Original Article

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STATUS OF SHORT COURSE CHEMOTHERAPY UNDER NATIONAL TUBERCULOSIS PROGRAMME*

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Summary. **Short Course Chemotherapy (SCC) was introduced under the National Tuberculosis Programme (NTP) in 1983-85, on a pilot basis, in 18 districts of the country. Government of India started its extension in rest of the districts from 1986-87 onwards in a phased manner. SCC is provided only to smear positive patients, aged 15 years and above, irrespective of their previous history of treatment. Two types of regimen-an intermittent supervised regimen of 6 months' duration (Regimen A) and a self-administered oral regimen of 8 months duration (Regimen B)-are offered to the patients under SCC. By the end of 1992, 252 out of 390 (65%) District Tuberculosis Programmes (DTPs) in the country have been covered under SCC. While 248 DTPs under SCC are monitored by National Tuberculosis Institute (NTI), Bangalore, four are being monitored by Tuberculosis Research Centre (TRC), Madras. In the 248 SCC-DTPs monitored by NTI, only 47% of the implemented Peripheral Health Institutions (PHIs) on the average, and 75% of the total PHIs available in the districts are covered by SCC.**

Based on the received quarterly reports, the average overall efficiency in terms of sputum examination is more than 100% at District Tuberculosis Centres (DTC) and 67% at PHIs. The corresponding figures in respect of case detection efficiency are 83% and 51% at DTC and PHI levels respectively. Smear positivity rates in the SCC-DTPs are 14% at DTCs and 6% at PHIs. In all, 74,459 smear positive cases 49.4% of the total smear positive cases, diagnosed in the SCC-DTPs have been put on SCC regimens. A cohort analysis of the treatment results (for the cohort period January-December 1991) revealed that 45% of the patients put on Regimen A and 53% of those put on Regimen B achieved satisfactory level of treatment (i.e. ≥ 75% of expected drug collections). Among them and where the result of final follow up sputum examination was available, 90% of patients put on Regimen A and 96% put on Regimen B had become smear negative.

Introduction

The advent of SCC in the early 70's can be considered as a turning point in the evolution of chemotherapy of tuberculosis. It raised optimism among those in-charge of tuberculosis control programme, besides brightening the prognosis of patients suffering from tuberculosis. Enthused by the impressive results of controlled clinical trials with SCC in different parts of the world, the Government of India and Tuberculosis Research Centre (TRC), Madras, introduced SCC, on a pilot basis in 18 districts in 10 States, in two phases, between 1983 and 1985 to study its operational aspects. Subsequently, SCC was extended further under the National Tuberculosis Programme (NTP) in a phased manner. Initially, 44 districts were covered between 1983 and 1987 but by the end of December 1992, 252 districts had been covered.

The SCC regimens introduced were : (a) a fully supervised biweekly regimen of 6 months' duration - $2S_2H_2R_2Z_2/4H_2R_2$ (regimen A) and (b) a self administered oral regimen of 8 months' duration - 2EHRZ/6TH (Regimen B), with drugs to be collected on a fortnightly basis in the intensive phase of 2 months, and monthly in the continuation phase. Efficiency of the programme before the introduction of

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SCC was assessed to be 39%[1] in case-finding and around 31% for satisfactory treatment completion. The introduction of SCC was expected to improve the performance in terms of treatment outcome. The performance of the districts covered under SCC, along with the others, is being monitored by the NTI through periodic (quarterly/annual) reports.

Objective

This paper aims at providing the current status of the performance of SCC-districts in terms of implementation, reporting, performance of case-finding and treatment for the year 1992 and the treatment outcome of the patients' cohort for the year 1991.

Material and Methods

Four quarterly reports on case-finding and treatment activities received from 248 SCC districts each for the year 1992 and the annual report on treatment results achieved for the cohort period 1991 from 234 districts under SCC constitute the material for this paper. Only correct and complete reports were included for analysis : 603 quarterly reports out of 992 reports expected (about 61%) and only 89 (38%) out of the 234 expected annual reports on cohort analysis of treatment results have been considered. The application of tests of statistical significance has not been considered necessary.

Efficiency of a DTP is assessed by comparing its achievements with the expectations. The expectations of the various activities are as follows :

(A) SCC Implementation : The ultimate aim is to cover all the DTPs, in a phased manner, and complete coverage of all the implemented PHIs with SCC in each SCC-DTP.

(B) Reporting : Complete 100% reports received from both DTC and PHIs.

(C) Case Finding : (a) In respect of sputum examination and detection of smear positive cases, the expectation is calculated according to (i) Population aged 5 years and above (as per 1991 census, (ii) Prevalence rate of bacteriologically positive cases (0.4%), (iii) Action taking pattern by the TB patients (iv) Proportion of PHIs offering tuberculosis services and (v) Case-finding as well as case-holding achievements of a reasonably well performing DTP in the country.

(b) Sputum smear positivity rate : On the basis of experience, the expectation is fixed as 18% for DTC and 8% for PHIs.

It is expected, therefore, that in an average district with a population of 1.8 million, DTC detects 500 smear positive cases per year @ 18% of the total number of sputum examinations conducted and PHIs detect 2,000 smear positive cases @ 8% smear positivity based on the achievements of a reasonably well performing DTP. These expectations are slightly lower than the potentials which were estimated in the operational studies conducted at NTI[2,3].

(D) Initiation on SCC : The expectation is that 100% of the smear positives will be put on SCC.

(E) Treatment Outcome : (a) *Treatment Completion rate* is the percentage of patients completing 75% and above of the expected drug collections. Here, the expectation is 100% because a cure rate of 85%[4] and above can be achieved only when all the patients achieve the collection/consumption of ≥ 75% of the expected drug collections.

(b) *Cure rate* is the percentage of smear positive patients converted to negative status at the end of treatment period, out of those initiated on treatment. The expected cure rate is ≥ 85% among the newly diagnosed patients, based on the WHO guidelines[5].

The performance of DTPs under various activities is classified as good, satisfactory or poor depending upon the percentage ranges of efficiency achieved (Annexure).

Findings

A. SCC Implementation

(a) *DTPS* : Out of 390 DTPs in the country 252 (65%) have been covered under SCC. The 4 DTPs monitored by TRC, Madras were excluded leaving 284 DTP for analysis Gujarat, Tamil Nadu, Maharashtra, Andhra

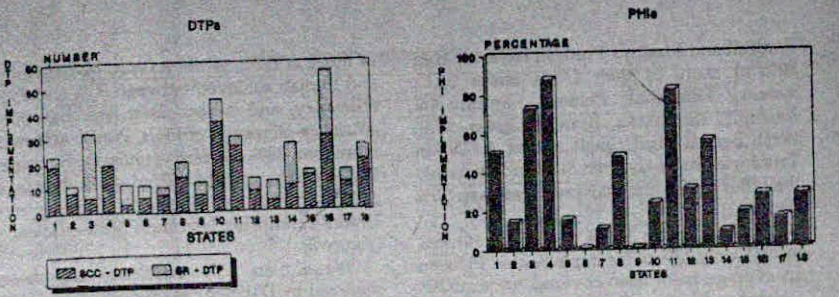

Fig. 1. Implementation under SCC-1992 – DTPs and PHIs
1. A.P.; 2. Assam; 3. Bihar; 4. Gujarat; 5. Haryana; 6. H.P.; 7. J & K; 8. Karnataka; 9. Kerala; 10. M.P.; 11. Maharashtra; 12. Orissa; 13. Punjab; 14. Rajasthan; 15. T.N.; 16. U.P.; 17. W.B. 18. SS & UTs

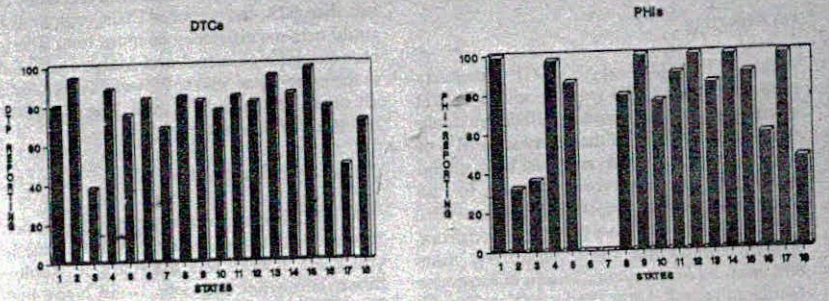

Fig. 2. Reporting in SCC-1992 DTPs and PHIs (Percentage)
Serial numbers indicate the same States as in Figure 1

