The Value of Chemotherapy for Active Pulmonary Tuberculosis in Out-patient Clinic

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Introduction

Recent advancement in the treatment of tuberculosis especially chemotherapy has brought a considerable change in the concept of this dreadful disease. Before the era of chemotherapy, rest was considered the most important portion of the treatment of pulmonary tuberculosis, however, since the introduction of effective drugs, the value of rest has apparently decreased. Thus it causes less economic burden for the care of tuberculosis individually as well as nationally. It is particularly significant in those areas where sufficient hospital facilities are not available for all discovered active pulmonary tuberculosis patients. In recognition of this advantage of applying chemotherapy, since late 1954, out-patient clinics have been operated as a control measure for over 800,000 pulmonary tuberculosis patients against 22 million population in Korea. This paper is to report the results of our investigation on the ambulatory chemotherapy for active pulmonary patients for a period of two years at the two largest clinics.

It may be necessary to state clearly that the majority of patients reviewed here continued their normal life during the course of treatment due to economic reasons so that perhaps the results presented here may not be quite comparable to the results obtained in those areas where other necessary measures besides chemotherapy could be adequately provided.

Method of Investigation

Material for the investigation was that of 5,793 patients who received chemotherapy among 7,020 diagnosed active pulmonary tuberculosis patients at Korea's two largest Tuberculosis Clinics of National Tuberculosis Center and Severance Chest Clinic in Seoul from January 1, 1955 to August 31, 1957. The number of patients received chemotherapy over 12 months and 24 months were 1,014 and 276 respectively. This low rate of continuing chemotherapy indicates the difficulties we are facing in the care of tuberculosis and felt the need of strong socio-economic support to these patients to continue their valuable treatment.

Four regimens of chemotherapy have been employed: 1. Streptomycin-isoniazid 254 patients (25 per cent) of total treated patients, 2. PAS-isoniazid 571 patients (58 per cent), 3. Streptomycin-PAS 149 patients (15 per cent), 4. Twenty-eight patients also received triple drug combina-

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tion treatment in consideration of the seriousness of the disease. The isoniazid alone was 12 patients (1 per cent).

There are three important items from the viewpoints of public health on this table: namely, 87 per cent of all patients who have visited clinics showed moderately or far advanced disease and more than a half of the patients received chemotherapy regularly or irregularly before they visited clinics, furthermore, only 1,014 patients actually continued chemotherapy over 12 months out of 5,793 patients who initiated treatment at the clinics.

Result

A. Bacteriologic Results: As Table II shows, in 673 of the total of 1,014 patients sputum culture were positive for tubercle bacilli at the time treatment was begun, and in 252 (37 per cent) were negative on culture following 12 months of chemotherapy, however, reversion in sputum culture was also found in 32 patients (11 per cent), but a little difference in the sputum status was observed at 24 months compared with 12 months results. However, in the group of patients previously untreated showed 49 per cent sputum conversion rate against 25 per cent of previously treated group at 12 months and showed only 41 per cent and 36 per cent respectively at 24 months.

B. Roentgenographic Results: Little difference was observed in the rate of roentgenographic improvement at 12 and 24 months as Table III shows.

In the group of 12 months observation, patients with no previous chemotherapy showed 78 per cent of improvement in comparison with 51 per cent in the group of patients with the history of previous chemotherapy and

<table>
<thead>
<tr>
<th>Culture report at start</th>
<th>Culture report at 12 &amp; 24 months</th>
<th>Per cent converted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Positive</td>
</tr>
<tr>
<td>Positive</td>
<td>673/209</td>
<td>416/129</td>
</tr>
<tr>
<td>Negative</td>
<td>281/34</td>
<td>32/6</td>
</tr>
<tr>
<td>No report</td>
<td>60/13</td>
<td>5/0</td>
</tr>
</tbody>
</table>

*12 months/24 months

TABLE II
BACTERIOLOGIC RESULTS
almost the similar results were observed at 24 months in 82 per cent and 54 per cent respectively among the two groups observed.

