent of patients showing improvement.									
96-100%	47.1	17.2	50	15.6	45.6	8.1	31.6	4.9	23.5	3.3
>75%	0	0	0	0	0	0	0	0	0	0
>50%	5.1	10.9	5.2	9.4	1.8	6.5	5.3	6.6	9.1	4.9
>30%	1.7	0	0	0	1.8	0	3.5	0	1.8	0
<30%*	45.9	71.9	44.8	75	50.9	85.4	59.6	88.5	65.5	91.8

% of pts.
showing
>50%52.2**28.152.2**2547.4**14.636.9**11.532.6**8.2
improvement
T.A. Alkaloids of *Tylophora indica* P = Placebo
**=Highly significant; ($p<0.01$);

*Less than 30 percent improvement has been shown together to save space, since only patients who experienced 50 to 100 percent improvement in the Tylophora and placebo groups are compared.

Table 5 shows the degree of total improvement *computed from scores* of symptoms, need based drug consumption and physical signs. The number of patients who showed 50 to 100 percent *total clinical improvement* at the end of first week were 57.7 percent in the *Tylophora group* against 23.5 percent in the placebo group. The respective figures at the end of second week were 51.4 percent against 20.4 percent; at four weeks 41.7 percent against 14.6 percent; at eight weeks, 31.9 percent against 9.9 percent and at twelve weeks 23.7 percent against; 9.8 percent.

TABLE 5

Results of Double-Blind that with Total Alkaloids of *Tylophora Indica* on 123 Asthmatics

Period	1st week		2nd week		4th week		8th week		12th week	
Drug	TA	P	TA	P	TA	P	TA	P	TA	P
Pts. followed	59	64	58	64	57	62	57	61	55	61
Based on improvement.	Percent of patients showing 50 to 100%									
Symptom scores	57.6	23.5	48.3	20.3	38.2	14.7	33.4	11.6	26.8	8.3
Medication Scores	61.3	23.5	58.7	23.3	43.9	16.2	38.1	11.5	32.8	9.9
Ronchi Scores	52.2	28.1	55.2	25.0	47.4	14.6	36.9	11.5	32.6	8.2

Computed mean of total scores	57.7**	23.5	51.4**	20.4	41.7**	14.6	31.9**	9.9	23.7**	9.8

TA=Total Alkaloids of *T. indica 0.5* mg daily for 6 days only; P=Placebo.

**=HighIy significant (P<0.01); NS=Not significant.

Only patients who-experienced 50 to 100 percent improvement in the *Tylophora* and placebo groups are compared.

Table 6 shows the degree of improvement in pulmonary functions in the two groups during the follow up period of 12 weeks. The number of patients who showed more than 15 percent increase in FEV1 at the end of the 1st week were 34 percent in *Tylophora* group against 15 percent in placebo group. The respective figures in the two groups at the end of 4th week were 26 percent against 3.8 percent; at the end of 8th week, 22.2 percent against 3.8 percent and at the end of 12th week, 17.3 percent against 3.8 percent.

The number of patients who showed more than 20 percent increase in PEFR at the end of one week, were 64.3 percent in the *Tylophora* group against 22.4 percent in the placebo group. The respective figures in the two groups at the end of 4th week, were 46.3 percent against 10.5 percent; at the end of 8th week, 40.7 percent against 10.7 percent and at the end of 12th week, 28.8 percent against 8.9 percent.

TABLE 6

Results of pulmonary function tests in the two groups of double-blind trial *with* alkaloids of *tylophora indica* and placebo

Period	1st week		4th week		8th week		12th week	
Drug	TA	P	TA	P	TA	P	TA	P
Total Pts. followed	56	58	54	57	54	56	52	56

% of pts showing <15% increase in FEV_1	34*	15	26**	3.8	22.2**	3.8	17.3*	3.8
% of pts showing >20% increase in PEFR	64.3*	22.4	46.3*	10.5	40.7**	10.7	28.8**	8.9

TA=Total alkaloide of *Tylophora indica;* P=Placebo; FEV*=first second Forced Expiratory Volume; PEFR=*Peak Expiratory Flow Rates;*—Significant ($0.01 < P < 0.02$);**—Highly Significant ($P < 0.01$)

TABLE 7
Incidence of Temporary side effects

Side Effects	TA	Placebo
	Percent of patients who experienced one or more side effects	
Nausea	10.8	2.6
Vomiting	9.5	2.6
Soreness of mouth	1.4	0
Partial loss of taste for salt	1.4	1.3
Total % of pts showing side effects	18.9*	5.3*

TA= Alkaloids of *Tylophora Indica*

*= a few patients experienced more than one side effect.

Table 7 shows the incidence of temporary side effects like nausea, vomiting, soreness of mouth and partial loss of taste for salt. It will be seen that nausea is the most frequent side effect

occuring in about 10.8 percent of the *Tylophora* group against 2.6 percent of the placebo group. The respective figures of vomiting in the two groups were 9.5 percent against 2.6 percent. In those, where vomiting occurred, it was usually once in the day within 2 hours of taking the alkaloids and not necessarily on each subsequent days. It was prevented when necessary by giving stemetil 25 mg at bed time of the previous night. All the symptoms disappear within a day or 2 after stopping the drug, except soreness of the mouth which disappears between 3-4 days. But this is very infrequent.

Discussion

Statistical analysis of the results of this double blind trial in 123 asthma patients, showed that with respect to symptoms scores (Table 2), the difference between the two groups was highly significant ($P<0.01$) upto 8 weeks, but was just significant ($0.01<p<0.05$) at the end of 12th weeks. Similarly, with respect to need-based drug consumption scores (Table 3) and with respect to ronchi scores (Table 4), the difference in the results of two groups were highly significant for all the 12 weeks ($p<0.01$).

Table 5 presents the degree of total improvement computed from scores of Tables 2, 3 and 4. The statistical analysis of the computed mean of all the scores showed that the difference in two groups was highly significant ($p<0.01$) for the 1st, 2nd, 4th and 8th weeks, but was just short of the significance level for the 12th week. There appears to be a gradual loss of improvement after a short 6 days course of *Tylophora indica* with the passage of time.

Statistical analysis of the results of pulmonary function tests in the two groups in Table 6 show that, with respect to more than 20 percent increase in PEFR, the difference in the two groups was significant for the 1st week and highly significant for the 4th, 8th and the 12th week. Whereas, with respect to more than 15 percent increase in *FEV1* the difference between the two groups was

significant for the 1st and the 12th week and highly significant for the 4th and the 8th week.

However, in some patients, the subjective improvement in symptoms occurred earlier and was also greater than the objective improvement in FEV1. Similar lack of coordination in perennial asthma, where ventilatory functions are not fully reversible, has been reported by some other workers also8. Further we also found that improvement in PEFR values recorded during follow-up were greater than the improvement *in* FEV1 values performed at the same time in the same patients.

The results of this double blind study seem to indicate that in the total alkaloids of *Tylophora indica,* we have a new anti-asthmatic drug. When administered in small dose, for a brief period of six days, it provides prolonged relief in statistically significant number of asthma patients as judged by various parameters prescribed above. Its main draw back is that when administered by mouth, it is accompanied by some temporary side effects which are being looked into to find out whether they can be eliminated by chemical manipulation of its molecule, if possible.

Its exact mode of action is not yet known, but several experiments in our Laboratory indicate that it does not have any specific antagonistic action against histamine, acetyl-choline, 5 HT and bradykiain, although it has some effect in relaxing plain muscle and inhibiting its spontaneous contractions.9'10 It does not block antigen antibody reactions, mediated by IgE or IgG in rat11 or guinea pig,10 or antigen skin test and P.K. reactions in man.11 it is not a broncho-dilator.1'3 But it definitely relieves the symptoms for varying periods in significant number of symptomatic asthma patients as seen in this and 2 earlier double blind studies2'3 and also provides definite protection against identical inhalation challenge with specific allergens in significant number of symptom-free asthmatics.4'5 It probably acts by prolonged blocking of some, as yet, unrecognized receptors (perhaps of the afferent limb), in broncho-pulmonary tree which may be responsible for the constitutional hyper-reactivity of the respiratory tract invariably present in asthmatics.

Summary

A double blind study has been conducted by a new scoring method in 123 asthma patients with total alkaloids of *Tylophora indica.* The dose of the alkaloids was 0.5 mg in glucose once a day for six days only. Assessment of each patient initially as well as during the follow-up period of 12 weeks was done by alloting scores for each 24 hours, for duration of dyspnoea at rest, need-based consumption of prescribed drugs ; and amount of ronchi at the time of examination. The percentage of improvement was calculated by an equation from the scores for the 3 parameters prescribed above.

In addition, pulmonary function tests (FEV1and PEFR) were performed at the same hour of the day, every day for the first one week and then at regular intervals upto 12 weeks.

The statistical analysis of the computed results, based on scores of difference between the *Tylophora* and the placebo groups was highly significant not only at the end of one week but also for several weeks of the follow-up, after stopping the drug on 6th day. The results of the pulmonary function tests for all the 12 weeks were highly significant in favour of *Tylophora indica.*

Acknowledgements

The authors are grateful to Mr. J.D. Gupta for isolating the total alkaloids from the leaves of *Tylophora indica* for this study and to Dr. M.P.S. Menon for some suggestions during the course of this work.

References

1. Shivpuri, D.N.; Menon, M P.S. and Prakash, Dharm. : Preliminary studies on leaves *of Tylophora indica* in the treatment of asthma and allergic rhinitis. Jour. Assoc. Physicians India 16 : 9, 1968.
2. Shivpuri, D.N. ; Menon, M.P.S. and- Prakash, Dharam : Cross-over double blind study on leaves *of Tylophora indica* in the treatment of asthma and allergic rhinitis. Jour. Allergy 43 : 145, 1969.
3. Shivpuri, D.N. ; Singhal, S.C and Prakash, D.: Treatment of asthma with *an alcoholic extract of Tylophora indica.* A cross-over double blind study. Ana. Allergy. 30 : 407, July 1972.