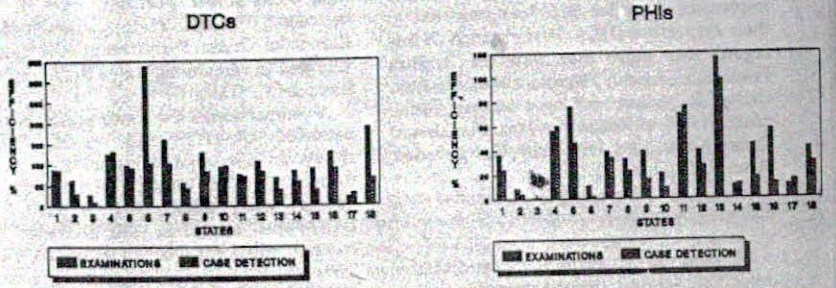

Fig. 3. Case finding efficiency, 1992
Sputum Examinations & Case Detection
Serial numbers indicate the same states as in Figure 1

Pradesh and Madhya Pradesh have covered 80% or more of their DTPs under SCC; Assam, Himachal Pradesh, Jammu & Kashmir, Karnataka, Kerala, Orissa, U.P. West Bengal, and Small States & Union Territories have covered 50% to 79% while the other states have covered less than 50% (Figure 1).

(b) *PHIs :* In the 248 SCC-DTPs monitored by NTI, only 47% of the implemented PHIs on an average have been covered under SCC. Gujarat and Maharashtra have covered more than 80% of their PHIs under SCC, Andhra Pradesh, Bihar and Punjab have covered between 50% and 79% while other States have covered less than 50% (Figure 1).

(B) Reporting

(a) *DTPs* : Out of 992 DTP quarterly reports expected, 785 were received at NTI amounting to 79% reporting efficiency. Only 603 reports (i.e. 77% of the received or 61% of the expected) have been analysed because the remaining reports were found to be inconsistent and/or defective. More than 90% of the DTP reports have been received from Assam, Punjab and Tamil Nadu, less than 80% from Bihar, Haryana, Jammu & Kashmir, Madhya Pradesh, Uttar Pradesh, West Bengal and Small States & Union Territories while the other States have reported in the range of 80%–90% (Figure 2).

(b) *PHIs* : Overall, 89% of the PHIs implemented under SCC had reported to their respective DTCs. Performance in this regard was more than 90% for Andhra Pradesh, Gujarat, Kerala, Maharashtra, Orissa, Rajasthan and West Bengal, in the range of 80% to 90% in Haryana, Punjab and Tamil Nadu, and less than 80% in other States/UTs (Figure 2).

(c) Case-Finding

(a) *Sputum Examination and Case-detection :* Overall, the efficiency in sputum examination is more than 100% at DTCs and about 67% at PHIs. Eleven out of the seventeen big States and all the small States & Union Territories achieved efficiency of 80% or more at DTC, while Assam, Maharashtra and Punjab achieved between 50% and 79% efficiency, and others even less than 50% efficiency. In respect of PHIs, Punjab achieved more than 80% efficiency, Gujarat, Haryana, Maharashtra, and Uttar Pradesh in the range of 50% to 79% and all the small States and Union Territories less than 50% efficiency (Figure 3).

Overall, an 83% efficiency has been achieved by DTCs in case detection and 51% by PHIs. Nine big States achieved more than 80% efficiency in case detection by DTCs, Maharashtra, Rajasthan and small States & UTs registered efficiency in the range of 50% to 79%, while all other States had efficiency of less than 50%. In respect of PHIs, only Punjab could achieve efficiency of more than 80% in case detection, Gujarat and Maharashtra fell in the category of 50% to 79% efficiency, while all other States & UTs had less than 50% efficiency of case detection (Figure 3).

(b) Smear Positivity Rate

In DTC, smear positivity rate is more than 18% in the States of Gujarat, Madhya Pradesh, and West Bengal, less than 10% in Assam, Bihar, Himachal Pradesh, Tamil Nadu and Small States & Union Territories, and in the remaining States in the range of 10% to 18%. In PHIs, the States of Gujarat, Maharashtra, Rajasthan and West Bengal registered more than 8.0% smear positivity rate. It was between 5.0% and 7.9% in Andhra Pradesh, Karnataka, Orissa, Punjab and Small States & UTs and in remaining States the figure was less than 5% (Table 1).

A comparison of the smear positivity rates between SCC-DTPs and non-SCC DTPs shows an appreciably higher rate in the former, both at DTCs and PHIs. At DTC, the average smear positivity is 14.1% in SCC DTPs and 11.6% in SR districts. The corresponding rates for PHIs are 6.1% and 3.5% respectively. Smear positivity rates in SCC-DTPs are generally higher than non-SCC DTPs of the same State (Table 1).

Initiation On SCC : Overall, 75,459 smear positive patients (i.e. 49.4% of the newly diagnosed smear positive cases) were put on

Table 1. *Smear positivity rates - 1992*

Sl No.	States/ UTs	DTPs with SR only			DTPs with SCC		
		DTCs	PHIs	DTPs	DTCs	PHIs	DTPs
1	2	3	4	5	6	7	8
1.	Andhra Pradesh	8.3	1.2	2.9	17.6	5.4	9.2
2.	Assam	6.3	2.3	4.4	8.4	3.5	6.3
3.	Bihar	9.2	0.8	4.0	6.1	4.5	5.9
4.	Gujarat	*	*	*	18.8	8.5	10.7
5.	Haryana	11.7	3.6	7.6	16.4	4.8	7.3
6.	Himachal Pradesh	5.4	3.-0	4.5	5.3	1.6	4.4
7.	Jammu & Kashmir	4.8	4.2	4.8	11.7	4.9	8.2
8.	Karnataka	8.2	7.4	7.7	13.6	5.6	6.9
9.	Kerala	12.0	2.9	6.1	11.5	3.2	6.7
10.	Madhya Pradesh	16.4	2.7	6.4	18.3	3.6	9.0
11.	Maharashtra	21.0	1.9	3.9	16.5	8.7	9.8
12.	Orissa	12.3	3.4	5.6	13.6	5.4	7.9
13.	Punjab	11.4	4.5	6.3	10.2	6.7	7.1
14.	Rajasthan	16.8	5.2	10.4	12.2	8.4	10.7
15.	Tamil Nadu	3.5	6.1	4.6	7.6	3.0	4.1
16.	Uttar Pradesh	10.4	4.0	5.5	12.6	1.8	5.3
17.	West Bengal	8.4	7.7	8.0	23.1	11.0	14.7
18.	Small States & UTs	8.6	1.6	5.2	6.5	5.7	6.0
	Total	11.6	3.5	5.8	14.1	6.1	8.0

* All DTPs are with SCC

SCC-2.8% under Regimen A and 46.6% under Regimen B (Figure 4). 33,604 patients were in DTCs (i.e. 52.6% of the cases diagnosed at DTCs) 2.6% under Regimen A and 50.0% under Regimen B with the percentage of patients put on SCC being more than 90% in Tamil Nadu and Bihar, 81% in Maharashtra and less than 80% in other States. In the PHIs, there were 41,855 patients (47% of the smear positive patients diagnosed at PHIs) 2.9% under Regimen A and 44.2% under Regimen B-(Figure 4) of whom the percentage of patients put on SCC was high in Bihar but less than 80% in other States but in some the number of patients put on SCC even exceeded the number of new cases detected (Figure 4).