C. Final Results: Table IV shows the over all status after 12 and 24 months of chemotherapy, and clinical classification was made by 1955 National Tuberculosis Association Classification and Diagnostic Standards. At the end of 12 months chemotherapy, only 144 patients among 1,014 patients (14 per cent) became inactive, and in general, more favorable changes were observed in the minimal lesions, in the patients with no history of previous chemotherapy and in patients with more recent diseases, that 53 per cent of minimal become inactive but only 13 per cent of moderately advanced, and almost none of the far advanced cases became inactive.

However, following 24 months of chemotherapy, the rate of inactivation in the diseases was much higher as Table IV shows. In all patients, 27 per cent became inactive compared with 14 per cent at 12 months. Especially, in the patients with minimal lesions 71 per cent became inactive. And even more in those patients with moderately or far advanced lesions became inactive 36 per cent and 11 per cent respectively.

It was also found that previous chemotherapy influenced the results markedly that at 12 months 31 per cent of patients with no history of previous chemotherapy became inactive while only 24 per cent of patients with history of previous chemotherapy and the similar findings were also seen at 24 months that 53 per cent and 39 per cent respectively. Thus, the confirmatory results of more favorable changes in the patients with no history of previous chemotherapy was observed.

TABLE III
ROENTGENOGRAPHIC CHANGES AT 12 & 24 MONTHS

<table>
<thead>
<tr>
<th>Stage at start of treatment</th>
<th>Total</th>
<th>Roentgenographic Status at 12 &amp; 24 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Improvement</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Number</td>
</tr>
<tr>
<td>*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimal</td>
<td>134/17</td>
<td>108/14</td>
</tr>
<tr>
<td>Mod. Adv.</td>
<td>486/133</td>
<td>399/110</td>
</tr>
<tr>
<td>Far Adv.</td>
<td>394/126</td>
<td>296/94</td>
</tr>
<tr>
<td>All Pts.</td>
<td>1,014/276</td>
<td>793/218</td>
</tr>
</tbody>
</table>

*12 months/24 months

TABLE IV
FINAL RESULT (CLINICAL DIAGNOSIS) AT 12 AND 24 MONTHS

<table>
<thead>
<tr>
<th>Stage of start of treatment</th>
<th>Total</th>
<th>Classification at 12 and 24 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Number</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Percentage</td>
</tr>
<tr>
<td>*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minimal</td>
<td>134/17</td>
<td>63/5</td>
</tr>
<tr>
<td>Mod. Adv.</td>
<td>486/133</td>
<td>422/85</td>
</tr>
<tr>
<td>Far Adv.</td>
<td>394/126</td>
<td>385/112</td>
</tr>
<tr>
<td>All Pts.</td>
<td>1,014/276</td>
<td>870/202</td>
</tr>
</tbody>
</table>

*12 months/24 months
DISCUSSION

There is a world-wide trend to use chemotherapy on unhospitalized or domiciliary tuberculosis patients increasingly as the successful demonstration of value of chemotherapy on these patients. It does not indicate the unnecessity of sanatorium care for the treatment of tuberculosis. Nevertheless, it has lessened the value of rest in the course of treatment of tuberculosis. However, even during the course of chemotherapy, in case of the patients with active clinical symptoms, it is needless to say that a considerable period of strict rest is also needed while it may shorten the period of rest by chemotherapy. The groups of 1,014 patients who received chemotherapy for 12 months or more and 276 patients for 24 months or more among 7,020 patients diagnosed active pulmonary tuberculosis were entirely dependent upon chemotherapy and they could not take proper rest because of socio-economic reasons. The results we have obtained were that 78 per cent at 12 months and 79 at 24 months roentgenologic clearing, and 37 at 12 months and 38 at 24 months in sputum conversion rate from positive to negative. Roentgenologic clearings are referable to the results obtained from sanatorium or hospitalized patients but sputum conversion rate was considerably lower.

