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TREATMENT OF PHARYNGEAL DIPHTHERIA AND PHARYNGITIS WITH TRADITIONAL CHINESE MEDICINE

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Foreword

Epidemics of diphtheria had occurred in China during eighteenth century. At that time, the western medicine introduced in China was very much limited and not popularized in clinical practice. The therapeutics for diseases including diphtheria was chiefly relied on Traditional Chinese Medicine. The ancient Chinese physicians had accumulated abundant clinical experiences written in medical classics concerning diphtheria and other disorders.

Since the year 1959, we have tried using some recipes of compound herbal medicine from those medical classics written in Qing dynasty to treat pharyngeal diphtheria instead of diphtheria antitoxin (D A T) thereapy which had been defined almost as a routine treatment for diphtheria formerly. We found that two of these recipes were fairly effective.

In the years 1963 – 1965, we had made a few more modifications about the old prescriptions and fixed the composition of herbs together with a new- fashioned preparations of a herbal decoction which was named "Anti-diptheria mixture" (A. D.M) and approved by the Ministry of Health, People's Republic of China (P. R. C.) in 1965, as a scientific research product of the Ministry.

Clinical Studies and Methods

During the years 1963 – 1965, in Tian – Jing municipal Isolation Hospital (Iian – Jing M. I. H), we had treated 192 cases (Group B) of pharyngeal diphtheria with only A. D. M. The other two groups of the same disorder, one consisting of 200 cases (Group A) were treated by herbal decoction (Herb Dec)* combined with Penicillin and another consisting of 269 cases (Group C) treated by D. A. T. together with Penicillin. The therapeutic effects of the three groups of patients were about the same. There were no significant difference in statistics about the effective rate (%) between groups A and B or groups B & C. See table (3).

During the same period, repetitions of the same clinical studies were carried out in Chong – ging M. I. H. (south – east territories, P. R. C) Chang – chun M. I. H. (north – east territories, P. R. C). The former treated 200 cases while the latter treated 80 cases of pharyngeal diphtheria with this same A. D. M. The therapeutic

effects in these two hospital were similar and satisfactory as our studies in Tian – jing.

Furthermore we got the similar effectiveness in treating 124 cases of acute pharyngitis and acute tonsilitis with the same A. D. M. in Tian – jing M. I. H.

Criteria for diagnosis:

The diagnosis of pharyngeal diphtheria is established provided one of the two criteria must be fulfilled.

1) Cultures for K. L. B. are positive but the symptoms and signs are also comparatively typical, such as higher body temperature, sore-throat, nausea, anorexia, pharyngeal pseudo-membranes appearing grayish-white in colour and surrounded by mild congestion. The pseudo-membranes confluent into pieces and not easily erased by a tongue-depressor but easily bled following erasures.

   *Herbs in the prescriptions were not fixed and prepared by traditional boiling with water.

2) Cultures for K. L. B. are negative but the above symptoms and signs are rather typical.

Clinical types:

The pharyngeal diphtheria is classified in to 3 types according to the severity of the disease.

1) **Localized type:**

   The pseudo – membranes limited on one or two tonsils; cervical lymph glands mildly enlarged.

2) **Diffused type:**

   The pseudo – membranes mostly occupying both tonsils and extending to palates, uvula or postpharyngeal wall; cervical lymph glands mildly enlarged; face appearing pale.

3) Symptoms and signs more severe, onset sudden, severe sore-throat, conspicuous facial pallor, nausea and vomiting, pseudo – membranes similar to diffused type, submaxillary and cervical lymph glands marked enlarged.

Among the group (B) 192 cases treated by us with A. D. M. 142 cases, 74% were classified as localized type; 16 cases, 8.3% and 30 cases, 15.6% as diffused and toxic types respectively. In addition, there were 4 cases, 2.1% belonging to pharyngolaryngeal diphtheria in this group. Throat cultures positive for K. L. B. were 85 cases, 44.3%; negative for K. L B. 34 cases, 17.7% and positive for Streptococcus hemolytics or Staphlococcus aureus 73 cases, 38%. The clinical symptoms and signs of all the patients in this group were comparatively typical and corresponding to the criteria of the diagnosis.

Analysis of the therapeutic effects of 3 groups of patients suffered from this disorder:

Group A: 200 cases, treated by herbal decoctions combined with Penicillin.

Group B: 192 cases, treated by A. D. M.

Group C: 269 cases, treated by D. A. T. and Penicillin.

All the patients in these 3 groups were cured by means of their different remedies.

Age distributions:

Group A: > 1yr and <11 yrs : 44% > 11 yrs. And < 20 yrs. : 56%.

Group B : > 1 yr. and < 11 yrs. : 37.5 > 11 yrs. And < 20 yrs : 62.5%

Group C: > 1 yr. and < 11 yrs : 74%; > 11 yrs and < 20 yrs. : 26%.