(E) Treatment Outcome

(a) *Treatment Completion rate :* The smear positive patients diagnosed during the cohort period January to December, 1991 and having an equal opportunity for completing treatment by October, 1992 at the latest have been analysed. Out of the 234 SCC-DTP annual reports expected, only 120 (51.3%) were received and 89 (72.4%) of the expected reports could be analysed (38.0%). Of about

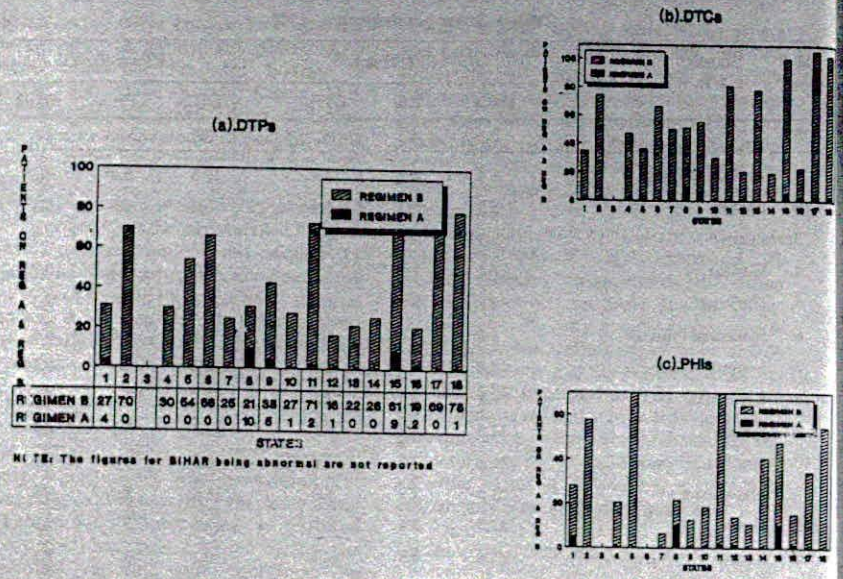

Fig. 4. Patients on SCC, 1992 (Percentages)
Serial numbers indicate the same States as in Figure 1

45,000 patients put on treatment in the 89 SCC-DTPs, the treatment completion pattern of only 36,281 patients was available (2,036 patients on Regimen A and the remaining 34,245 patients on Regimen B).

Out of 2,036 patients put on Regimen A, 44.5% collected consumed ^ 75% doses and could be considered to have completed a satisfactory level of treatment. Likewise, 53.2% of 34,245 patients put on Regimen B made ^ 75% of the expected collections.

With regard to Regimen A, only Karnataka and small States & UTs could achieve treatment completion of above 50% while all the other States achieved less than 50% treatment completion rate. As regards Regimen B, only Jammu & Kashmir achieved more than 75% completion rate. In Gujarat, Maharashtra, Punjab, Rajasthan, West Bengal and small States & UTs, the treatment completion rate was between 50% and 74% and all the other States had treatment completion rate of less than 50% (Table 2).

(a) *Cure Rate* : Out of the 2,036 smear positive patients on Regimen A, the results of smear examination at the end of chemotherapy were reported only for 498 (24.4%) patients. Likewise, out of 34,245 patients on Regimen B, results of smear examination were available only for 14,541 patients (42.4%). Under the circumstances, it has not been found possible to calculate the cure rate. In view of the impracticability of arriving at the cure rate, an alternative method is to calculate the cure rates from studies relating them to observed treatment completion rates. An overall assessment of States with regard to various activities is presented in Table 3.

Discussion

The introduction of SCC in NTP from 1986-87 onwards was an important milestone.

Table 2. *Report of cohort analysis-SCC regimens (patients diagnosed from Jan. to Dec. 1991)*

Sl. No.	States/ UTs	SCC DTPs	Report on cohort analysis			Regimen A		Regimen B	
			Received	Analysed	Analysed (%)	Pts. included	Completed %	Pts. included	Completed %
1	2	3	4	5	6	7	8	9	10
1.	Andhra Pradesh	19	15	13	86.7	391	47.3	4380	46.3
2.	Assam	8	8	6	75.0	0	–	378	43.9
3.	Bihar	6	1	0	–	–	–	–	–
4.	Gujarat	16	16	12	75.0	56	35.7	8732	56.1
5.	Haryana	2	1	1	100.0	0	–	25	32.0
6.	Himachal Pradesh	6	2	1	50.0	0	–	35	0.0
7.	Jammu & Kashmir	7	1	1	100.0	0	–	155	78.1
8.	Karnataka	14	11	11	100.0	911	53.0	1291	40.0
9.	Kerala	7	6	4	66.7	6	33.3	1190	43.4
10.	Madhya Pradesh	33	5	1	20.0	25	40.0	258	46.9
11.	Maharashtra	23	15	9	60.0	0	–	11869	56.1
12.	Orissa	7	4	4	100.0	140	29.3	1201	40.3
13.	Punjab	4	4	1	25.0	0	–	289	65.4
14.	Rajasthan	10	4	2	50.0	40	0.0	308	59.7
15.	Tamil Nadu	14	8	7	87.5	415	33.0	1885	48.6
16.	Uttar Pradesh	27	7	4	57.1	23	8.7	351	43.9
17.	West Bengal	11	3	3	100.0	14	28.6	1361	61.4
18.	Small States & UTs	20	9	9	100.0	15	66.7	537	56.8
	Total	234	120	89	72.4	2036	44.5	34245	53.2

The rate of coverage can be considered as fairly rapid in view of the fact that only 44 districts were covered under SCC between 1983-1987 and the number rose to 252 by the end of December, 1992.

The fact that only about 47% of the implemented PHIs in these 252 districts were covered under SCC is a matter of concern because the PHIs have to detect and treat around 80% of the cases in each district. The SCC coverage gets reduced to 35% (47% × 75%) taking into consideration that on an average only 75% of the available PHIs in a district are implemented to offer tuberculosis services. All the States except Gujarat, Maharashtra and Punjab need to intensify efforts to cover more PHIs in their districts with SCC.

Though reporting by PHIs to SCC DTCs (89%) was somewhat satisfactory, the reporting by SCC DTCs to higher level (only 79%) was inadequate. This may be due to lack

Table 3. *Assessment of SCC DTP activities-performance levels*

Sl. No.	State	Performance levels												
		Implementation		Reporting		Sputum exam		Case detection		Smear positivity		Patients put on SCC		Treatment completion
		DTC	PHI	DTC	PHI	DTC	PHI	DTC	PHI	DTC	PHI	DTC	PHI	DTP
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1.	Andhra Pradesh	A	C	B	A	A	C	A	C	B	A	C	C	C
2.	Assam	B	C	A	C	B	C	C	C	C	B	C	C	C
3.	Bihar	C	B*	C	C	C	C	C	C	C	B*	A*	A*	NR
4.	Gujarat	A	A	B	A	A	B	A	B	A	A	C	C	B
5.	Haryana	C	C	C	B	C	B	A	C	B	B	C	C	C
6.	Himachal Pradesh	B	C	B	C	A	C	A	C	C	C	C	C	C
7.	Jammu & Kashmir	B	C	C	C	A	C	A	C	B	A	C	C	A
8.	Karnataka	B	C	B	C	B	C	C	C	B	B	C	C	B
9.	Kerala	B	C	B	A	A	C	A	C	B	B	C	C	C
10.	Madhya Pradesh	A	C	C	C	A	C	A	C	A	A	C	C	C
11.	Maharashtra	A	A	B	A	B	B	B	B	B	A	B	C	B
12.	Orissa	B	C	B	A	A	C	A	C	B	B	C	C	C
13.	Punjab	C	B	A	B	B	A	C	A	B	B	C	C	B
14.	Rajasthan	C	C	B	A	A	C	B	C	B	A	C	C	B
15.	Tamil Nadu	A	C	A	B	A	C	B	C	B	A	C	C	B
16.	Uttar Pradesh	B	C	C	C	A	B	A	C	B	B	C	C	C
17.	West Bengal	B	C	C	A	C	C	C	C	A	A	A	C	B
18.	Small States & UTs	B	C	C	C	A	C	B	C	C	B	A	C	B

Note : (i) A = Good; B = Satisfactory; C = Poor; NR = Not Reported
(ii) For different performance levels, see ANNEXURE
(iii) *Based on very few reports.

of trained Statistical Assistants or diversion of trained staff because 23% of the reports were rejected for analysis due to defects/ inconsistencies. Therefore, the reported conclusion can be considered to represent only 61% of the SCC-DTPs. The annual reporting of cohort analysis of treatment results was still more deficient.

Considering DTCs, 11 big and all the small States & UTs, achieved an efficiency of more than 80% in respect of sputum examinations. This can be considered as good. While the States of Bihar and West Bengal with less than 50% efficiency need to intensity their efforts in subjecting the chest symptomatics to sputum examination, all other States should aim at the achievable 80% efficiency. The reported more than 100% efficiency is perhaps due to indiscriminate selection of cases for sputum examination (Figure 3).