Kinoshita of Japan has reported the results of ambulatory chemotherapy that his group observed, 60-70 per cent of maximum sputum conversion rate at six months and roentgenologic clearing was 80-90 per cent at 12 months of chemotherapy, Robinson et al. have reported the results of chemotherapy on nonhospital tuberculosis patients that 56 per cent at 12 months and 58 per cent at 24 months chemotherapy in sputum conversion rate. In comparison with the above mentioned two groups of investigators, our results especially sputum conversion rate is considerably low. It is because of inadequacy in proving sufficient nutrition and rest, especially mental rest. In addition the group we have studied included more moderately or far advanced cases than those two groups of investigators. It is an important fact especially from the viewpoint of public health that 40 per cent of the comparatively severe patients who received chemotherapy for more than 12 months became non-infectious. The differences between the results of chemotherapy at 12 and 24 months in both roentgenological and bacteriological changes were not significant, and they are comparable to the above mentioned two groups of investigators. We believe that unless the patient shows stabilization of active symptoms and signs of pulmonary tuberculosis within 12 months of chemotherapy, continuous chemotherapy will achieve little, and it is especially true to the patients with history of previous chemotherapy. The patients with no previous history of chemotherapy showed 49 per cent of sputum conversion rate against 25 per cent in the patients with history of six months or more previous chemotherapy. It is however agreeable to the other investigators that maximum sputum conversion will be achieved by chemotherapy within the first six months. But the significant bacteriologic improvement will continue to occur until 12 months.

Thus, there will be no argument or objection to administer chemotherapy to all the active pulmonary tuberculosis patients, but, if no satisfactory results are seen, within 12 months of chemotherapy the continuation of the same regimen of chemotherapy will not be significant, and other possible therapeutic measures such as surgical intervention, if applicable, should be considered. For those inoperable cases, combination of drugs is to be changed in accordance with the results of sensitivity test. The patients with the lesion, inoperable or incurable with chemotherapy alone, must be given rehabilitation program with hope of giving the patients psychological release.

SUMMARY

1. The results of chemotherapy at the end of one and two years on 1,014 and 276 patients among 5,793 proved active tuberculosis patients in 7,020 who visited two of Korea's tuberculosis Clinics of National Tuberculosis Center and Severance Chest Clinic during the period between January 1, 1956 and August 31, 1957 are reported.
2. Forty-eight and 39 per cent of total investigated were moderately or far advanced cases respectively.
3. Sputum negative conversion rate was 37 and 38 per cent at 12 and 24 months chemotherapy respectively.
4. Roentgenographic improvement was seen in 75 and 80 per cent at 12 and 24 months respectively.
5. It is believed that adequate bed rest is important in pulmonary tuberculosis patients given chemotherapy on ambulatory basis.
6. In general, more favorable therapeutic effects were observed in the less advanced, more recent, previously untreated cases.
7. There was not much difference between the results obtained at 12 and 24 months chemotherapy. Therefore, at the end 12 months of chemotherapy, a complete evaluation will be necessary.
8. Ambulatory chemotherapy on pulmonary tuberculosis is a proper therapeutic measure, especially in the region where sufficient hospital facilities are not available for all the active pulmonary tuberculosis patients.

RESUMEN

1. Este es un relato de los resultados de la quimioterapia en 1,014 y 276 enfermos, entre un número de 5,793 de tuberculosis activa demostrada en 7,020 personas que
acudieron a dos grandes clínicas del Centro Nacional de Tuberculosis en Corea, así como en Severance Chest Clinic durante el período de Enero 1o. de 1955 y Agosto 31 de 1957.