4. Shivpuri, D.N. and Agarwal, M.K. : Effect *of Tylophora indica on bron-chial* tolerance to inhalation challenges with specific allergens". Ann. Allergy 31 : 87, Feb. 1973.
5. Shivpuri D.N. ; Narula, S,; Chandra Rekha and Pal, T.K. A new anti asthmatic *Ty/ophora indica* compared with Disodium Cromoglycate in 81 asthmatics (Duration of protection against induced asthma)" Presented at the VIII International Congress on Allergology Oct. 14-20, 1973, Tokyo,
6. Shivpuri, D N.: Methods in clinical research in bronchial asthma and allied conditions. Aspects of Allergy and Applied Immunology Vol. 7:15,1974..
7. Shivpuri, p.N. and Dua, K.L.: Hypo-senstization Treatment of 250 patients with bronchial asthma in India against local allergens (A 7 years follow up) Ann. Allergy 22 : 632, 1964.
8. Woolcock , A J. and Read, J.: Improvement in bronchial asthma not reflected in forced expiratory volume. Lancet 2<: 132-3j 1965;
9. Agarwal, M K. and, Shivpuri, D.N. : Preliminary studies on bronchial tolerance to histamine. and raethacholine chloride inhalation challenge before and after 6 days treatment with leaves *of Tylophora indica.* Aspects of Allergy and Applied Immurxology 5 : 62, 1971.
10. Agarwal, * M.K, ; Shivpuri, D.N.; Gupta, M. and **Ray,tG,N. :** Studi.es on the effect .of *Tylophora indica* on the responses of plain muscle to spas-mogens and on the immunologic reaction in rats and *in vitro.* Aspects of Allergy and Applied Immunology 6 :107,1973.
11. Menon, M.P.S. ; Shivpuri, D.N.; John C.J.; Prakash, D. and Gupta, J.D.: A Clinical study on the effect of *Tylophora indica* on the immunologic reactions in man. Aspects of Allergy and Applied Immunology 6: 100, 1973.
12. Shivpuri, D.N. : A new approach in the treatment of bronchial asthma with *Tylophora in^ic^* Aspects of Allergy pnd Applie4 Immunology 6; 33J, 1973.

Reference of the article
Volume 7 Aspects of Allergy and Applied immunology 1974 PP 166 - 179

This study proved scientifically that the alkaloids of the Tylophora -Indica is effective in the treatment of Bronchial Asthma. This is the first study in medical science with alkaloids of the plant Tylophora-Indica in the treatment of Brochial Asthma. Previously there were studies with the leaves and alcoholic extracts of the leaves of the plant Tylophora-Indica.

My clinical observations were quoted in many authentic international medical journals including the prestigious medical journal 'Thorax' of British Medical Journal (Thorax 2000 : 55 : 925-929)

Metronidazole in Primary Cholangitis

K.K. MATHEW

Primary cholangitis is an uncommon disease characterised by obliterative inflammatory fibrosis of the biliary tract. It can involve intrahepatic as well as extrahepatia ducts (Bartholomew etal, 1963; Russel et at., 1980). The disease generally follows a progressive course eventually leading to cirrhosis, portal hypertension and death from liver failure (Chapman etal., 1980s); Reported series of patients with primary cholangitis have been small until the advent of percutaneous and endoscopic cholangiography. The aetiology of this disease is unknown and there is no satisfactory medical treatment tor this disease.

A case of primary cholangitis presenting as progressive jaundice, treated at different hospitals and not responding to any of the medical treatment, is described here.

Case Report

Mrs. K. M, aged 32 years was admitted to St. Thomas Mission Hospital, Kattanam in April 1979 with complaints of progressive jaundice of 6 mouths duration. She also complained of severe itching all over the body, weakness and irregular fever for the last few months. She was very sick and was mentally very upset as she knew that she was having an incurable disease.

Her complaints started 6 months ago as mild fever, itching and yellowish discolouration of urine. She was admitted to a private hospital with provisional diagnosis of Infective hepatitis. As the disease was progressing she was referred to the District hospital and was investigated and treated there. Later she was referred to one of the major medical college hospitals of Kerala State with the diagnosis of obstructive jaundice. She was admitted to the Gastroenterology Department of the Medical College Hospital and was fully investigated. As the patient's condition was deteriorating in spite of having treatment with all medicines including antibiotics and corticosteroads, she was referred to the surgeon for laparotomy.

The discharge card given from the Medical College Hospital showed that the laparotomy could not give any clue for the diagnosis and there was no evidence of malignancy. The percutaneous transhepatic cholangiography done at the Medical College Hospital showed diffuse involvement of the intrahepatic biliary ducts. The right intrahepatic ducts showed dialatation while the left intrahepatic ducts showed stricture and obstruction. The liver biopsy done there was reported as "extensive cholestasis". As the patient's condition was very bad and nothing more could be offered for her she was discharged from Medical College Hospital after 3 months. The patient was again admitted to a Mission Hospital at Neyyoor in Tamil Nadu and she had treatment for a short time. At last she came to our hospital in a very critical condition.

Examination—She was febrile, toxic and deeply jaundiced, liver was palpable for about 6 cm. below the right costal margin. It was firm in consistency but was not tender. There was no intercostal enderness. Spleen was just palpable. All other systems were within normal limits.

Investigation—Blood picture showed haemoglobin level of 8 g.%, total leucocyte count-32000/c.mm. with polymorphs-67%, lymphocytes—23-%, eosinophils—10%. ESR—160 mm./ 1st hour. Liver function tests showed total serum bilirubin level 36 mg.%, serum proteins— 6 g.% with albumin—2.8 g.%, SGPT—10 units, serum alkaline phosphatase—72 King-Armstrong units. Thymol turbidily 6.6 units. Urine showed presence of bile pigment. Cholangiography and liver biopsy were not repeated as the patient was very sick.

A provisional diagnosis of primary cholangitis was made.

Management—The patient was given full dosage of Metronidazole orally 800 mg. thrice daily for 10 days with other supportive treatment.

There was a dramatic improvement in her condition. Her health showed marked improvement. The fever subsided and she developed good appetite and serum bilirubin level came down

to 10 mg.% on the 11th day of treatment. Liver also regressed by about 2 cm. and she became completely asymptomatic after 2 weeks. She was discharged from the hospital after 6 weeks and at that time her serum bilirubin level was 2.7 mg.%.

About 6 months after discharge she again started developing itching, fever and signs of mild jaundice. Again she was given a course of Metronidazole and she became symptom-free after the treatment. Since then she was perfectly all right and the follow-up studies for 2 years and 3 months did not show any rise in her serum bilirubin level. Now she is attending her routine just like any other housewife.

Discussion

In primary cholangitis all parts of the biliary tract may be involved by chronic fibrosing inflammatory process. When the smaller biliary ducts in the liver are involved this condition is called Pericholangitis (Sherlock, 1975). Inflammation of the larger major extrahepatic bile ducts is termed as Sclerosing cholangitis (Sherlock, loc. cit.),

The degree of involvement of different parts of biliary tract varies from patient to patient. Pericholangitis may be found with or without sclerosing cholangitis and the reverse. It may be impossible to define the parts affected without surgical exploration. The disease may occur alone or in association with ulcerative colitis (Warren etal., 1966; Thorpe etal, 1976).

The aetiology of this disease is unknown. There is no specific treatment for Primary cholangitis. Corticosteroids, antibiotics, immunosuppressants and cholecystogue alone or in combination have been tried but the results with all have been disappointing (Russel et al, loc, cit.).

In this particular case, the clinical history, physical findings and investigations were in favour of the diagnosis of Primary cholangitis-Pericholangitis. There was no evidence of Amoebiasis. Metronidazole was started after putting forward a postulation that the aetiology of this disease is anaerobic bacteria. The anaerobic bacteria can get entry into the portal vein from the gastro-intestinal tract producing portal tract bacteraemia and it can produce inflammation of the portal tract with proliferation

of ductules. This postulation was based on the author's experience with a similar case a few years ago which was treated successfully with metronidazole.

Summary

A case of primary cholangitis which has responded to metronidazole is presented. The theory that anaerobic infection may be the aetiology of this disease is put forward.

Acknowledgement

The author is grateful to, the Medical Superintendent St. Thomas Mission Hospital, Kattanam for her kind permission to publish this case.

References

1 BARTHOLOMEW, L.G., CAIN, J.C., WOOLNER, L.B., UTZ, D.C. AND FERRIS, D.O. - New Eng. J. Med., 269:8, 1963.

2 CHAMPAN, R. W.G., BANNAR BORGH, J.M., RHODES, JASUMMER, FIELD, DICK, R., SCHENER, P.J. AND SHERLOCK, S.-Gut, 21 : 870, 1980

3 RUSSEL, H., WIESNER, NICHOLAS AND LA RUSSO, F.- Gastroenterology, 79:200, 1980.

4 SHERLOCK, S.- Diseases of the Liver and Billiary System, 5th Ed., 1975, Blackwell, Oxford, P.657.

5 THORPE, M.E., SCHENER, P.J. AND SHERLOCK, S.-Gut, S : 433, 1976.

WARREN, K.M., ANTHIHANASSIADES. S. AND MONGE, J.-Amer. J. Surg., 111 : 23, 1966.

Reference of the article

Volume 80 No. 2 Journal of the Indian Medical Association. 1983 PP 31 - 33

This is the first article of its kind in medical science. Primary Cholangitis is a dreadful disease causing obliterative inflammatory fibrosis of the whole of the biliary tract. It is a progressive disease leading to biliary cirrhosis and liver failure. The patients having this disease live only for a short span of time varying from few months to few years.

In this scientific article, I have proved that the drug Metronidazole is effective in the treatment of Primary Cholangitis. I have put forward the theory that anaerobic infection in the gut is the cause of the disease.

Dr. Dame Sheila Sherloc, the world authority on liver diseases and the chief professor of 'The Royal Free Hospital', London has described my scientific article as 'most interesting'.

A panel of world-renowned American physicians who are the editors of the prestgious postgraduate medical book 'Harrison's Principles of Internal Medicine' appreciated my scientific observation and took it to their attention.

My scientific observation was quoted in many international medical journals. Thirty years after the publication of my article, Dr. James H. Tabibian and associates of Mayo Clinic of North America published their clinical trial with the drug Metronidazole in patients of Primary Cholangitis in the prestigious international journal 'Alimentary Pharmacology and Theraputics' and they concluded that the drug Metronidazole demonstrated efficacy in patients of primary sclerosing cholangitis.

My clinical obervation was quoted by Dr. James H. Tabibian and Associates of Mayo clinic, North America in their scientific article 'Role of Microbiota and Antibiotics in primary sclerosing Cholangitis' in the prestigious international journal Bio Med Research International (Volume 2013 - Article 1D 389537, 7 pages)

Radiological Pulmonary Opacities and Shock

K.K. MATHEW

Introduction

Shock can occur in lung infection as a complication. Shock and circulatory failure in cases of lung infection including pneumonia may occur due to toxic tissue injury and perhaps to cardiac muscle.[1] The peripheral blood vessls loose their tone, the blood pressure falls and the limbs become very cold and clammy.[2] Such patients are desperately ill.

This article deals with the clinical study of an interesting type of lung infection which we come across in Kerala. The patients affected by this disease present to the physician with a very short history of febrile illness and they develop shock very quickly. Majority of these patients are referred to the physician by the local doctors as cases of myocardial infarction with shock. This disease is more common in middle aged individuals.

Material and Methods

Thirteen patients admitted to our hospital over a period of three years with a history of short febrile illness and with radiographic pulmonary shadows and presenting clinically with shock comprise the materials of the study. Nine patients were in shock at the time of hospitalisation and four developed shock after hospitalisation. The duration of the presenting complaints was one to four days.