As regards PHIs, the sputum examination performance of only Punjab was good, that of Gujarat, Haryana Maharashtra and Uttar Pradesh, satisfactory while that of all other States in need of vast improvement (Fig. 3).

Overall, the case detection efficiency was 83% at DTC, and only 51% at PHIs. At DTCs, the performance of Andhra Pradesh, Gujarat, Haryana, Himachal Pradesh, Jammu & Kashmir, Kerala, Madhya Pradesh, Orissa and Uttar Pradesh could be considered as good, that of Maharashtra, small States & UTs satisfactory and that of all the other States in need of great improvement. At PHIs, the efficiency of case-detection was alarmingly low in all the States except Gujarat, Maharashtra and Punjab. In Himachal Pradesh, Jammu and Kashmir, Kerala, Orissa, U.P. and Small States & UTs, the efficiency of case detection at DTCs was not commensurate with the high efficiency of sputum examination.

DTCs in 6 States could attain the expected rate of 18% and in all other States sputum positivity rate was variable, calling for an inquiry into the likely reasons. The performance of PHIs could be regarded as distressing in the sense that only 4 out of the 17 big States could achieve the expectation of 8% positivity. **Strengthening of the laboratory services, both at DTCs and PHIs and adequate supervision are the obvious needs. A higher percentage of smear positivity was noticed both at PHIs and DTCs of SCC-DTPs compare to SR-DTPs (Table 1) This needs to be viewed cautiously. The likely possibility of "motivated positivity" in the eagerness to put patients on SCC needs to be kept in mind (Table 1) and further investigated.**

Only 49.4%, on the average, of the smear positive patients diagnosed in DTPs were put on SCC-2.8% on Regimen A and 46.6% on Regimen B. **The low acceptability of Regimen A may perhaps be due to the inability of the patients to attend twice a week for supervised administration of drugs. It is also possible that staff opted for the operationally more convenient self-administered oral Regimen B.** The coverage of all PHIs with SCC needs to be intensified before extending SCC to other districts. In DTCs, the percentage of patients put on SCC was below 80% against the expectation of 100% in all the states except Bihar, Maharashtra, Tamil Nadu, West Bengal and Small States & UTs. In some States where the percentage exceeded 100%, possibly some old patients were also put on SCC. At PHIs, none of the States crossed 80% level except Bihar where the percentage was deceptively high, based on very few reports.

Out of the total of 75,459 patients put under SCC, 5,080 patients (6.7%) in the country had to change over to the long term standard regimen, mostly due to non-availability of SCC drugs. It is imperative to procure and supply adequate SCC drugs so that there is no interruption of treatment.

It was expected to achieve a higher treatment completion and consequently a higher cure rate with the use of SCC. This requires a prompt follow up smear examination at the end of chemotherapy and proper reporting of results for a given cohort period. Out of about 45,000 smear positive patients put on SCC regimens, during the cohort period Jan-Dec 1991 (in 89 SCC-DTP reports analysed), the final follow up smear results of only 15,039 patients who had completed satisfactory level of drug collection were available for analysis. In view of this

limitation, it was not possible to arrive at a reliable cure rate. However, among these 15,039 patients, 90% of patients on regimen A and 96% patients on Regimen B (not given in Table) had become smear negative. This result is almost in conformity with the findings of another study conducted by NTI[4]. It, therefore, calls for intensified efforts on the part of medical and para-medical personnel in DTPs to subject all the patients to smear examination at the end of chemotherapy, by proper motivation, and then proper recording and reporting of the results.

The alternative method of studying the treatment outcome through study of drug collection pattern is less reliable. None the less, out of about 45,000 patients put on treatment under SCC regimens, during 1.1.91 to 31.12.91 details of drug collections were available only for 36,281 patients; for about 20% the treatment cards were not available. Of these 36,281 patients, only about 45% and 53% of the patients put on Regimens A & B respectively had completed a satisfactory level of treatment. Besides small States & UTs, only one State could achieve a treatment completion rate of above 50% in respect of Regimen A while for Regimen B, only one State could achieve more than 75% treatment completion rate. Five big States and small States & UTs achieved completion rate in the range of 50%-74% and all other States were below 50% rate (Table 2). This gain is not substantial taking into consideration that even for standard chemotherapy, 41%[6] of the patients have satisfactory level of treatment completion and the aim of SCC is a cure rate of ≥ 85%.

The above conclusions drawn from smear conversions and treatment completion patterns derived from truncated reports cannot be generalised or extrapolated to all the SCC-DTPs. Regular periodic supervision by the higher level officers can go a long way in the overall improvement of all the activities under the DTP including their reporting which alone can lead to more realistic conclusions.

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Annexure

Assessment of DTP Activities

Activity	Performance Levels		
	Good	Satisfactory	Poor
1	2	3	4
Implementation			
(a) DTC	≥ 80%	50-79%	< 50%
(b) PHI	≥ 80%	50-79%	< 50%
Reporting			
(a) DTC	> 90%	80-90%	< 80%
(b) PHI	> 90%	80-90%	< 80%
Case-Finding			
(i) Sputum Examination :			
(a) DTC	≥ 80%	50-79%	< 50%
(b) PHI	≥ 80%	50-79%	< 50%
(ii) Case Detection :			
(a) DTC	≥ 80%	50-79%	< 50%
(b) PHI	≥ 80%	50-79%	< 50%
(iii) Smear Positivity Rate :			
(a) DTC	≥ 18%	10-17.9%	< 10%
(b) PHI	≥ 8%	5-7.9%	< 5%
Patients put on SCC			
(a) DTC	> 90%	80-90%	< 80%
(b) PHI	> 90%	80-90%	< 80%
Treatment outcome			
Percentage of patients completing ≥ 75% of drug collection/consumption.	≥ 75%	50-74%	< 50%

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RESULTS OF TREATMENT WITH A SHORT COURSE CHEMOTHERAPY REGIMEN USED UNDER FIELD CONDITIONS IN DISTRICT TUBERCULOSIS PROGRAMME

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Summary. **The treatment results of an unsupervised Short Course Chemotherapy (SCC) regimen used under conditions of District Tuberculosis Programme (DTP) are presented. The District Tuberculosis Centre (DTC) Kolar and six of its peripheral health institutions (PHI) formed the study area. No extra efforts except ensuring of adequate availability of drugs at the participating centres were made to obtain patients' compliance. In all, 584 smear positive tuberculosis patients were diagnosed during the study period but 28.3% of the patients could not be initiated on treatment with the chosen self-administered SCC regimen –2EHRZ/6TH (EH). Of the 382 put on treatment, only 33.2% completed over 75% drug collections in both intensive and continuation phases. The pattern of treatment compliance did not vary with the place of treatment, i.e. DTC or PHI. Irrespective of treatment compliance, nearly 72–77% of the patients attained smear negative status at the end of the period of treatment, there being no difference between PHI and DTC. However, deaths were higher in the PHI patients. This could be attributed to a significantly higher proportion of aged patients taking treatment at PHI than at DTC. Patients with drug sensitive bacilli had a higher rate of culture negativity (70%) as compared to those with drug resistant bacilli (48%). It was concluded that unsupervised SCC could give encouraging results in a DTP setting provided adequate drug supply was ensured.**

Introduction

Short Course Chemotherapy (SCC) is being gradually introduced in the District Tuberculosis Programme (DTP) since 1986. However, its initial acceptability, extent of treatment compliance, and the resulting efficacy of treatment, obtained under the organizational structure and functional efficacy of DTP appear to be important considerations which are making the results of treatment obtainable under DTP conditions vastly different from those under controlled clinical trial situations.[1,2] The earlier studies conducted by the National Tuberculosis Institute on the efficiency of SCC were done mostly in urban centres. The present study was meant to find out the treatment results of an SCC regimen in a largely rural DTP under the routine operational situations.

Objectives

The objectives of the study are to observe :

(*i*) Treatment compliance with a self administered SCC regimen in a DTC and its PHIs, and

(*ii*) Response to treatment assessed in terms of bacteriological status on completion of the period of treatment and relating the treatment response to the initial sputum culture and drug sensitivity status.