2. Cuarenta y ocho por ciento y treinta y nueve por ciento respectivamente, fueron moderadamente o muy avanzados.

3. La conversión de los espumis a negativos, fue de 37 por ciento y 38 por ciento a los 12 y 24 meses respectivamente.

4. La mejoría radiológica se observó en 75 por ciento y 80 por ciento a los 14 y 24 meses respectivamente.

5. Se cree que el responso en cama adecuado, es importante en los enfermos que se les da quimioterapia ambulatoria.

6. En general, se observó más favorable resultado en los menos avanzados, más recientes y no tratados previamente.

7. No hay mucha diferencia entre los resultados obtenidos a los 12 y a los 24 meses. Por tanto, al cabo de los 12 meses se necesita una revaluación completa.

8. La medicación ambulatoria de la tuberculosis es apropiada especialmente en las regiones en que no hay suficientes camas de hospital para todos los enfermos de tuberculosis activa.

RESUME

1. Les auteurs rapportent les résultats de la chimiothérapie à la fin d'une période d'un à deux ans sur 1.014 et 276 malades, parmi 5.973 malades atteints de tuberculose évolutif prouvée, sur les 7.020 qui vinrent en consultation aux deux plus importantes cliniques tuberculeuses de Corée, du Centre National Tuberculose et à la Clinique Thérapeutique Severance entre le 1er Janvier 1955 et le 31 août 1957.

2. 48% et 39% du nombre total des malades examinés étaient respectivement des cas modérément ou très avancés.

3. Le taux de négativation de l'expectoration fut respectivement de 37% et 38% entre 12 et 24 mois de chimiothérapie.

4. Une amélioration radiologique fut constatée dans 75% et 80% des cas aprèse respectivement 12 et 24 mois de traitement.

5. Les auteurs croient qu'un repos au lit approprié est important chez les malades atteints de tuberculose pulmonaire, traités par la chimiothérapie administrée d'une façon ambulatoire.

6. En général, les effets thérapeutiques plus favorables furent observés dans les cas les moins avancés, les plus récents, et sans traitement antérieur.

7. Il n'y eut pas beaucoup de différence entre les résultats obtenus après 12 et 24 mois de chimiothérapie. C'est pourquoi à le fin de 12 mois de chimiothérapie, un bilan complet s'avère nécessaire.

8. La chimiothérapie ambulatoria dans la tuberculose pulmonaire est un boyen thérapeutique convenable, particulièrement dans la région où on ne dispose pas de capacités hospitalières suffisantes pour tous les malades atteints de tuberculose pulmonaire évolutif.

ZUSAMMENFASSUNGEN


2. Bei 48% und 33% aller untersuchten Kranken handelte es sich um mässige, beziehungsweise weit fortgeschrittene Krankheitsformen.

3. Die Sputumkonversionsrate betrug 37% und 38% nach 12 Monaten und nach 24 Monaten Chemotherapy.

4. Röntgenologische Besserung war erkennbar in 75% und in 80% nach 12, bezw. 24 Monaten Behandlung.

5. Es wird die Annahme ausgesprochen, dass adäquate Bettruhe von Wichtigkeit ist für solche Kranken mit Lungentuberkulose, die eine ambulante Chemotherapy erhalten.

6. Im allgemeinen konnte man mehr günstige therapeutische Effekte beobachten bei den weniger fortgeschrittenen, frischeren unbisher behandelten Fällen.

7. Es bestand kein großer Unterschied in dem Ergebnissen, die nach 12 und nach 24 Monaten Chemotherapy von 12 Monaten eine komplette auswertung notwendig sein.

8. Ambulante Chemotherapy bei Lungentuberkulose ist eine geeignet therapeutische Massnahme, besonders in Gegenden, in denen ausreichehende Anstaltunterbringung für alte aktiven Lungentuberkulöse-Kranken nicht zur Verfügung steht.

REFERENCES

1 Kinoshita, A. K.: Out Patient Care for Pulmonary Tuberculosis, Japan, Clinical Tuberculosis, June, 1956.