The radiographic pulmonary opacities of these patients taken for the study were in the form of (a) homogenous or non homogenous shadows which may appear as rounded or regular density, (b) irregular infiltrate.

The following criteria were taken in to account to diagnose shock in these patients.

(a) Hypotension (b) rapid and thready pulse (c) apathy or restlessness (d) weakness (e) pale and cold extremities (f) oliguria. All the causes of shock other than lung infection were excluded by taking detailed history and doing careful physical examination and relevant, investigations. None of the patients showed any evidence of deep vein thrombosis or phlebitis or heart disease. Special care was taken to exclude any cause for pulmonary embolism in these patients.

Observations

All these patients complained of irregular fever of one to four days duration. Seven of them had mild fever while six of them complained of high grade fever. All patients complained of cough with expectoration and the sputum in the majority of them was thick and tenacious. Two patients had mild haemoptysis. One patient complained of breathlessness.

Nine patients had chest pain and in five, pain was substernal.

TABLE. I
Age distribution of the patients

Age group	*Number* of *patients*
Above 50 years	2
Between 40 and 50 years	9
Below 40 years	2
10 were males and 3 females	

TABLE. 2
Presenting symptoms of Patients

Symptoms	*Number of Patients*
Fever	13
Chest Pain	9
Cough with expectoration	13
Breathlessness	1
Mild haemoptysis	2

Clinical Sings

Nine patients were in shock at the time of hospitalisation. Blood pressure was not recordable and the pulse was very feeble in six of them. Extremities were cold. Clinically none of the patients showed signs of dehydration. Four patients developed shock after hospitalisation. Out of thirteen patients only five showed signs of respiratory pathology. They had scattered fine crepitations heard over some parts of the chest. In others clinically, the respiratory system was within normal limits.

Investigations

Blood Examinations :- Marked leukocytosis with incresed neutrophil count was seen in all the patients. E.S.R. was raised moderately in all of them. Haemoglobin level was only 10 gm% in two patients. Blood sugar and Blood urea were within normal limits and urine analysis was normal in all patients.

TABLE. 3
W. B. C. Count of the patients

Total W. B. C, Count	*Number of patients*
Above 20 thousand/Cu mm	9
Above 15 thousand/Cu mm	2
Above 10 thousand/Cu mm	2

In all cases, the differential count showed that the neutrophil count was above 80 percent. Blood culture, sputum culture and urine culture were done before starting antibiotic therapy. But in all patients, blood culture and urine culture did not grow any pathogenic organism.

TABLE. 4
Sputum culture report of the patients

Pathogenic organisms grown	*Number of Patients*	*Antibiotics To which the organisms were sensitive*
Klebsiella Pneumoniae	5	Gentamycin, Kanamycin Streptomycin
Klebsiella Pueumoniae & Staphylococcus aureus	1	*Klebsiella :-* Gentamycin, Kanamycin Streptomycin *Staphylococcus:* Cloxacillin, Erythromycin, Gentamycin. Cephaloridine
Bordetella Para pertusis	1	Gentamyrin, Kanamycin Streptomycin Neomycin
Streptococcus pneumoniae	1	Penicillin, Septran, Ampicillin, Gentamycin.
No growth	3	

Electrocardiograph was within normal limits in all patients.

x-'ray of chest showed characterestic finding in all patients.Homogeneous shadows were seen in lungs.The shadow may appear as rounded or irregular density or irregular infiltrate.

Treatment

All patients were given intravenous fluids mainly glucose saline and electrolite maintenance solution with a close watch on the cardiac status.Majority of them were given three to five litres of fluid in the first 24 hours. All patients were given initially a combination of two antibiotics intravenously-Benzyl Penicillin in the dose of 20 lacs every six hours and Gentamycin 80 mg every eight hours.Appropriate changes in the antibiotic therapy were made when the sputum culture report was ready.The antibiotics were given for ten days. All patients were given Corticosterids intravenously for the first few days-Inj Hydrocortisone 100 mg intravenously every six hours initially and it was tapered and stopped when the blood pressure rose to normal level and the signs of shock have completely disappeared. within forty eight hours after starting the treatment.Then the administration of intravenous fluids was discontinued.None of the patients was given any vasoactive drugs to counteract shock. Repeat X-'ray of chest was taken after ten days and all patients showed complete clearing of the opacity and all of them were discharged after two weeks.Repeat sputum culture was negative in all patients at the time of discharge.

Discussion

Shock and peripheral collapse can occur in the terminal stage of serve pnenmonia[3].septic shock can occur early in some cases of staphylococcal pneumonia.[4] Except for this,majority of patients with lung infection including pneumonia, present with charcterestic clinical symptoms and radiographic signs of penmonia and shock is terminal complication. Here is an interesting combination of radiographic pnlmonary opacity and shock is presented. The differential diagnosis of these conditions are mainly two. (a) Primary lung infection - Pneumonia with bacteremic shock (b) pulmonary embolism with shock. Both conditions can present with same clinical, laboratory and radiographic findings. But the presence of pulmonary embolism can be excluded in these patients by the following reasons.

a) Absence of evidence of deep vein thrombosis or phlebitis or of heart disease in any of these patients.
b) Short history of febrile illness before the onset of shock.
c) Chest X-ray of some of the patients showed pulmonary shadows before they developed shock
d) Majority of the patients had a total W.B.C. count above 15 thousand/cu mm,
e) Sputum culture of the majority of the patients grew different pathogenic micro-organisms.
f) Theraputic response of the patients to antibiotic therapy.

Special investigations like lung scanning and pulmonary angiograpy are needed to confirm the diagnosis.[5] The early development of shock makes this condition interesting.

This may be due to the high virulence of the pathogenic micro-organism and the early liberation of endotoxin to the blood stream producing bacteremia. Bacterial endotoxin exerts its major effects on small vessels with sympathetic (alpha receptor) innervation. Although blood culture is negetive in all patients, it is quite clear that these patients had developed bacteremic shock. Bacteremia may be intermittent and blood culture may be negative. Further some of patients, may have received antimicrobial drugs before hospitalisation. A negetive blood culture does not exclude the diagnosis of bacteremic shock[4].Culture of the primary focus may be helpful but here again it may be altered because of previous therapy. Many of the patients developed chest pain probably because of the early pleural involvement.

Although the over all mortality of bacteremic shock remains 50 percent[4] we could save all patients probably because of early diagnosis of this condition and early initiation of treatment before patients developed irreversible shock. All patients responded to treatment. It is observed that the early diagnosis of this condition is very important. There should not be any delay in the initiation of treatment. Many of the patients can be mistaken in the rural hospitals as cases of ischaemic heart disease with shock. It is observed that Gentamycin is the the most effective antibiotic in

all cases and a combination of penicillin and gentamycin is the best combination of antibiotics to start treatment.

Intravenous administration of Corticosterords was also found to be effective in treatment of these patients with bacteremic shock because corticosterords can overcome the increased peripheral resistance, mitigate cellular injury evoked by endotoxins[6,7]. Although vasoactive agents like alpha receptor blocking agents or beta stimulants may be useful in the treatment of bacteremic shock[8], there was no need of administering any of these agents in our experience.

Summary

The clinical study of thirteen patients with radiographic pulmonary opacities who developed shock at a very early stage is presented. All patients showed characterestic signs in the chest X'ray and in the majority of them sputum culture grew different pathogenic bacteria. Clinical studies and investigations of these patients and their theraputic response to antibiotic therapy show that the pulmonary opacities are due to primary lung infection and subsequently they develop bacteremic shock. It is presumed that the virulence of the infecting microorganism is very high and the bacterial endotoxin is liberated to the blood stream very early, producing bacteremic shock. It is observed, that with early diagnosis and prompt treatment, this disease can be managed successfully.

Acknowledgement

I am grateful to Dr. Baben Mathai, St. Thomas Mission Hospital, Kattanam, for his suggestions.

References

1. John Grofton and Andrew Douglas: Res-piratory Diseases. Black well, scientific publications. Second edition: 128, 3, 1977.
2. Tiliostion j. R. and Lernerah: Pneumonia caused by gram negative bacilli. Medicine 45, 65, 1962.
3. AVardle N : Bacteremic and, endotoxic shock, J. appl. Med 6:373, 1980. 4 Petersdorfj R, G f Dale, D. C : Harrison's principles 6f Internal medicine", 9th edition, Mcgraw Hill Kogakusha Ltd., Tokyo P, 561, 1980.]

5. Figlay, MI M. Gerdes, A J. and Ricketts, H. J : Radiographic aspects of 'pulmonary embolism, jsen - Roentgenol 2: 389.
6. Christy J. HN: Treatment of gram negative shock. A. M. J. Med 50:77, 1971.
7. Ledingham IMGA, MC Ardle C. S : Prosp-ective study of the treatment of shock, Lancet 1, 1194, 1971.
8. V. Tarazi R.j G :, Sympathomimetic agents in the treattnent of shock, Ann Intern Med 81, 364, 594.

Reference of the article

Volume 24 No. 4 Kerala Medical Journal 1983, PP 105-108

This scientific article is the first of its kind in medical science. Since the bacterial endotoxin produced by the bacteria enters the blood stream at an early phase, these patients develop bacteremic shock very early. The pneumonic lesions are found in the hilar area of the lungs. The infection was mostly caused by the organism Klebsiella pneumoniae.

Micrococcus Ureae Bacteremia and Hypouraemia

K.K.MATHEW, A.ABRAHAM
MARIAM GEORGE

Introduction

Micrococcus urea is a member of the family micrococcaceae and can be isolated from a variety sources such as dust, air, water, soil, human and animal sources. It is a gram positive coccus, spherical or oval in shape with an average diameter of 0.8 u to 1u arranged in pairs or tetrads or octads. This organism is larger than staphylococcus and can be distinguished from staphylococcus by special tests.[2] This organism is a contaminent of urine and is a harmless commensel and saprophyte. It very rarely causes opportunist infection. [3]

Case Report

Mr. G. K., 52 years old male was admitted to the hosptial on 22. 9. '82 with complaints of sudden episode of restlessness, profuse sweating and change in sensorium of few hours duration. He was a known case of diabetes mellitus and rheumatoid arthritis and was on ayurvedic treatment for joint pain for sometime.

Physical Examination showed that he was febrile, disoriented and dehydrated. He was sweating profusely and his extremities were cold. His pulse and B. P. were normal. Systemic examination did not show any other positive finding.