Material and Methods

The district of Kolar was selected since it is a typical Indian district in terms of its development, urban-rural demography as well as a predominantly dry land area. The centres selected for the study were District Tuberculosis Centre (DTC), Kolar and six of its peripheral health institutions (PHI) namely Gauribidnur, Bagepalli, Kaiwara, Chintamani, Nyamagondlu and Chikkaballapur. The period of intake of patients lasted from April, 1988 to June, 1989.

All patients aged 15 years and more, diagnosed freshly as sputum positive cases of tuberculosis on direct smear examination at DTC Kolar as well as the six PHIs were eligible for intake irrespective of the history of previous treatment. In all, 584 sputum positive patients were diagnosed, of whom 51 were

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not eligible for inclusion in the study. Of the remaining 533 patients, treatment with the SCC regimen could not be initiated in 151 (28.3%) because either the patient did not come back for result of examination (21.6%) or refused (6.8%) to be treated with the drug regimen offered (Figure in Appendix), leaving 382 patients for analysis.

Pre-treatment Investigations

Apart from the initial sputum smear examination done at the DTC/PHI just before the intake, one spot specimen of sputum was collected by the PHI/DTC staff at the time of initiation of treatment to be independently examined at the National Tuberculosis Institute (NTI) laboratory, by direct smear and culture. These specimens were stored at the respective centres in a refrigerator till collected by NTI messengers, once a week.

SCC Regimen

The study patients were offered the following self-administered 8-month oral SCC regimen (2EHRZ/6TH or 6 EH) which is also the regimen B recommended for DTP :

(*a*) *Intensive Phase*	2EHRZ			
Ethambutol	(E)	1g	All drugs consumed together, daily, for 2 months	
Isoniazid	(H)	300 mg		
Rifampicin	(R)	450 mg		
Pyrazinamide	(Z)	1.5 g		
(*b*) *Continuation phase*	6TH or 6EH in case of hypersensitivity to Thioacetazone			
Isoniazid	(H)	300 mg	Both drugs taken orally, together, daily, for 6 months	
Thioacetazone or Ethambutol	(T)	150 mg		
	(E)	800 mg		

Drugs were issued to the patients fortnightly for self-administration at home. The treatment period was eight months, without additional time granted to defaulting patients for completing the prescribed treatment, as is done in the DTP.

The supply of antituberculosis drugs in adequate quantities was ensured by NTI.

Management of Drug Default

A patient was considered a defaulter if he did not attend the centre on the due date for drug collection. First defaulter action was a letter posted on the due date itself or the next day. Second action was taken on the fourth day of default, as a second letter or home visit or message sent through a multipurpose health worker (MPW).

Adverse Reactions

The prescribed regimen was continued inspite of minor adverse reactions like itching, nausea, vomiting, etc., which subsided with or without symptomatic treatment. Major reactions like anaphylactic shock, jaundice, exfoliative dermatitis, etc. were managed by withdrawal of the offending drug.

Follow-up Examination

Two follow-up examinations, one at the end of the intensive phase and the other at the end of chemotherapy were to be done. Sputa collected at the respective centres were examined at the NTI laboratory by direct smear & culture and drug sensitivity tests were performed for positive cultures. While the spot/overnight sputum specimen at the end of "intensive phase" was collected within 15 days of the due date, the "treatment end" sputum specimen was collected between 15 days prior to and $1^1/_2$ months after the prescribed date of end of chemotherapy. In case of death, special efforts were made to obtain the history of previous treatment and the probable cause of death, from the relatives.

Results

Table 1 gives the age/sex distribution of the 382 patients analysed.

Table 2 gives the coverage for sputum follow up examination after the end of treatment. It is seen that 297 (77.7%) patients could be followed up, of whom 45 were dead (15.2%) and sputum was examined for 252 persons (84.8% of eligibles).

Level of Treatment Compliance

Table 3 shows the distribution of patients by levels of treatment compliance. A patient making less than 75% of drug collections due in the intensive phase as well as in the continuation phase was considered to be in the compliance level 1. Those making less than 75% of the due collections in intensive phase, but 75% and more in continuation phase were considered to be in level 2. Of the total

Table 1 *Distribution of patients by age and sex*

Age group	DTC			PHIs			Total		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
15-24	11 (12.8)	6 (15.4)	17 (13.6)	21 (12.1)	18 (21.4)	39 (15.2)	32 (12.3)	24 (19.5)	56 (14.7)
25-44	42 (48.8)	25 (64.1)	67 (53.6)	60 (34.7)	42 (50.0)	102 (39.7)	102 (39.4)	67 (54.5)	169 (44.2)
45+	33 (38.4)	8 (20.5)	41 (32.8)	92 (53.2)	24 (28.6)	116 (45.1)	125 (48.3)	32 (26.0)	157 (41.1)
Total	86	39	125	173	84	257	259	123	382

Difference in age structure of patients between PHI & DTC significant (X^2 = 6.93, df 2, P < 0.05)

Table 2 *Coverage for sputum examination at follow up on conclusion of treatment period*

	Initially sensitive patients	Total patients
Followed up	148(79.6)	297(77.7)
Examined	125(84.5)	252(84.8)
Dead	23(15.5)	45(15.2)
No response	38(20.4)	85(22.2)
Total	186	382

(Percentages in brackets)

382 patients who were initiated on treatment, 86 (22.5%) had made less than 75% of drug collections in the intensive phase, irrespective of the collections in the continuation phase. They (levels 1 and 2) were not eligible for analysis under the study. Therefore, their compliance with treatment in the continuation phase is not presented and patients in levels 1&2 have been combined in Table 3. Their follow up results at the end of treatment period have, however, been presented.

In the third level of treatment compliance, (i.e. ≥ 75% collections in intensive phase but < 75% of due collections in continuation phase), there were 169 patients (44.2%). Compliance level 4 comprised

Table 3 *Distribution of cases by level of drug collection & initial culture status*

Compliance level	Proportion of expected no. of collections made during 8 months		Number of patients			Total
	Intensive phase	Continuation phase	Sensitive	Resistant	Others	
1	<75%	–	44	20	22	86* (22.5)
2	<75%					
3	≥75%	<75%	79	43	47	169 (44.2)
4	≥75%	≥75%	63	30	34	127 (33.2)
Total			186	93	103	382

(Percentages in bracket)
*No. of patients not eligible for continuation phase-86 (see text)

patients who had collected 75% or more drugs due in both the intensive as well as continuation phases. Of the patients initiated on treatment, 127 (33.2%) had completed the fourth level of treatment compliance.

There is no difference in the treatment compliance patterns between the patients collecting drugs at the PHIs in comparison with those at the DTC (Table 4).

Bacteriological response related to treatment compliance levels

Table 4 presents the status of 382 patients at the end of treatment period, by place of treatment, compliance level, and bacteriological response as judged by sputum smear examination. For the Kolar district, out of the 382 patients, 36 could not be followed up and 45 were dead. Thus, sputum could be examined by direct smear only in 301. Of these, 228 were sputum negative after the completion of treatment period (75.7%); the proportion for DTC Kolar was 72.8% and for all PHIs taken together, 77.3%. However, considering that death is an unfavorable outcome of treatment, the proportions having favourable results i.e. those in whom sputum was negative, excluding only the non-response group from the denominator, 69.4% could be seen to have favourable result at the DTC compared to 64.3% at PHIs.

Considering sputum conversion on the basis of smear results, according to levels of treatment compliance for Kolar District as a whole 58.5% with compliance levels 1&2, 70.2% for level 3 and 88.7% with level 4 had converted. There were no differences between these proportions, i.e. treatment compliance at various levels and sputum conversion by these levels, between DTC & PHIs.

Also in Table 4, the deaths are shown according to place of treatment and compliance level of treatment. Five of the 125 (4%) patients undergoing treatment at Kolar DTC had died; only one of them was in the treatment compliance level 3 and none in level 4. Of the 257 undergoing treatment at PHIs, 40 had died (15.6%) and half of them were in levels 3&4. The proportion of deaths was higher at PHIs than at DTC but not high enough to affect the respective proportions of favourable results. The distribution of deaths by age and sex as proportion of patients put on treatment showed no difference (Table not put up).