There were no significant difference of the durations between onset of the illness and the admission.

The number of severe patients in Group B was somewhat more than the other two groups. See table (1).

The evaluation of the therapeutic effects among the three groups of cases had been expressed by comparing their effective rates in fulfillment of the following criteria; body temperature recovered to normal, sorethroat and pseudo-membranes disappeared within 1 – 3 days after the treatment. See Table (4).

Further comparison of the therapeutic effects among the cases with positive cultures for K. L .B. in these three groups had been done similarly as above. See Table (5).

The therapeutic effects of the three groups as shown in Table (4) and (5) are apparently similar.

In the years 1963 – 1965 we admitted 124 patients suffering from acute pharyngitis and acute tonsillitis. They were treated by A. D. M. Within 1 – 3 days after this remedy, we found that the fever, sorethroat and the pharyngeal exudations (Sometimes resembling diphtheria pseudomembranes) were all subsided or disappeared in majority of these patients.

Composition of Antidiphtheria Mixture (A. D. M).

This mixture is a modified preparations processed on the basis of old traditional prescriptions consisting of Radix scrophulariae, Fructus forsythia etc.

TABLE – I

Distribution of types of patients

Groups	**A** **R x Herb dec. + Penicillin**		**B** **R x A. D. M.**		**C** **R x D. A. T. + Penicillin**	
Clinical types	**Cases**	**%**	**Cases**	**%**	**Cases**	**%**
Localized:	175	87.5	142	73.9	223	83.0
Diffused:						
Toxic :	1	0.5	16	8.4	23	8.5
1st. d.	20	10.0	28	14.7	22	8.1
2nd.d.	1	0.5	2	1.0	1	0.4
Pharyngolaryngeal diphtheria	1	0.5	4	2.0	0	0

Nasal diphtheria	2	1.0	0	0	0	0
Total	200	100	192	100	269	100

TABLE II

Other conditions of the 3 groups

Condition of groups	A (200 cases)	B (192 cases)	C (269 cases)
% of Throat cultures positive for K. L. B.	45%	44.3%	32.4%
D. A. T. prior to ad.	No	No	No
No. of cases received only one dose of antibiotics before ad.	97	119	138
No. of cases immunized with diphtheria toxoid only once but not regularly in past history	21	20	29

TABLE III

Complications in the 3 groups

Complications in groups	A (200 cases)	B (192 cases)	C (269 cases)
Mild myocarditis shown by E. C. G. No Clinical manifestations	1	2	8
Myocarditis with both clinical and E. C. G. Findings	0	0	4
Cases with ocular and palatal paralysis	0	0	1
Serum sickness due to inj. of D. A. T.	0	0	6
Immediate reaction due to inj. of D. A. T.	0	0	1

TABLE IV

Groups	**A (200 cases)**	**B (192 cases)**	**C (269 cases)**
R X	**Herb dec. + Penicillin**	**A. D. M.**	**D. A. T. + Penicillin**
No. of cases fulfilling the above criteria	171	172	232
Effective rate	85.5%	89.6%	86.2%
Difference of effective rates	Between A and B :		Between B and C:
Between 2 groups	4.1		3.4
T value	1.2		1.1
Significant difference in statis	No		no

TABLE V

Groups	**A (90 cases)**	**B (85 cases)**	**C (87 cases)**
R X	**Herb + Penicillin**	**A. D. M.**	**D. A. T. + Penicillin**
No. of cases fulfilling the above criteria	76	68	69
Effective rate	84.4%	80.0%	79.3%
Difference of effective rates	Between A and B :		Between B and C:
Between 2 groups	4.4		0.7
T value	0.77		0.11
Significant difference in statis	no		no

TABLE VI

Product No. of A. D. M. (Zhong – lian Pharm. Works, Wu-Han)	Antitoxic Effects (K. L B. Toxin No. 55 – 44, 200 M. R. D. / ml)	Bacteriostatic Effect (K. L. B. Strain No. 38009)	Bacteriocidal Effect (K. L. B. Strain No. 38009)
18	2,000	100	200
49		100	200
59	2,000+	100	200
7, 10, 37	2,000	100	<200
58	2,000 +	100	<200

Oral Administration and Dosage

Adults and children above 10 years of age : for first 2 days; 25 cc. 4 id; then, 25 c.c bid; Children below 10 years of age: each dose may be 15 – 20 c.c. The dosage may be increased according to severity of the diseases.

No toxic or side reactions have been reported relating to this mixture.