Investigations

On admission, blood examination showed that his Hb was 10.5gm% Total WBC count was 66000 / cumm DLC was Neutrophils 94%, Lymphocytes 4%, Eosiniphils I%, Basophils I%. ESR was 115mm/1st hour. His blood urea was 5mg% (repeat estimations also confirmed the same value). Serum creatinine was 2 mg%. Random blood sugar was 251 mg%[s] Liver function tests showed, serum protein 6gm%, albumin 4gm% Globulin 2gm%: S. G. P. T. 24 units; serum alkaline phosphatase 11 KA

units; serum bilirubin - 0.8mg%. C. S. F. study showed Total cells - 4 lymphocytes / cumm; Protein 30mg%; Glucose-60 mg%; Chloride 730 mg%, Urine analysis showed presence of glucose (+). urine microscopy was normal. E. C. G. and chest X'ray were within normal limits. Urine and sptum culture did not grow any pathogenic organism.

Blood culture report showed heavy growth of the organism micrococcus ureae which was sensitive to Gentamycin, Amoxycillin and Aerosporine. Repeat blood culture also grew the same organism. Gram staining from the colonies revealed large gram positive cocci arranged in tetrads and octads and pairs. The biochemical tests done on it confirmed the identification of the organism micrococcus ureae.

Patient was given I. V. fluids, 20% mannitol and soluble insulin. Antibiotic therapy was started by a combination of two antibiotics -Injection Crystalline penicillin 20 Lacs IV Q6H and Injection Gentamycin 80 mg IV Q8H. patient regained consciousness within 12 hours. When the blood culture and sensitivity report was ready, Injection Crystalline Pencillin was stopped and Amoxycilline was given orally in the dose of 500mg Q8H. The antibiotics were continued till the blood culture report became normal. Patient had tremendous clinical improvement and he was discharged from the hospital after one month. It was an interesting thing to note that the blood urea level started rising gradually during the course of treatment and at the time of discharge his blood urea was 18 mg%; Serum creatinine was 0.9 mg%; Total WBC count was 8000 / cu mm.

Discussion

In this patient we could not find out any other cause other than micrococcus ureae, bacteremia as the cause of hypouraemia. His dietary habit has been good before. His liver function tests including serum proteins were within normal limits. Micrococcus ureae can very rarely cause bacteremia in man and can affect internal organs[4]. The production of an enzyme urease is characterestic of this cocus. The biochemical test namely urease;

test is considered to be a confirmatory test for Micrococcus ureae, It is. based on the principle that the bacteria growing naturally in an environment exposed to urine may decompose urea by means of the enzyme urease to Ammonium carbonate[5]. Although we do not come accross any report of hypouraemia in cases of bacteremia by the organism Micrococcus ureae, it is believed that the organism in the blood stream thrives on the blood urea and breaks down the blood urea in to Ammonium carbonate. Hence the blood urea level registers a sharp fall. The blood urea level rises when the infection is being controlled. The Ammonium carbonate probably volatalises, resulting in the patient feeling cold,

Summary

A rare case of bacteremia by the organism Micrococcus ureae is presented. It was found that the blood urea of the patient was very low and serum creatinine was high. Patient responded remarkably to treatment and it was seen that when the infection was fully controlled the blood urea rose to normal level. It is presumed that the organism micrococcus ureae decomposes blood urea to Ammonium carbonate and causes hypouraemia.

References

1 Bird, Parker A. C; The basis for the present classification of staphylococcus and.micro-coccus. Ann. N.Y.A cad sei 1974. 236 : 7-14

2. Recommendation, Sub committee on toxonomy of Staphylococci and micrococcL' Int, Bull, Bad, Nomenclat, Taxon 1965. 15 : 109-110.

3. William, D.N; Lud M. E and Blazevie D.J; Significance, of urinary isolates of coagulase negative micrococcaeae. J. clin microbiol 1976: 3:'556-559.

4. Baily and Scott's Diagonostic microbiology; sydney M Finegold, william J. martin, Elvyn G Scott, fifth edition, The, C.V. Mosby company, 1978, P. 128.

5. Grand Wohls clinical Laboratory methods and diagnosis. 1976. vol. II P. 1891.

Reference of the article
Volume 24 No. 5 Kerala Medical Journal 1983,
PP 147-148

Effect of *Micrococcus ureae* on blood urea level

K.K.MATHEW, MARIAM GEORGE

Abstract

This is an in vitro study to observe the effect of the bacteria Micrococcus urea on blood urea level. When this organism was tested against pure urea solutions the strengths of the solutions were reduced. The control samples did not show any change. The same procedure when repeated with human blood samples collected at random showed marked reduction in the blood urea levels while control samples did not show any change. This proves that Micrococcus urea is capable of breaking down blood urea.

Introduction

Micrococcus urea is a gram positive coccus arranged in pairs or tetrads or octads and it is a member of the family

Table 1

S.No	mg %	OD before inoculation	OD after inoculation	Urea level in mg %
1	10	0.03	0.00	0
2	20	0.06	0.00	0
3	30	0.10	0.05	17
4	40	0.13	0.07	23
5	50	0.17	0.11	33
6	60	0.20	0.15	45
7	70	0.22	0.17	50
8	80	0.26	0.20	60
9	90	0.30	0.22	70
10	100	0.34	0.22	70
11 Control	100	0.34	(uninoculated) 0.34	100

Micrococcaceae.[1] It is a harmless commensal and a saprophyte.[2] It is usually a contaminant of urine and can rarely cause infection in man with lowered resistance.[2,3] The present study was carried out to observe whether this organism is capable of lowering blood urea levels in vitro. It is known that Micrococcus urea can split urea to Ammonium carbonate in vitro by means of an enzyme Urease.[4,5]

There is a report on the effect of this microorganism on blood urea level.[6]

Materials *and* Methods

Venous blood was aseptically drawn from a patient of Micrococcus urea bacteremia and immediately inoculated into sterile brain heart infusions and bile broth containers. These were first incubated at 37°C for 24 hours. The plates revealed a heavy uniform type of growth on blood agar plate. All routine identification studies of the morphology and staining characters, colony characters and biochemical reactions of the growth confirmed that the organism was Micrococcus urea.

Table 2

S.No	OD before inoculation	mg % Urea	OD after inoculation	Urea level in mg %
1	0.02	60	0.11	33
2	0.08	25	0.03	10
3	0.29	93	0.02	60
4	0.05	17	0.00	0
5	0.13	40	0.07	23
6	0.15	45	0.08	25
7	0.02	60	0.13	40
8	0.32	95	0.22	70
9 Control	0.29	93	0.29	93

The present study was divided into 4 stages

Stage I

The isolate obtained from the blood culture of the patient was kept at room temperature. The culture was checked for purity and then it was subcultured on nutrient agar. The growth was harvested and washed in sterile normal saline to free the coccus from the nutrients. The deposit obtained after centrifuging was suspended in sterile nutrient broth containing 0.5% glucose and 0.1% urea and incubated at 37 C for 24 hours.

Stage II

25ml. of culture form Stage I was removed and centrifuged to obtain the cells and it was suspended in just enough sterile saline to obtain a clear opalescent fluid to be used in the next stage.

Stage III

(A) Setting up of a standard solution of urea

l00mg of pure analytical grade urea was dissolved in 100ml sterile distilled water. From the solution other standards were prepared to contain varying amounts of urea. These solutions were treated within the standard method of blood urea estimation to determine the optical densities of the solutions. The solution strengths and corresponding optical densities (OD) were tabulated and recorded. Each set of standards was treated with the inoculum (0.2ml) and incubated at 37 C for 24 hours. The next day, blood urea estimation was repeated to obtain a new set of OD values and were recorded. The urea level was read off from the standard curve. Table -1 shows the result of this stage.

(B) Treatment of unknown strength solution of urea with inoculum

A series of urea containing unknown amounts of urea were treated the same way as in A. The urea levels prior to and after inoculation with the cocci were obtained from the standard curve. Results recorded are given in Table 2.

Table 3

S.No	OD before inoculation	mg % Urea	OD after inoculation	Urea level in mg %
1	0.07	23	0.04	1 3
2	0.07	23	0.04	1 3
3	0.06	20	0.02	6
4	0.06	20	0.02	6
5	0.06	20	0.03	10
6	0.08	25	0.05	17
7	0.06	20	0.02	6
8	0.05	17	0.01	3
9	0.08	25	0.03	10
10	0.08	25	0.05	17
	Control (Uninoculated)			
2	0.07	23	0.07	23
6	0.08	25	0.07	23
7	0.06	20	0.06	20

Stage IV

Blood samples of 10 persons were obtained by venous puncture. The anticoagulant used was E.D.T.A. Urea levels of these blood samples were determined. The blood samples were inoculated with 0.2ml of the inoculum and then were incubated. Following incubation the urea levels were again determined. Results were tabulated and are given in Table-3.

Control samples

Before the samples were inoculated with the bacteria a few samples were selected at random and a small quantity (0.5ml) was siphoned off to serve as control. These were not inoculated. All the control and test samples were incubated under identical conditions. The result of the controls were also tabulated. See Table - 3.

Results

The results of the study are recorded in the Tables.

Discussion

It is obvious from Table - 1 that the inoculum used has brought about a significant reduction in the urea levels of standard solution. The control showed no change in the urea level. It is also evident that in the levels above a certain range the rate of break down decreased, probably because the total number of cells involved were not sufficient to cope with the excess urea.

It is clear from Table - 2 that the urea level of unknown strength solution was reduced by the bacteria following their inoculation and incubation. The control showed no change in the level.

Table -3 also shows that the urea levels after inoculation and incubation with the organism showed a marked reduction. It is interesting to note that while most of the samples tested prior to inoculation showed a normal value range, the same samples were reduced in their urea content after treatment with the inoculum. The control samples however, did not show any significant change in their blood urea level. This proves that Micrococcus urea is capable of breaking down blood urea.

Acknowledgements

The authors are grateful to Dr. A. Abraham for his help.

References

1. Bird, Parker AC: The basis for the present classification of Staphylo-coccus and Micrococcus'. Ann. A.Y.A. Cadsei; 1974, 236: 7-14.
2. Recommendation, Sub-committee on taxonomy of Staphylococci and Micrococcf. Int. bull, Bad, Nomenclat, Taxon; 1965; 12:1, 109-110.
3. William, DN Lud ME and Blaze vie DJ: Significance or Urinary isolates of Coagulase negative micro-coccacae'. J. Clin microbiol; 1976, 3: 556-559.
4. Baily and Scott: *Diagnostic microbiology* 5th Edn.; Sydney: The C.V. Mosby Company; 1978; 129.
5. *Wohls clir\ical laboratory methods and diagriosis;* Grand vvohls clinical Laboratory; 1976, 2: 1891.
6. Mathew KK, Abraham A, Mariam George: *Micrococcus urea bacteremia and hypouraemia[1]. Kerala Medical Journal; 1983; 50:147-148.

Reference of the article

Volume 38 No. 5 Kerala Medical Journal 1996, PP 18-20

These scientific articles are the first of their kind in medical science.

I could prove by in-vivo and in-vitro studies that the bacteria Micrococcus ureae can lower blood urea level drastically. It is found out that the bacteria produces an enzyme named urease which in turn decomposes blood urea in to Ammonium Carbonate and water. This results in marked decrease of blood urea level.