Table 4 *Fate of patients at the end of treatment period by compliance levels & place of treatment*

Treatment compliance level	8th month sputum smear status				
	Neg.	Pos.	Dead	ND	Total
Kolar District					
1&2	31 (58.5)*	22	24	9	86 (22.5)
3	87 (70.2)*	37	20	25	169 (44.2)
4	110 (88.7)	14	1	2	127 (33.2)
Total	228 (75.7)*a	73	45	36	382 (100.0)
DTC					
1&2	11 (50.0)*	11	4	5	31 (24.8)
3	26 (66.7)*	13	1	10	50 (40.0)
4	38 (90.5)*	4	-	2	44 (35.2)
Total	75 (72.8)*b	28	5	17	125 (100.0)
PHIs					
1&2	20 (64.5)*	11	20	4	55 (21.4)
3	61 (71.8)	24	19	15	119 (46.3)
4	72 (87.8)*	10	1	-	83 (32.3)
Total	153 (77.3)*c	45	40	19	257 (100.0)

*Proportion among sputum examined after excluding deaths and not followed up
ND Not done
a,b,c : Proportion of favourable results (death being unfavorable outcome)
a-65.9 b-69.4 c-64.3

Bacteriological response according to treatment compliance level and drug sensitivity status.

Table 5 presents the bacteriological response to treatment at various levels of compliance according to drug sensitivity status at start of treatment. Out of 382 patients, the initial culture was positive only in 279, whose results are presented in Table 5. In the remaining 103 patients, culture was either not done

Table 5 *Bacteriological response at various levels of treatment compliance according to initial drug sensitivity*

Treatment compliance level	8th month culture status					
	Neg.	Pos-S	Pos-R	Dead	Not done	Total
Initially drug sensitive						
1 2	11	10	6	11	6	44
3	31	15	3	11	19	79
4	46	2	1	1	13	63
Total	88 (70.4)*a	27	10	23	38	186
Intially drug resistant						
1 2	6	1	4	7	2	20
3	12	3	11	5	12	43
4	11	1	11	-	7	30
Total	29* (48.3)*b	5	26	12	21	93
All	117 (63.2)*c	32	36	35	59	279**

*Proportion among sputum examined; ($P<0.05$)
a,b,c : *Proportion of favourable results (death being unfavorable outcome)
a-59.5
b-40.3 ($P<0.05$)
c-53.2
**Initial culture neg/contaminated/not done, excluded-103
S-Drug sensitive; R-Drug resistant

or was contaminated. However, 10 of the 103 patients were dead; 54 were culture negative; 13 were culture positive (resistant 9), and in 26 patients the follow-up examination could not be carried out at the end of treatment period (not on Table).

Of the 279 patients in whom pre-treatment culture was positive, 220 alone could be followed up (Table 5). Of the latter, 117(53.2%) were culture negative, 35(15.9%) were dead and 68(30.9%) were still culture positive at the end of the period of treatment (drug resistant 36). Therefore, unfavorable response was 46.8%; by leaving out the dead and non-response group from the denominator, 63.2% were found to have converted compared with 53.2% over all result.

Of the 186 initially drug sensitive patients, sputa could be cultured for 125 at the end of treatment period. Of them, 88(70.4%) were converted. However, the proportion of favourable results (in 88 out of 148 patients) fell to 59.5% when death was considered as an unfavourable result.

Among the initially resistant group of 93 patients, follow-up sputa could be examined for 60. Of them, 29 were culture negative at the end of treatment period (48.3%). Considering death as unfavourable result, 29 out of 72 patients (40.3%) had favourable results.

Major toxic and side effects were infrequent in the study; only 7 required stoppage of treatment due to these (1.8%) reactions.

Discussion

The present study was conducted to investigate the efficiency of a short course regimen, accepted for DTP, in terms of initial acceptance, treatment compliance and result of treatment in a typical Indian district. While carrying out the study, no interference was made by NTI research staff, either at the DTC or PHIs except that adequate drugs supply was maintained at the respective centres for the study period. Care was taken at the outset to explain to the programme staff the criteria of admission of patients to the study and other requirements. Therefore, the situation was similar to any DTP using short course regimens but lack of drug supply was not allowed to become a constraint.

Despite the methodology of the study having been fully explained to the participating medical officers, 28 patients otherwise eligible were excluded by them without valid reason and 23 were correctly excluded from 584 patients diagnosed during the period.

Of the remaining 533 patients, 151(28.3%) either did not come back to receive the results of investigations or refused the SCC regimen. It is not known why such a substantial proportion of patients behaved as they did. The place of treatment (DTC or PHI) did not matter because the proportions not initiated on treatment were 32.4% and 26.1% respectively (not on Table).

Of the 382 patients in whom the SCC could be initiated, 22.5%, 44.2% and 33.2% respectively complied with the treatment at levels 1 and 2, 3 and

4 respectively. There was no difference in the pattern of treatment compliance, whether the patient was treated at DTC or at PHIs (Table 4). The proportion of patients complying at level 4 was only about one third of the patients initiated on SCC, whether at the DTC or PHIs.

In spite of the low compliance at level 4, the sputum smear negativity achieved at the end of period of treatment, among those for whom sputa could be examined ranged between 73% and 77% (Table 4), irrespective of the level of compliance, initial drug sensitivity status, and whether the patients was treated at the DTC or PHIs.

In Table 5, it could be observed that the patients with drug sensitive organisms initially achieved a significantly higher rate of sputum culture negativity (70.4%), than those with drug resistant bacilli (48.3%). Further, among 49 out of 63 patients with sensitive organisms initially who completed level 4 of treatment and whose sputa could be examined, 46 were culture negative (93.8%). The corresponding figure for patients with drug resistant bacilli was only 47.8% (11 of 23). Thus, SCC can achieve good sputum culture negative status in patients with initial drug sensitive bacilli even in patients taking unsupervised but adequate treatment, i.e. the patients in level 4. Even the overall treatment result of 75.7% (Table 4), expressed as sputum smear negativity and without considering level of treatment compliance, is quite considerable. Besides, deaths were almost equal in both the sensitive and resistant groups (12.4% and 12.9% respectively). The results, though far short of the expectations raised by controlled clinical trials, are, nevertheless, favourable keeping in mind the operational conditions of the programme, where culture and sensitivity test are not applicable.

Deaths among patients put on treatment were higher at the PHIs (16%) compared to DTC (4%). However, considering that death is an unfavourable result of treatment, along with persistent sputum positivity among the patients followed up, the proportion of those who had favourable result, on smear examination, was similar for the DTC and the PHI, i.e. DTC : 69.4% and PHI : 64.3% (Table 4). The possible reason for higher death rate at PHIs despite similar drug compliance patterns observed at DTC and PHI is not clear. One possibility is that a significantly higher proportion of aged patients were on treatment at the PHIs than at the DTC (Table 1).

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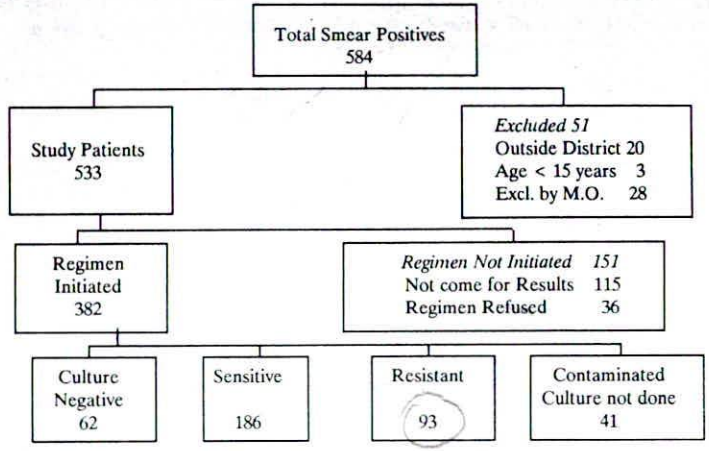
Appendix Table : Age-Sex distribution of smear positive patients

Age Group	DTC			PHI			Total		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
15-24	16 (12.9)	6 (9.8)	22 (11.9)	22 (9.5)	23 (19.8)	45 (12.9)	38 (14.7)	29 (16.4)	67 (12.6)
25-44	56 (45.2)	42 (68.9)	98 (53.0)	80 (34.5)	55 (47.4)	135 (38.8)	136 (38.2)	97 (54.8)	233 (43.7)
45+	52 (41.9)	13 (21.3)	65 (35.1)	130 (56.0)	38 (32.8)	168 (48.3)	182 (51.1)	51 (28.8)	233 (43.7)
15+	124	61	185	232	116	348	356	177	533*

*Excluding 51 not eligible for intake

APPENDIX FIGURE

Classification of smear positive patients diagnosed during April 1988 – June 1989



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NTP/DTP is a complex program requiring

System inputs — of PHI
uninterrupted drug supply of 4 drugs
microscopes + stains

Staff - trained / motivated
Health educ' - of pts / families / communities

Patient inputs
confidence in PHI / staff
understanding of the disease

NTI Bulletin 1995,31/1&2,1-6

DYNAMICS OF TREATMENT : UNDER VARIOUS CHEMOTHERAPY SITUATIONS IN THE TUBERCULOSIS CONTROL PROGRAMME*

P Jagota**

A review of the functioning of the District Tuberculosis Programme (DTP) in various states in India has revealed that these are functioning at different levels. At present neither case-finding nor the treatment activity can be considered as satisfactory.