Discussion

Diphtheria has been brought gradually under control in occurrence over all the territories through prophylactic measures in our Country. However, some of our clinicians seem to be still in need of this herbal A. D. M. at present moment. As a matter of fact, the differential diagnosis between pharyngeal diphtheria and acute pharyngitis or tonsillitis are not so easy some times especially for some of the rural or even some of the urban young clinicians as far as their limited clinical experiences are concerned. Besides, the results of K. L. B. cultures usually need 24 – 48 hours to be achieved. In addition, the positive findings of both the cultures and the direct smears examinations for K. L. B are not 100%. The clinicians may hesitate in making accurate diagnosis for these pharyngeal disorders. Most of them are afraid of the possible complications such as myocardial damage or neuroparalysis due to K. L .B. exotoxin if the diphtheria antisera are not injected at the earliest time to the diphtheria patients. For this reason, the diphtheria antitoxin (D. A. T) AND Penicillin are not properly administered for these patients. Although the therapeutic effects of this antiserum combined with Penicillin (or other antibiotics) are satisfactory for both diseases as mentioned, but there would be the possible chances to produce antiserum anaphylaxis or Penicillin hypersensitivity to the patients even though incidentally.

A. D. M. may be indicated for tonsillitis without unnecessary hesitation in diagnosis and without worrying about the complications of diphtheria as well as the hypersensitiveness to antiserum or

antibiotics. Financially this herbal mixture is much cheaper than antiserum and antibiotics. The way of oral administration of this mixture is more convenient and comfortable than injections and skin test.

In the development of medical methodology as a whole, the A. D. M. might be considered as another therapeutic method beneficial to a certain part of patients. This mixture probably is conducive to some clinicians wherein if necessary.

Appendix for Reference:

Our laboratory studies for A.D.M. are in a preliminary stage and on trial basis. Up to the present day we are in the process of studying it and not in favour of drawing any conclusion of the mechanisms of its role or effectiveness. We have encountered considerably intractable and complicated factors concerning the analysis of this herbal prescription especially the elucidation of traditional Chinese Medicines theories which are entirely different from that of modern medicine. The following laboratory works are only for reference.

The Pharmaceutical Studies in Vitro:

The antitoxic, bacteriostatic and bacteriocidal effects of this mixture are shown in table (6). Seven groups of this laboratory study were repeated with approximately similar results.

Antitoxic effects is equivalent to neutralization of the number of M. R. D. per ml. of this mixture.

Bacteriostatic and bacteriocidal effects are equivalent to number of Penicillin I. U. per ml. of this mixture.

The Other Laboratory Studies:

Since the ulcerations and pseudo membranes over the pharynx due to radiation therapy for 8 cancer patients were much improved after administration of A. D. M., by Ri-Tan Hospital (Institute of Oncology, Beijing) we have been interested in the assumption whether or not there might be any relationship between carcinoma and this herbal mixture.

Thenceforth we have done the following laboratory studies on trial basis:

1) The leucopenia in mice injured by a lethal dose of Co^{60} radiation was improved by feeding A. D. M. as compared with controls in three groups of repeated experiment.

2) The nucleated myelocytes in borne marrow of mice following similar radiation damage as above were increased in cellular counts after the same feeding (Repeated two times)

3) The vitality of polyenergetic stem cells in the bone marrow of mice injured by the similar radiation was invigorated by administration of A. D. M. as shown by marked increasing spleen weights and microscopic findings of spleno – proliferation as compared with spleno – atrophy of the controls. A. D. M. also prolonged the lives of mice debilitated by radiation compared with the mortality of the controls. (Repeated two times).

4) Rate of Inhibition of Transplanted me – mela – noma of mice was 47% ($P < 0.05$) by feeding each mice with 0.4 ml. of A. D. M. as compared with weights of the tumor masses between the treated group and control group.

5) The combination in use of A. D. M. and cyclophosphamide inhibited the growth of sarcoma and ascetic carcinoma of S_{180} in mice around 60.7% and 63.0%. ($P < 0.01$; $P < 0.05$) respectively. (Repeated two times, with controls).

   The synergetic effect of these two remedies revealed the prolongation of survival time of mice transplanted with leukemia (L_{1210}) accounting for 70.0% ($P < 0.05$) and 65% ($P<0.05$) in two groups of experiments with controls.

   On the other hand, the use of only one of these two remedies would show less effect than the above as compared in other groups of experiments.

6) The co-ordination of A.D.M. and cyclophosphamide also increase the cAMP contents of tumor cells as well as cAMP / cGMP ratio value of mice transplanted with ascetic carcinoma of S_{180} (Shown by 3 groups of experiments with controls).

   The synergic effects of these two therapies as mentioned in (5) and (6) are parallel with each other.

7) A. D. M. inhibited the synthesis of D N A and R N A in ascetic carcinoma of S_{180} transplanted in mice up to 97.6% (by 3 H – T d R incorporation) and 96.7% (by 3H – UR incorporation) with a concentration 12.49 mg/ml. equivalent to raw herbs of A. D. M.