The editors of the prestigious postgraduate medical book, 'Harrison's Principles of Internal Medicine' have given their appreciation to my clinical observation.

Metronidazole in Endometriosis

K.K. MATHEW

Endometriosis is a condition where there is the presence of ectopic endometrium outside its normal location namely, lining of the cavity of the uterine body.[1] Two cases of endometriosis which responded to metronidazole are presented here.

Case Reports

Case No. 1

Indira, an unmarried lady aged 32 years, complained of severe lower abdominal pain, irregular bleeding per vagina and dysmenorrhoea since the past 3 years. She was investigated at Medical College Hospital and laparoscopic examination done there confirmed that she had Endometriosis of uterus and right ovary. She was advised to have hysterectomy.

Clinical examination showed presence of pallor and bimanual examination showed a tender retroverted uterus. The utero-sacral ligaments and pouch of douglas felt thickened. Routine examination of blood showed - Hb 10 gm%, ESR 40 mm/1st hour and total count 10200/cumm with P *65%* L 30% E 5%. Urine analysis was normal.

Treatment

Patient was given tab Metrogyl 400 mg thrice daily for 10 days.

She had a dramatic clinical improvement. Her abdominal pain and bleeding subsided completely. She had marked relief of dysmenorrhoea. The follow-up study for two years showed marked relief of all her symptoms.

Case No. 2

Ambily, aged 30 years, complained of severe abdominal pain and dysmenorrhoea since the past 4 years. She was married for 10 years and was treated for primary sterility at Medical College Hospital. Laparoscopic examination done there showed

endometriotic bullous lesions on the posterior surface of the uterus. She did not get any relief of her symptoms with the treatment given to her.

Bimanual examination showed a tender fixed retroverted uterus. Multiple small nodules were palpable through the posterior fornix. The routine investigations of blood and urine were within normal limits.

Treatment

Patient was given tab Metrogyl 400 mg thrice daily for 10 days.

She had marked relief of her abdominal pain and dysmenorrhoea subsided. About 8 months after treatment she started complaining of severe abdominal pain again. She was again given a course of Metronidazole and the abdominal pain subsided. The follow-up study for one year showed marked relief of her abdominal pain and dysmenorrhoea.

Discussion

There is no specific treatment for Endometriosis. Danazol suspension and Leuprorelin acetate depot are reported to be effective in the treatment of Endometriosis.[2,3] Here Metronidazole is found to be effective in controlling bleeding and to relieve abdominal pain. The role of anaerobic bacteria in the pathogenesis of Endometriosis is to be investigated. Metronidazole can be tried to relieve the symptoms of endometriosis.

References

1. Thomas EJ: 'Endometriosis, 1995 - confusion or *sense?'IntJGynaecol-Obstet48(2):* 149-55, 1995.
2. Sidorov IS, Guriev TD: 'Danazol in the treatment of endometriosis'. *Ter-Arkh* 66(10): 55-7, 1994.
3. Schinder AE *et al:* Treatment of endometriosis with the GnRh agonist leuprorelin acetate depot'. *Zentraalbl-Gynakol* 116(12): 679-86, 1994.

Reference of the article

Volume 38 No. 1 Kerala Medical Journal 1997, PP 4

I could prove that the drug Metronidazole is effective to relieve the symptoms of Endometriosis especially the abdominal pain.

After the publication of this article, I could treat few more patients with Endometriosis with this drug. They also got relief of pain for few months. When they got recurrance of the symptoms, I repeated a full course of the drug and they got relief again for few more months. In one patient, it was found, there is a reduction in the size of the cysts in the ovaries after taking a course of the drug.

I could not continue my studies because I am a Physician, not a Gynaecologist. I could reveal the 'root' to the medical community for further studies.

Imipramine in persistent vomiting

K.K. MATHEW

A 21 -year-old female presented with persistent vomiting for last 3 years. She had all the investigations done including gastroscopy but there was no abnormality detected. She was tried earlier with medicines prescribed in a medical college or a private nursing home. The cause of vomiting was thought of psychogenic. She was advised imipramine 25mg thrice daily and responded to the treatment favourably.

[J Indian Med Assoc 2006; 104: 641]

Key words: **Nausea, vomiting, psychological, imipramine.**

Persistent vomiting, a problem in clinical practice, does not give any clinical clue for the diagnosis and the treatment fails. In case of persistent vomiting, in the absence of any clinical or psychological abnormality, a detailed psychological scanning is indicated[1]. Imipramine can be tried in cases of persistent vomiting where there is no clinical abnormality detected. Here one case of persistent vomiting treated at different hospitals without any relief, responded to imipramine, is presented.

Case Report

(Miss) SS, a 21-year-old college student presented with persistent vomiting, loss of appetite and loss of weight since the past 3 years. She used to get continuous vomiting approximately fifteen days a month. The vomiting was projectile in nature. The vomiting started as soon as she took meal or just after it was completed. She was investigated in the department of Gastroenterology of a medical college hospital in Kerala. All the investigations including Gastroscopy done were reported to be normal.

She was investigated again in the department of Gastroenterology of a private nursing home. No abnormality was detected there also. She did not get any relief of vomiting with any of the drugs administered at both the centres. A detailed psychiatry consultation done elsewhere also could not help her. The vomiting continued during the three years. She became very weak and depressed.

Examination — The patient was sound, mentally. She had marked reduction of weight. Clinical examination did not show any abnormality. All systems were normal. As she was fully investigated twice before, none of the investigations was done again.

Management- With the probable diagnosis of psychogenic vomiting, she was put on tablet Imipramine 25 mg thrice daily and advised to continue.

Follow-up — There was marked improvement in her condition and the vomiting stopped completely. The follow-up studies for one year was uneventful. She is completely healthy now. She has gained 8 kg of weight in one year. She still takes the drug in the same dosage. Special caution was taken not to administer any of the drugs which will interact with Imipramine during the treatment and the follow-up period. During the follow-up period routine haematological examinations were done repeatedly. They were within normal limits. Electrocardiography was done repeatedly. All were normal. Liver function tests along with phosphatase, blood urea and serum creatinine levels were all within normal limits.

Discussion

Three cases of persistent vomiting which responded to imipramine was reported by the author earlier[2]. Psychogenic vomiting is a clinical syndrome in which psychosocial factors interact to produce symptoms of vomiting which may be mistaken for organic disorders[3]. The characterestic clinical features are repeated vomiting which typically occurs soon after meal has

begun or just after is completed. The illness is usually chronic[4]. Anorexia nervosa and Bulimia may be associated with vomiting and weight loss. The antidepressant effect of Imipramine is important to alleviate the symptom.

References

1 Nampoothiry KMJ — Depression in disguise. *Kerala Med J* 2001; 42: 8.
2 Mathew KK — Persistent vomiting. *Kerala MedJ* 2000; 4t:10.
3 Ahuja N, Ahuja S — A Short Book of Psychiatry. 4th ed. New Delhi: Jaypee Brothers, 1999; 137.
4 Friedman LS, Isselbacher KJ — Nausea, vomiting and indigestion. In: Fauci AS, Braunwald E, Isselbacher KJ, Wilson JD, Martin JB, Kasper DL, *et* a/, editors. Harrison's Priciples of Internal Medicine. Vol 1.14th ed. New York: McGraw-Hill, 1998:230-6.

Reference of the article
Volume 104 No. 11 Journal of the
Indian Medical Association 2006, PP 10

I could prove that the drug Imipramine is effective in the treatment of a special type of persistent vomiting which does not respond to any medicine. This is the second article of this type, published in medical literature.

My clinical observation was quoted in many international publications. One of them is Journal of the Formosan Medical Association (2011, 110(1):62-66)

Dr.Kurt.J.Isselbacher,world renowned Gastroenterologist and Distinguished Mallickrodt Professor of medicine of Harvard Medical School,has approved my observations.

Persistent Vomiting

K.K. MATHEW

Abstract

Three cases of persistent vomiting, which responded to imipramine, are presented.

Introduction

Persistent vomiting is a problem in clinical practice. Sometimes investigations do not give any clue and treatment fails. Three cases of persistent vomiting treated at different hospitals are presented here.

Case Report

Case 1

This 64 years old married female complained of persistent vomiting since the past 3 weeks. She was investigated and treated as inpatient in the department of Gastroenterology of a private Nursing Home for the past two weeks. All investigations including Gastroscopy done there were reported to be normal. Since the patient did not get any relief with treatment, she was referred to the Medical college Hospital . But she preferred to come to this centre.

Patient complained of vomiting immediately after ingestion of food. Clinical examination was normal, she did not show any sign of dehydration or weight loss. She was mentally sound and had no psychological problems.

Case 2

A 35 years old married male complained of persistent vomiting for the past 4 years. He was treated at different hospitals without any relief. Investigations done there were reported to be normal.

He was clinically normal and did not have any psychogenic problem.

Case 3

A 32 years old married male who is a Gulf returnee, complained of continuous vomiting for the past 2 years. He was investigated and treated at Gulf. All investigations done there were reported to be normal. But vomiting did not stop. Hence he returned home for treatment. Clinical examination did not show any abnormality. He did not have any psychological background.

Treatment

These patients were administered with Imipramine 25mg thrice daily. All of them showed dramatic improvement and vomiting stopped. These patients are taking Imipramine daily and are perfectly well now.

Discussion

Psychogenic vomiting is a clinical syndrome in which psychosocial factors interact to produce symptoms of vomiting which are mistaken for upper Gastrointestinal tract disease, Anorexia nervosa, Dissociative (conversion) disorder, somatisation disorder or malingnany. The characteristic clinical features are repeated vomiting which typically occurs soon after meal has begun or just after it is completed. Vomiting often occurs in complete absence of nausea or retching. Despite repeated vomiting, the weight loss is not significant. The course of illness is usually chronic.

References :-

1. Ahuja N, ahuja S. A short Textbook of Psy-chiatry, 4th edition. New Delhi, jayee Broth-ers publication 1999; 137
2. Lawrence S, Isselbacher KJ Nausea, Vom-iting and Indigestion. In (Eds) Fuci As, Braun Wald. E. and Isselbacher KJ. Hanison's principles of internal Medicine. 14th edition. New York. Mc-Grow Hill. 1998 1:231.

Reference of the article

Volume 41 No. 4 Kerala Medical Journal 2000, P 10

Essential Thrombocythaemia

K.K.MATHEW, FERNANDEZ,
CHITHRA SHENOY

A case of essential thrombocythaemia which responded to aspirin and hydroxyurea is presented.

Key words : Essential thrombocythaemia, aspirin, hydroxyurea.

Essential thrombocythaemia is characterised by abnormal proliferation of megakaryocytes. This disorder is rare, most frequently seen in persons in middle adult life and affects men and women with equal frequency[1]. Marked increase in megakaryocyte number, total megakaryocyte mass and mean megakaryocyte volume are characteristic[2]. Platelet production may be increased even up to 15 times[3].