Improvement in the functioning of the DTP can considerably improve case-finding but cannot possibly influence treatment results. Improvement in case-holding demands that its technical and organizational methodology will have to be improved to obtain better completion and thus better treatment efficacy. This is a decisive factor in the treatment delivery system if one were to avert a situation of already diagnosed cases continuing to form part of later prevalence cases, so aptly described by Grzybowski[1] as "epidemiological mess". I will take up this aspect in a little more detail later.

There have been two crucial breakthroughs in the field of anti- tuberculosis treatment in the recent past. The first one by Tuberculosis Chemotherapy Centre, Madras, in the fifties, was the demonstration of the efficacy of domiciliary chemotherapy which made it amenable to be self-administered. The second has been the development of Short Course Chemotherapy (SCC) in the seventies.

1) **Domiciliary treatment:** When domiciliary treatment with Standard Regimen (SR) was introduced, it needed a change from hospital to ambulatory system. From the sanatorium mode of treatment in vogue, one had to develop an 'organization' for treatment delivery. A machinery had to be built to place patients on treatment, to make it available to them as conveniently as possible, to work out a method of identification of defaulters and their retrieval, as well as to document treatment results and their effect on reducing pool of transmitters in the community. In other words, the system had to be developed to deliver public health and to measure its efforts. Individualistic medicine was to graduate into having an epidemiological consideration in it. Thus the concept of 'organization' and 'treatment delivery' came to the fore. This was a new system altogether. Advent of SCC did not necessitate a change in the system nor even a special reorganisation. This aspect has been stressed by Wallace Fox.[2] Why I choose to highlight it, is because one must realise that the organization for delivering effective SCC, like as it is in SR, means improving the organization for chemotherapy 'delivery', and not creating a new system. Thus delivery is crucial to both. To quote Fox, "it is vital to apply SCC in an efficient organizational frame work" and "the organizational aspect of chemotherapy cannot be over emphasised[2]".

2) **Short course chemotherapy**: Introduction of SCC is considered as a technical advancement of the seventies. Its epidemiological and sociological gains are supposed to be so far reaching that we for the first time, find ourselves talking of the possibility of ridding human bodies of the tubercle bacilli i.e., 'cure', instead of 'quiescence'. However, the efficient delivery of SCC is one of the pre-requisites to chemotherapy programme, much more crucial than it had been anytime in the past. The benefit of SCC is summarised below:[2]

Advantages of SCC

1. Reduction in the total duration of treatment:
   a) Less chronic toxicity
   b) Cost effective
2. Reduction in the work load on the health services.
3. Better attention for case-finding and case-holding.
4. Low relapse rate even after incomplete treatment.

To this we could also add and operational advantage of SCC that the outcome of chemotherapy at the end of treatment is not dependent on mid term follow-up. It is

* Dr P.V. Benjamin Memorial Oration delivered at 21st Andhra Pradesh Tuberculosis & Chest Diseases Conference held at S.V. Medical College, Tirupathi, on 9th July 1994.

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seen from a study at the NTI[3] that irrespective of sputum being negative or positive in two or three monthly follow-ups, in an overwhelming majority, cases would turn negative at the end of treatment.

Efficiency of Treatment Delivery

The all important requirement of SR or SCC thus is the efficiency of treatment delivery, not merely that 'efficacy' of the regimen. It must again be realised here that the difference is not for etymological distinction only. Nagpaul, as early as in 1972, has found it useful to distinguish between 'efficacy' and 'efficiency' of the chemotherapy of tuberculosis[4]. The former was defined by him as related to results obtained with drug regimens in controlled clinical trials, denoting the maximum that was attainable under favourable conditions. 'Efficiency', on the other hand, could be recognised as what could actually be achieved with varying technical, operational as well as organisational conditions, which could not essentially be controlled. He had recognised that 'efficiency' could vary widely, whilst 'efficacy' of a particular regimen would not. A gap between efficacy and efficiency of chemotherapy may be expected. It was 'fond hope' of the clinicians that whatever treatment results could be demonstrated in clinical trials, would be achieved among the patients treated by them. It was of course not so, since therapeutic efficacy was but only one aspect of the complexity of tuberculosis treatment.

Similarly, those who had conceptualised the DTP were shocked to realise that the term 'efficiency' under programme conditions was not a standardised unindimensional factor.

Potential & Performance

It was envisaged that National Tuberculosis Institute (NTI) should do operational studies to find out the maximum efficacy by following the recommendations laid down in the manuals for the District Tuberculosis Programme (DTP). The results of these studies were defined as **potential efficacy**, a parameter which could be used to compare the results of DTP units with wide range of conditions i.e., actual efficiency of individual DTP or **performance**.

It is important for us to understand the dynamics of treatment situations in the country, as it would enable us to adopt appropriate chemotherapy policy. Starting from a naturally occurring one, where no organised intervention was carried out to a fairly well organised situation with SCC in the programme.

The fate of the smear positive patients in various situations as given in table 1 was as follows:

In the sputum positive patients, initially diagnosed on a house to house survey under a situation where neither a communication was made to the patients on their diagnosis, nor any effort was made to treat them, 27.8% became culture negative, 30.2% died and 42% remained culture positive at the end of eighteen months. At the end of five years 18% were still culture positive and while about half of them were dead[5]. This study provided excellent data on the 'no intervention situation' referred to here as 'Natural Dynamics'. In a study conducted by NTI, treatment was given in accordance with the guidelines for DTP at an urban District Tuberculosis Centre (DTC). At the end of 12 months, irrespective of level of drug collection, 63% became culture negative, 10% died, 27%

Table 1 Fate of cases as reported in several operational studies on chemotherapy

Chemotherapy situations	At the end of chemotherapy			At the end of five years		
	Favourable outcome	Unfavourable outcome		Favourable outcome	Unfavourable outcome	
	Culture negative	Dead	Culture positive	Culture negative	Dead	Culture positive
Natural dynamics[5]	27.8	30.2	42.0	32.5	49.2	18.3
Potential of regimen						
SR at DTC[4,6]	63	10	27	59	30	11
SCC at DTC[7]	90	0	9	76.2	2.7	21.1
Performance Under DTP						
SCC[8]	66	13	21	–	–	–
Under DTC						
SR[9]	–	–	–	45.7	40.5	13.8
SCC	–	–	–	80.8	12.1	7.1

continued to be culture positive. The five year follow-up results of these patients showed 59% culture negative, 30% died and 11% remained culture positive[6].

Thus it could be seen that natural dynamics could be improved after introduction of SR on domiciliary basis. Potential of SCC was further studied under the same urban DT.[7]. It was seen from the table 1 again that at the end of treatment 90% became culture negative, none died and 10% were culture positive. The two year follow-up results of these patients showed that 76.2% remained culture negative, 2.7% died and 21.1% were culture positive.

The point to observe in such a comparative study is that as compared to SR, SCC was found to have a considerably lower fatality and nearly 20% improved negativity status on sputum examination at the end of the treatment as well as at the end of follow-up.

In another study on SCC, the performance was evaluated under DTP. The treatment was given in a real field situation where none of the organisational factors were controlled except drug supply. It was observed that at the end of 8 months of treatment period, 66% were culture negative, 13% had died and 21% continued to be culture positive[8]. The results were thus inferior to potential.