Case Report

Mrs RM aged 78 years presented in 1984 with elevation of platelet count noticed since December,1983. Significant past history included episodes of blue toes 3 years and one year ago.

Examination — Physical examination was unremarkable . There was no enlargement of liver, spleen or lymph nodes. Peripheral pulses were present and were normal.

Investigations — Blood counts were as follows: Haemoglobin 12 g%, RBC 4.32 x 10^6cmm, MCV 82fl, reticulocytes 1.4% , platelets 783,000/cmm and monocyte 10%. Platelet anisocytosis and giant platelets were noticed in peripheral blood. Subsequent work up revealed Leukocyte alkaline phosphatase 77 u/l vitamin B_{12} binding capacity 1099 ng/l, serum B_{12} 627 *ng/l* and folic acid 13 ug/l, platelets aggregation studies with ADP, epinephrine and collagen were within normal limits. The method of study was platelet factor 3 availability assay (PF3availability). No spontaneous aggregation was noted . Liver and spleen scans did not reveal any hepato-splenomegay

Bone marrow biopsy showed areas of hyper cellularity but fat cells were preserved. All series were represented. Numerous

bizarre megakaryocytes, isolated and in clusters, were present. There was also one fair large nest of lymphocyte. The reticulin stain showed small focal areas of increased reticulin.These findings were consistent with essential thrombocythaemia.

Management—- Treatment was started with aspirin 325 mg daily to prevent platelet aggregation. Enteric coated aspirin was used as the patient gave a history of gastric intolerance to regular aspirin. The patient was also put on hydroxyurea 1 g per day. Aspirin was continued at the same dosage. Patient was seen at 2 weekly interval. After 7 weeks of therapy with aspirin and hydroxyurea, platelet count decreased to 285,000/cmm

. WBC count at this time was 4100/cmm. At this point hydroxyurea and aspirin were discontinued. Four weeks later the platelet count increased to 576,000/cmm.

Hydroxyurea was restarted at a dose of 500 mg per day along with aspirin 325mg per day. This regime was continued for 8 weeks; Her platelet count decreased to 220,000 then discountinued temporarily.

Follow-up The patient had generally felt well throughout the follow-up period. She did not develop any complication. She was not administered any drug during the last 4 years as her platelet count remained within normal limits throughout this period .

Discussion

The diagnosis of essential thrombocythaemia was made based on the observations of increased platelet count, giant platelet form on peripheral blood, history of blue toes in the past, the bone marrow biopsy finding and the feature of platelet count to return to normalcy in the absence of overt infection, malignancy or bleeding. Radioactive phosphorus- and alkylating agents such as melphalan, busulfan[4] and antimitotic drugs[5] have been used in thrombocythaemia. In the present case, it is found that a combination of aspirin and hydroxyurea was effective.

References

1 Gunz FW—~ Hemorrhagic thrombocythemia: a critical review. Blood 1960; 15:706-23.
2 Harker LA, Finch CA —Thrombokinetics in man. J clin invest 1969; 48:963-74.
3 Fountain JR, Losowsky MS Haemorrhagic thrombocythaemia and its treatment with radioactive phosphorus. *QJM*1961; 31:207-20.
4 Bensinger TA, Logue GL, Bundles RW—Hemorrhagic mrornbocythemia; control of postsplenectomy thrombocytosis with melphalan. Blood1970;36:61-9.
5 Killmann SA, Cronkite EP —Treatment of polycythemia vera wilh myleran. *Am J Med Sci* 1961; 241:218-24.

Reference of the article

Volume 10 No. 4 Journal of the Indian Medical Association 2002, PP 24

In this scientific article, we could prove that a combination of the drugs Aspirin and Hydroxy Urea is effective in the treatment of the dreadful disease Essential Thrombocythaemia. There are previous reports that Aspirin and Hydroxy Urea are effective in the treatment of Essential Thrombocythemia.

In Essential Thrombocythemia there is an abnormal multiplication of thrombocytes leading to thrombosis in different blood vessels, even in those supplying the internal organs of the body.

Acquired Hyper High-Density Lipoproteinemia

K.K. MATHEW

Abstract
A case of Acquired Hyper High-Density Lipoproteinemia is presented. The regular use of sesame oil for cooking is perceived to be the reason for this effect. Hyper High-Density Lipoproteinemia is a very rare condition.

Case report

In March 2003, a seventy year old lady withCoronary Artery Disease, treated at a different centre during the year 2002 came to this centre for treatment. She did not have any complaints. Physical examination did not show any positive finding. Investigations - Lipid profile : Total Cholesterol - 198 mg%, HDL - 60 mg%, LDL - 65 mg%, Serum triglyceride - 110 mg%, VLDL - 24 mg%. Haemogram including serum protein, serum bilirubin, serum alkaline phosphatase, SGPT, serum uric acid, Thyroid function test and Urine analysis were within normal limits. Electrocardiogram was normal. Treadmill test was negative for inducible ischaemia. Treatment - she was advised to continue Amlodipine 5 mg daily, Aspirin 75 mg daily and Atorvastatin 10 mg daily which she was taking regularly. It was revealed that she was using sesame oil for cooking in the past one month. Serum HDL level of her children, brothers and sisters were within normal limits.

Periodic check-up showed that her serum HDL level started rising and within one year it reached 115 mg%. From the year 2004 her HDL level was in between 105 mg% and 115 mg% and she became stable.

Discussion

This case appears to be a case of Acquired Hyper High-Density Lipoproteinemia because her serum HDL was within normal limits initially. The patient, a widow was staying alone and her relatives staying at far off places did not use sesame oil. The beginning of the rise of her serum HDL level coincides with the beginning of her consuming sesame oil in the year 2003. Hence one is justified to assume that the regular consumption

of the sesame oil is the cause of the abnormal rise in serum HDL level. There is no report to substantiate it. Sesame oil is extracted from sesame (Sesamum Indicum L) seeds. It is a rich source of antioxidants, linoleic acid, vitamin E, A, B1, B2, minerals including calcium, phosphorous and iron. It contains 13% of saturated fatty acid, 41% of mono unsaturated fatty acid, 45% of polyunsaturated fatty acid and 1% of omega 3 poly unsaturated fatty acid. It is reported that regular consumption of sesame oil can lead to drop in serum cholesterol and reduction in blood clots. The antioxidants in sesame oil namely sesaminol and sesamolinol protect fat from being oxidized. Sesaminol maintains the serum LDL level in an unoxidised state1. It is felt that sesaminol and sesamolinol cause the abnormal rise in HDL level. This postulation needs further studies.HDL particulars are thought to participate in the reverse transport of free cholesterol from peripheral tissues by HDL receptor. Ornam and coworkers report that APO A-I and A-II interact with this receptor2. This receptor mediated reverse transport could explain why patients with elevated HDL are less prone to coronary Artery Disease. There is a genetic condition associated with markedly high plasma levels of High-Density Lipoprotein (plasma HDL Cholesterol levels >100mg/dl). These patients have Cholesteryl Ester Transfer Protein deficiency. This is due to decreased HDL catabolism of Apo A-I and Apo A-II. Decreased HDL catabolism was reported in patients treated with a CETP inhibitor. There is another condition called Familial alphalipoproteinemia. A single unique kindred has been identified with markedly increased HDL and Apo A-I but normal Apo A-II levels. This proband was healthy and the kindred was consistent with longevity; however the number of kindred members was too small to make a definite conclusion. The markedly increased HDL in this proband was due to selective increase in synthesis of Apo A-I with normal Apo A-II production3. There is a report that Hyper High-Density Lipoproteinemia potentiated by prednisolone therapy is associated with Nephrotic Syndrome4. Alpha - adrenergic blockers such as prazosin may raise serum HDL level. Oestrogen tends to raise serum HDL while reducing serum LDL level.

Patients with Hepatic Lipase deficiency may also have increased serum HDL level and decreased catabolism5.

Conclusion

This case illustrates a progressive and marked rise in serum HDL - Cholesterol levels in an elderly lady from baseline levels over a period of a year with a possibility of sesame oil contributing to this phenomenon. Further studies are needed to assess the biochemical effects of sesame oil on lipid metabolism.

References :

1. Dhoon SS, Tripathy A.K. Sesame in nutrition therapy and health care: Indian Council of agricultural project on Sesame and Niger. 2003;6.
2. Oram JF, Brinton EA and Bierman EL. Regulation of High- Density Lipoprotein receptor activity in human fibroblasts and human arterial smooth muscles. J. Clin. Invest 1983; 72 : 1611
3. Rader DJ, Schaefer JR, Lohse P, etal. Increased production of apolipoprotein A-1 associated with elevated plasma levels of High - Density Lipoproteins, apo lipoprotein and lipoprotein A-1 in a patient with familial hyperalpha lipoproteinemia. Metabolism. 1993; 42: 1429-1434.
4. Saski J, Haraf etal. Nephrotic Syndrome associated with hyper High-Density Lipoproteinemia potentiated by prednisolone therapy. Nephron 1985; 41 : 110-113. 5. Rue IL, Coutier P, Cohn JS. Evidence that Hepatic Lipase deficiency in humans is not associated with proatherogenic changes in HDL composition and metabolism. J. Lipid Res. 2004; 45:1528-1537.

Reference of the article

Volume 5 No. 1 Kerala Heart Journal, PP 48-49

There is no medicine available at present which can raise the good cholesterol, the H.D.L. to an abnormal level. Many drugs were introduced but none got past the trial phase because of the side effects. An effective medicine without major side effects to increase HDL is a great boon to reduce cholesterol related diseases like Coronary Artery Disease, Cerebral Thrombosis etc. In this context my clinical observation that the use of sesame oil daily in cooking, can raise HDL level to an abnormal level, is an important one. I introduced a new condition named 'Acquired Hyper High-Density Liproproteinemia', for the first time, where the serum HDL rises to an abnormally high level resulting in much relief in the Coronary Artery Disease. This observation opens the door for further studies like clinical trials and biochemical studies and it can become a break-through in the treatment of Coronary Artery Disease. This scientific article is the first of its kind in medical science.

Alfacalcidol in Cervical Spondylosis - A Clinical Study

K.K. MATHEW

Abstract

The study is designed to evaluate the efficacy of the drug alfacalcidol in the treatment of cervical spondylosis. Seventy-five patients of cervical spondylosis were administered orally with 0.5 μg of alfacalcidol daily (capsule form) for a period of 12 months. It was observed that 81.3% of the patients were relieved of neck pain from the second month of the administration of the drug. Forty percent of patients who had brachial neuralgia got relief of neuritic pain, 36.4% having vertebrobasilar insufficiency had relief of vertigo, 37.3% of patients showed radiological regression of the osteophyte formation of cervical vertebrae, 12 months after the administration of the drug. Of the 30 patients randomly selected for bone densitometry test, majority showed significant improvement in T values, 9 months after the administration of the drug.

Keywords: Alfacalcidol, cervical spondylosis, osteophytes, osteopenia, osteoporosis, bone densitometry test.

Cervical spondylosis is a degenerative disease of cervical vertebrae, namely osteophytosis.[1] It is a progressive degenerative disorder usually seen in aging cervical spines.[2,3] It is a non inflammatory disc degeneration. This study is designed to evaluate the efficacy of the drug alfacalcidol in relieving the clinical symptoms of cervical spondylosis and to observe whether the drug produces any regression of the osteophyte formation of the diseased cervical vertebrae and to evaluate whether there is any improvement in the bone densitometry test score after the administration of the drug.

Material and Methods

Seventy-five patients of cervical spondylosis were selected based on the following criteria: (a) pain in neck especially on movement, (b) referred pain (if any), (c) neck muscle spasm (if any), (d) limitationof movements (if any) and (e) pathological changes seen in cervical vertebrae radiologically-mainly osteophyte formation; narrowing of disc space; thinning of vertebral body and narrowing of the foramen.3,4 The distribution of the patients based on age, sex and complications are shown in Table 1. All patients were administered alfacalcidol 0.5 μg daily orally in the capsule form for a period of 12 months. X-rays of cervical vertebrae were taken before the administration of the drug and were repeated after a period of 12 months. Bone densitometry tests were done in randomly selected 30 patients before treatment and were repeated 9 months after the administration of the drug. Although the study was completed in 12 months, all patients were advised to continue treatment throughout their life. Statistical evaluation was performed using IBM SPSS Statistics 20.0. For all the continuous variables, the results are given in mean ± standard deviation. To compare the means of continuous parameters between related sets of observations (following normal distribution), a paired *t*-test was performed. For all the categorical variables, the results are given in percentages. Pearson's correlation coefficient was computed between T values (before and after). Probability value (p value) is d"0.05 was considered for statistical significance. All tests of statistical significance were twotailed. The post-treatment clinical status of all 75 patients were observed for 3 months after the completion of the treatment for 12 months.

Table 1. Distribution of the patients	
Variable	**No. (%)**
Gender	
Male	31 (41.3)
Female	44 (58.7)
Total	**75**
Age (years)	
<40	8 (10.7)
40-50	15 (20.0)
50-60	40 (53.3)
>60	12 (16.0)
Total	**75**
Complications	
Brachial neuralgia	25 (33.3)
Vertigo due to VBI	11 (14.7)
Total	**75**

VBI = Vertebrobasilar insufficiency

OBSERVATIONS

Observations are shown in Tables 2-5 and Figures 1-4. Sixty One patients out of 75 (81.3%) got relief of neck in from the second month of the administration of the drug. Seven out of

Table 2. Percentage distribution of patients having relief from the corresponding condition and improvement of clinical sign after treatment		
Condition	**No. (%)**	**Total**
Neck pain	61 (81.3)	75
Referred pain	7 (70.0)	10
Neck spasm	3 (50.0)	6
Limitation of movements	Nil (0)	8
Brachial neuralgia	10 (40.0)	25
Vertigo due to VBI	4 (36.4)	11
Tenderness in neck Absence	2 (40.0)	5

Table 3. Percentage distribution of patients having reduction in pathological conditions (radiologically) after treatment

Condition	No. (%)	Total
Reduction in osteophyte formation	28 (37.3)	75
Reduction in narrowing of disc space	Nil (0)	15
Reduction in thinning of vertebral body	Nil (0)	8
Reduction in narrowing of foramen	Nil (0)	4

Table 4 (Paired *t*-test in used)

Variable	No.	Mean	SD	P Value
T value (Before)	30	-2.052	1.325	
T value (After)	30	-1.577	1.295	<0.001*

*The mean reduction in T values before and after the treatment is found to be statistically highly significant. Pearson's correlation coefficient between T values before and after is 0.948 ($p < 0.001$).

Table 5.

T value (Before)	T value (After) Osteoporosis No. (%)	Osteopenia No. (%)	Normal No. (%)	Total No. (%)
Osteoporosis	7 (63.6)	4 (36.4)	0 (0.0)	11 (36.7)
Osteopenia	1 (6.2)	9 (56.2)	6 (37.5)	16 (53.3)
Normal	0 (0.0)	0 (0.0)	3 (100.0)	3 (10.0)
Total	**8 (26.7)**	**13 (43.3)**	**9 (30.0)**	**30**

McNemar-Bowker test ($p = 0.020$).

10 patients (70%) who had referred pain were relieved of pain, three out of six patients (50%) having neck spasm had relief of spasm, none of the eight patients (0%) having limitation of neck movement got any relief, 10 out of 25 patients (40%) having brachial neuralgia got relief of the neuritic pain, four out of 11 patients (36.4%) having vertebrobasilar insufficiency (VBI) had relief of vertigo, two out of five patients (40%) having tenderness in neck had absence of tenderness, 12 months after the administration of the drug.

Twenty eight out of 75 patients (37.3%) showed reduction in osteophyte formation in vertebrae (Figs. 1 and 2), while there was no radiological improvement in any of the 15 patients having narrowing of disc space, eight patients having thinning of vertebral body and four patients having narrowing of foramen, 12 months after treatment.

In 30 patients randomly selected for the bone densitometry test, 11 (36.7%) had osteoporosis (T score below -2.5), 16 (53.3%) had osteopenia (T score between -1.1 and -2.5) and three (10%) had normal T value (score up to -1).

The average T value in 30 patients before treatment was -2.052 and it was -1.577, 9 months after treatment. It was observed that the number of patients having osteoporosis decreased from 11 to 8 (36.7% to 26.7%), the number of patients having osteopenia decreased from 16 to 13 (53.3% to 43.3%) and the number of patients with normal.

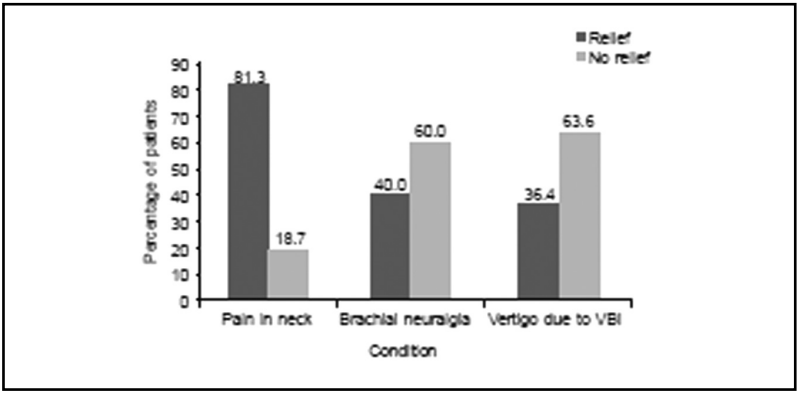

Figure 1.

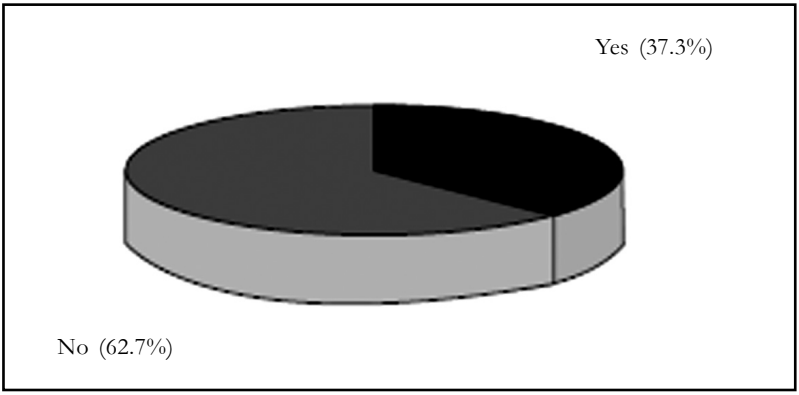

Figure 2. Percentage distribution of patients having reduction in osteophyte formation.

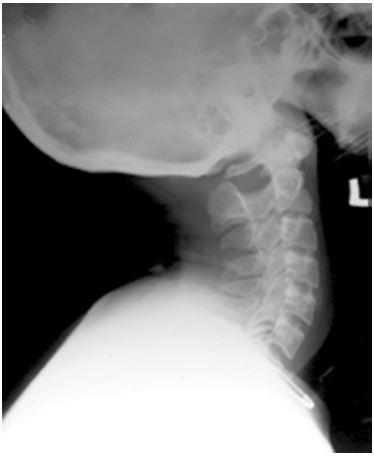

Figure 3.

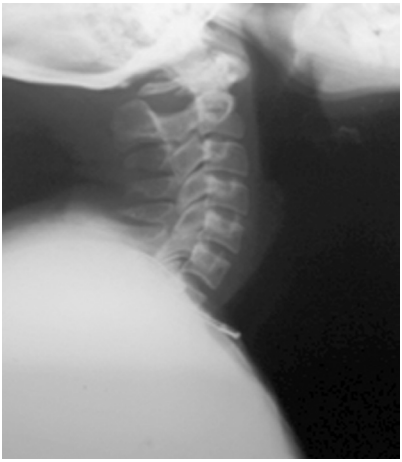

Figure 4.

T value increased from 3 to 9 (10% to 30%), 9 months after treatment.

It was observed that those patients who did not get any relief of clinical symptoms with treatment for 12 months did not have any improvement during the follow-up period of 3 months. Those

patients who were relieved of symptoms with treatment continued to have that relief during the follow-up period of 3 months. Those three patients who did not get any change in tenderness in neck during treatment continued to have no change in the follow-up period of 3 months.

DISCUSSION

In cervical spondylosis, analgesics, nonsteroidal anti inflammatory drugs (NSAIDs) and muscle relaxants have only limited role in relieving pain and spasm of cervical muscles.[3] Various exercises using proprioceptive strengthening, endurance or co-ordination exercises are found to be effective to some extent.[4,5] Epidural injection is considered in patients with intractable pain or radiculopathy, if surgical intervention is not an option.[6] This study proves that alfacalcidol is effective in relieving neck pain in 81.3% of the patients. It is observed that it can relieve the neuritic pain in patients with brachial neuralgia and relieve vertigo in patients with vertebrobasilar insufficiency. This drug can produce regression of the osteophyte formation in 37.3% of the patients selected for the study. Table 4 shows that there is significant improvement in T value after treatment. Table 5 also shows that the improvement in T value after treatment is highly significant.