Further in a retrospective study on performance of SR and SCC in the same urban DTC at the end of five years 45.7% of the patients on SR were found to be culture negative, 13.8% were culture positive and 40.5% dead. While in patients treated with SCC concurrently 80.8% became culture negative, 7.1% remained culture positive and 12.1% died. The gap between potential and performance with SR was wide while with SCC it was 10% only.

It can be seen from table 2 that in spite of very good results with SCC, the overall results under a situation of this mix of SR and SCC were 54.8% culture negative, 12.2% culture positive and 33% dead.

Reasons for Fall in Efficacy

Attempts were made to find out the reasons for loss of efficacy of the chemotherapy. Two key variables i.e., non-compliance and initial drug resistance were found to be associated with it. The patients were classified into two groups according to treatment status.

i) **Adequately treated group:** Those who were on SR and took 80% or more of the prescribed treatment (level 4 treatment). In case of SCC it was 75% or more.

ii) **Inadequate treated group:** Patients who took less than 80% on SR and less than 75% on SCC (level 1-3).

In the potential study on SR[4] the outcome according to the treatment status as seen in table 3 was as follows: those who took adequate treatment (level 4) irrespective of initial sensitivity status, 77.6% became culture negative, 20.5% remained positive and 1.9% dead, while in the other group with inadequate treatment 46.4% were culture negative, 34.7% remained culture positive and 18.9% were dead .

Similar observations were made on SCC from the DTP study[8] of the patients who took 75% of treatment (level 4); as seen from table 4, 88% became smear negative, 1% died and 11% remained positive, while in patients having less than 75% of treatment (level 1-3) only 53.4% became negative, 26.7% remained positive and 20% died[8]. Thus the loss of efficacy of regimens was mainly due to inadequate treatment.

Similar observations were made from another study on performance[9]. As per table 5, the patients on SR who had inadequate treatment, about half of them were dead after 5 years indicating that death was a major outcome.

The unfavourable outcome was mainly due to poor compliance by the patients on SR. It can be seen from the table that majority of the SR patients (79.5%) were lost from treatment, while those on SCC, only about 30% were

Table 2 Result according to SR and SCC mix

Regimen	Ratio SR SCC mix	No. of patients	Results after five years		
			Culture negative %	Positive %	Dead %
SR	80	368	45.7	13.8	40.5
SCC	20	130	80.8	7.1	12.1
Total SR+SCC	100	498 (100)	54.8	12.2	33.0

Jogota P et al: Ind J Tub 1994,41,223

Table 3 Treatment results at the end of 12 months according to level of treatment taken

Treatment group	Total	Culture negative %	Culture positive %	Dead %
Aquate ≥ 80% (level 4)	210	77.6	20.5	1.9
Inadequate < 80% (level 1-3)	196	46.4	34.7	18.9
Total	406 (100)	62.6	27.3	10.1

Nagpaul DR: WHO/TB/73.99, 1972

Table 4 Fate of patients on a SCC regimen at the end of treatment by level of compliance

Treatment completed	Outcome at the end of 8 months							
	Total	Smear status				Dead		Not done
		Negative		Positive				
		No.	%	No.	%	No.	%	
Adequate treatment ≥ 75 % Level 4	127	110	88.0	14	11.0	1	1.0	2
Inadequate treatment < 75% Level 1-3	255	118	53.4	59	26.7	44	19.9	34
Total	382	228	65.9	73	21.1	45	13.0	36

Chaudhuri K et al, Ind J Tub 1993 40/2, 83-89

Table 5 Results at the end of 5 years according to treatment status and regimen

Regimen and treatment status		No.	Culture negative %	Dead %	Culture positive %
SR	Completed	76	75.0	6.6	18.4
	Lost	292	38.0	49.7	12.3
	Total	368	45.7	40.5	13.8
SCC	Completed	90	86.7	9.8	3.5
	Lost	40	67.5	17.5	15.0
	Total	130	80.8	12.1	7.1

Jagota P et al; Ind J Tub 1994, 41, 223

lost from treatment. This helped in reducing the overall loss of patients from treatment marginally, as the number of patients treated with SCC were probably less.

The patients with initial drug resistant organisms had less favourable outcome in comparison with patients having sensitive organisms[4].

It will not be out of place here to report Grzybowski's observation on Chingleput BCG Trial as seen from table 7, where all the cases detected during each survey were treated with SR by the general health services. Treatment was so ineffective that out of total cases found in the fifth survey, only 29% were new and the remaining 71% were old cases detected during previous rounds, over a period of 12 1/2 years.

Table 6 Regimenwise treatment completion pattern of smear positive patients treated at urban district tuberculosis centre

Primary treatment	Number	Completed (%)	Lost (%)
SR	370	76 (20.5)	294 (79.5)
SCC	132	92 (69.7)	40 (30.3)
SR + SCC	502	168 (33.5)	334 (66.5)

Jagota P et al; Ind J Tub (accepted for publication)

Table 7 Proportion of culture positive old cases among patients found at fifth round of Chingleput BCG trial (after 12 1/2 years)

Status at previous round	No.	%
Culture positive	473	61
Active on X-ray	77	10
Normal X-ray	228	29
Total	778	100

Grzybowski S: Bull IUATLD 1991, 66, 193

We thus now have a replica of the situations commonly seen at an average DTP in India. Therefore, when computing the results it could be seen from table 8 that the patients who were treated with SR and were lost from treatment had fate exactly similar to the natural dynamics and as seen from table 5 patients belonging to SR completed group had results very near to the trial efficacy. Compared to SR, SCC was found to have a considerably lower fatality and nearly 20% improved negativity by culture on sputum examinations. Much more organisational effort is necessary to ensure compliance in patients on SR than on SCC. Moreover, results of patients lost on SCC were not as unfavourable as seen in the SR lost patients. These factors tilt the balance overwhelmingly in favour of SCC as the regimen of choice, not only for the clinicians but for public health use. There are some other decisive factors related to efficient treatment delivery system. One of them is availability of anti tuberculosis drugs, at all levels, at all times. This can be achieved by providing required funds and having indigenous production of the drugs. The other factor which is equally important to remember is that there is no likelihood of getting a new anti tuberculosis drug in the near future. Hence strengthening of the delivery system is the only way to get better results from the existing regimens.

Chakraborty et al (1992) in their model on variable efficiency of the DTP as a system showed that not only treatment results would differ depending on the

Table 8 Fate of smear positive patients in two different situations

Chemotherapy situation	Fate at the end of five years		
	Culture negative %	Culture positive %	Dead %
Natural dynamics	32.5	18.3	49.2
Performance			
SR lost group	38.0	12.3	49.7

SR lost group 38.0 12.3 49.7

operational efficiency of the treatment delivery system, but would also directly correlate with the case-finding efficiency[10]. Efforts to change the treatment efficiency only through selected augmented inputs, without improvement in case-finding efficiency, is hardly the way to control tuberculosis. However, whether a new system is to be developed for organised treatment administration under supervision, as distinct from the current system and practice of an organised treatment delivery, requires further research. Alternatively, it will be ideal to administer every dose under supervision to ensure the achievement of maximum efficiency. Revised strategy being organised currently in several parts of India will show whether or not the expectation for maximum efficiency is something more appropriate to remain enshrined on fungoid parchments.

To conclude, the SR incomplete treatment group had a serious outcome. the overall results in this group was almost similar to natural dynamics itself. Organised treatment delivery is thus of paramount importance, whether the treatment regimen is SR or SCC. When only a small proportion of patients in the community are put on SCC, its epidemiological impact could be minimal, even with the high cure rate.

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Points to Remember While Entering Treatment Outcome Results in Treatment Cards

A patient is said to have:

COMPLETED TREATMENT

- if a smear positive patient has completed the required number of drug collections but final follow-up smear result is not available.
- a smear negative extrapulmonary patient has completed the required number of collections.

CURED

- if a smear positive patient has completed treatment and is smear negative at the end of treatment.

LOST

- if the patient has not collected drugs for more than one month from the due date.

TRANSFERRED

- if transferred to another district.

FAILED TO TREATMENT

- if the smear is positive at the end of treatment also.

TREATMENT STOPPED

- if treatment stopped by Medical Officer due to adverse reaction or change in diagnosis.

DEAD

- if dies during treatment period.

Source: **National Tuberculosis Institute, Bangalore: Manual for Peripheral Health Institutions, ED-4, Bangalore, NTI, 1994.**