Alfacalcidol (1α-hydroxyvitamin D_3: 1α-(OH)D_3 undergoes rapid conversion to 1,25-hydroxyvitamin D_3, the vitamin D3 metabolite, which acts as a regulator of calcium phosphate.[7,8] Its main effects are:

The circulating 1,25-hydroxyvitamin D_3 levels increases intestinal absorption of calcium phosphate[9]

Promotes bone mineralization[10]

Increases bone absorption causing relief of bone and muscle pain

Produces additional activation of the bone tissue[11]

α

It may produce increase in the number and diameter of muscle cells[12]

It may produce an increase in the number of muscle strength by 24%, an average across all compartments.[13]

Retards corticosteroid-induced bone loss due to immunomodulating properties.[14,15]

This study proves that alfacalcidol is effective in relieving the clinical symptoms in patients of cervical spondylosis. This drug can produce regression of the osteophyte formation of the diseased vertebrae and improve bone densitometry score.

References

1. Cardall PH, Batzadarf U. Cervical spondylotic myelopathy. J Neurosurgery. 1966;25(1):57-66.
2. Ebersold MJ, Pare MC, Quast LM. Cervical spondylotic myelopathy. J Neurosurg. 1995;82(5):745-51.
3. Kim RC. Spinal cord pathology. In: Nelson JS, Parsi JE, Schochet SS (Eds.). Principles and Practice of Neuropathology. St. Louis: CV Mosby; 1993: p. 398-435.
4. Ferguson RJ, Caplan LR. Cervical spondylitic myelopathy. Neurol Clin. 1985;3(2):373-82.
5. Asgari S. Cervical spondylotic myelopathy. In: Palmar JD (Ed.).Neurosurgery: Manual of Neurosurgery. New York: Churchill Livingstone; 1966: p. 750-4.
6. In: Weinstein PR, Ehni G, Wilson CB (Eds.). Lumbar Spondylosis: Diagnosis, Management and Surgical Treatment. Chicago: Year Book Medical Publishers; 1997: p. 13-87.
7. Tsai KS, Heath H 3rd, Kumar R, Riggs BL. Impaired vitamin D metabolism with aging women. Possible role in pathogenesis of senile osteoporosis. J Clin Invest. 1984;73(6):1668-72.
8. Quesada JM, Mateo A, Jans I, Rodriguez M, Bouillon R. Calcitrol corrects deficient calcitonin secretion in vitamin D-deficient elderly. J Bone Miner Res. 1994;9(1):53-7.
9. Heaney RP, Dowel MS, Hale CA, Bendich A. Calcium absorption varies within the reference range for serum 25-hydroxyvitamin D. J Am Coll Nutr. 2003;22(2):142-6.
10. Muller K, Diamant M, Bendtzen K. Inhibition of production and function of interleukin-6 by 1,25-dihydroxyvitamin D3. Immunol Lett. 1991;28(2):115-20.

11. Simpson RU, Thomas GA, Arnold AJ. Identification of 1,25-dihydroxyvitamin D3 receptors and activities in muscle. J Biol Chem. 1985;260(15):8882-91.
12. Bischoff HA, Stahelin HB, Urscheler N, Ehrsam R, Vonthein R, Perrig-Chiello P, et al. Muscle strength in elderly: its relation to vitamin D metabolites. Arch Phys Med Rehabil. 1999;80(1):54-8.
13. Veenstra TD, Fahnestock M, Kumar R. 1,25-dihydroxyvitamin D3 regulates the expression of nerve growth factor gene. J Invest Med. 1977;45(3):249-51.
14. Kato T, Chen JT, Katase K, Hirai Y, Hasumi K, Ogata E, et al. Effect of 1 alpha-hydroxyvitamin D3 on loss of bone mineral density immediately after artificial menopause. Endocr J. 1997;44 (2):299-304.
15. Pouilles JM, Tremollieres F, Ribot C. Prevention of postmenopausal bone loss with 1 alpha-hydroxy vitamin D3. A threeyear prospective study. Clin Rheumatol. 1992;11(4):492-7.

Reference of the article

Volume 113 No. 11 Journal of the Indian Medical Association, PP 149-152

This scientific article proved that the drug Alfacalcidol is effective in curing the disease Cervical Spondylosis. At present there is no drug availabale in medical science which can arrest the progress of the disease. I could prove that there is regression of pathalogical changes in the cervical vertebrae of the patients treated with the drug. The regression of the pathological changes in the vertebrae is also proved by radiological studies and Bone densitometry tests.

After the completion of the study, I have treated hundreds of patients of Cervical Spondylosis with the drug, Alfacalcidol. My clinical observation is a break-through in the treatment of Cervical Spondylosis. This scientific article is the first of its kind in medical science.

Life after Death

K.K. MATHEW

A chapter of my book 'Mind and Peace' published in January 1985.

My observation in the study of 12 patients is almost identical with the observation made by the study of the researchers of the Southampton University in 2000 patients in the year 2014. [after 29 years]

Is there a life after death? This is a question we may ask ourselves. Some people believe that this life ends permanently with death . The religious books say that there is a life after death. We also believe that the person who lives a right and good life on earth goes to the heaven and the one who lives a sinful life goes to hell.

It is known to all, that when a person dies, his life is separated permanently from his body. But nobody knows clearly where the soul or the life goes after death. No one can give a clear answer to that. Our belief is based on religious books but there is no scientific proof Scince is not so developed or advanced as to give a satisfactory answer to this question

Now as a doctor, shall I point out some of my experiences in this field. During my whole professional life I had twelve very serious patients whose heart beats and respirations stopped for a lew seconds and whom I could revive back to normal life. Had they been allowed to remain for a few seconds more in that state they could be declared dead . I wanted to know what happened to these patients during this shortest period of time when their hearts and respirtation stopped for a short while. A few days after their revival, when they regained full consciousness, I had a close chat with them. I asked them whether they remembered anything which had happened to them during that time. I wrote down the experiences they narrated and obtained signatures to their statements.

Out of twelve patients, three did not know anything of what had happened . Seven patients gave identical versions while two patients gave a different version. All the seven patients narrated

identical experiences, said "Doctor, I feel that I was going down to the bottom of the earth or to the bottom ot the sea. There was nobody to help me . It was full of darkness. I got frightened . I started crying aloud . I could not breathe properly. There was no air I got suffocated . How much pain I could bear! I have never experienced such terrible pain during my whole life on earth . I prayed for my escape from this hell. I get frightened when I think about that experience. I do not remember anything more" .

Two patients gave a different version. "Doctor I felt that I was going up and up. I saw the sky; I saw the stars; I saw the moon. Again I went up. I saw the angels. I saw bright sunshine. I was filled with great joy which I have never experienced during my whole life on earth. What a great joy! I did not want to come hack to earth."

The narration of these patients can be interpreted as hallucinations or delusions by critics. Hallucnations are the feelings arising from a subconscious or unconscious mind I went one step forward. I went to their native places and verified for myself the background and the previous life of these patients. I was convinced fully by one fact that those seven patients who felt that they were all going down lived really an evil life in all respects .Those who felt they were going up lived a life of all goodness. The fact that those who lived a good life felt that they were going to heaven and those who lived an evil life, felt that they were going down to hell cannot be written off as hallucinations or as baseless data. It should be remembered that they had all these feelings at a time when the soul was getting separated from the body. These feelings remained at the bottom of their mind when they started living agian.

With the above data, I feel that I may not be wrong in stating that this is a scientific proof for the existence of heaven and hell. If you believe that there is heaven and there is eternal Joy and peace, why should you worry about your life on earth?

Healing of the Soul

K.K. MATHEW

This concept was published in my book 'Healing Of The Soul'. The publisher of this book, International Chavara Cancer Research Insitute, Nedumangad functions on my concept - 'If Healing of the soul is combined with modern medical science, treatment becomes complete'.

This concept is the first of its kind in medical science. My treatment of the sick patients since the past 42 years is based purely on this concept. I diagnose the diseases purely by intuition [the words of Jesus Christ] and treatment becomes very successful. The innovations I make, the poems I write, the novels and the stories I write, and the speeches I deliver, are all by what Jesus tells me and I just reproduce them. It is the truth of the truth.

Today we are witnessing the advancement of medical science and the latest devices in the treatment of human body and mind. But we do not hear about the treatment of a fundamental thing, that is the soul. The soul and body constitute the human being. Medical science treats the human body and mind, not the soul, ie medical science deals with the periphery and not the centre. It is as if we are spraying insecticides on the branches, leaves and fruits of a tree but not treating the disease of its roots. This is the incompleteness of medical science.

Many feel that treating the soul, is an insignificant matter, not worthy of a discussion. Many consider it, an irrelevent concept. But one should understand 'healing of the soul' has power to surpass medical treatment. The soul and the body are one and mutually dependent. Hence healing of the soul results in healing the human body.

Where is the human soul? How does it function? Medical science is quite ignorant of the answers to these questions. Hence one is justified to embank upon faith in God and the truths in the ancient scriptures like the religious books, the 'Puranas', the

'Upanishads' and the 'Vedas'. What we see in the ancient scriptures is the truth revealed by God from time to time. One living in this scientific era should accept the fact that faith in God and the truth in the ancient scriptures will nullify the incompleteness of medical science.

What are the ailments of the soul? How can they be treated? The ailment of the soul are countless. They are the passions of the person for this materialistic world and the worldly things. These passions act as a curtain separating the human being from the soul which is Godly. Science remains incapable of removing the passions. In fact the soul is immobalised inside the worldly passions. One should understand that these passions can be washed off only by total surrender to God and immutable faith in Him. The one who proceeds in the path towards God, will be distracted by countless numbers of tribulations and obstacles, but faith in God will come for rescue of that person. When faith in God becomes strong, the worldly passions covering the soul begin to vanish leaving the soul free from the bondage of the passions. This is the healing of the soul. Now the person comes fully under the control of the soul.

At present some of the diseases are incurable. The reason for this is that these diseases are the result of the ailments of the soul. The person having the healing of the soul becomes immune to diseases. Medical science says that some diseases are due to mental tensions. The root cause of the mental tension is the diseased soul when man is ruled by passions and desires.

A doctor with a healed soul is fully controlled by the soul without the influence of the worldly passions and so whenever he comes across patients having complicated diseases, he gets the correct diagnosis. This revelation is called intuition. The Nobel laureates discover only a very small fraction of the great craftsmanship of God. If one submits himself or herself to God, the mysteries of God will be revealed to that person. These mysteries of God cannot be measured by the scales of science. The doctor attains knowledge that God is the real wealth. The

doctor sees God in the patients who approach for help. The doctor becomes the 'visibile God' for the patients. They wait for hours together to the feel the touch of that 'God sent person'.

If one goes to the valleys near the mountain 'Kanchan ganaga' one can see hermits sitting under the shades of big trees meditating. Many of them are aged more than hundred years. They live by eating fruits and drinking water from the nearby streams. They are very healthy. They ascertain the existence of spiritual healing.

Modern medical science should accept spiritual healing because spiritual healing is not opposed to scientific principles. In fact it complements science. Science is the gift of God. By offering complete cure to every malady man faces, it becomes the finality of all scientific pursuits. If spiritual healing is combined with medical science, treatment becomes complete. Then wonders happen.