APEC CONFERENCE ON PREVENTION, CONTROL AND CARE FOR MDR-TB AND SUPPLY OF 2nd-LINE ANTI-TB DRUG

CHINESE TAIPEI

Provided by
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An Integrated Patient-centered MDR-TB Program Results in Favorable Outcomes

Background

The challenge of MDR-TB

- High mortality rates and loss to follow-up for MDR-TB treatment
- In an ageing population with a high proportion of comorbidities

Objective

To evaluate the hospital-initiated integrated multidisciplinary patient-centered management program for MDR-TB patients

Methods

Taipei MDR-TB consortium

- Wan-Fang Hospital-initiated consortium (5 general hospitals in Taipei area)

MDR-TB patients

- All the pulmonary MDR-TB patients in Taipei area (referred from public health system)

Enrolled period

- May 2007 ~ April 2013

Exclusion criteria

- More than 3 months treatment before enrollment (21 cases: 90.5% treatment success)
- Under 20 y/o (10 case: 100% treatment success)
- Transfer out (2 foreigners)

Integrated multidisciplinary patient-centered care

- Led by experienced pulmonary specialists
- Designated diligent case managers
- Cooperative and integrated medical groups
- Adopting individualized regimens
- Initially received in-patient treatment, followed by outpatient DOT in the community

The DOTS-plus mode

Allocation criteria

- TB history, cognition of disease, disease severity and sputum status, family support and patient's willingness

The Supporter (S-DOT) group

- Supporters visit the patients at prearranged time

The videophone (V-DOT) group

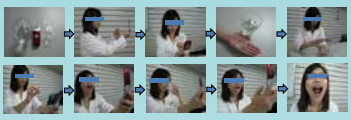
- Patients call the nurse at about prearranged time at anyplace
- All pills swallowed in view of the mobile videophone

The Mixed-DOTS group

The hospitalized/nursing home group

Treatment outcome evaluation

- 30 months after commencement of treatment



Conclusions

1. The hospital-initiated treatment consortium adopting individualized regimens with an integrated multidisciplinary patient-centered management program can result in favorable outcomes
2. The age group older than 65 years and comorbidities with cancer or DM were associated with unfavorable outcomes
3. Mobile videophones could be used as an effective modality in selected cooperative MDR-TB patients

Results

Table 1. Characteristics of 188 MDR-TB patients

	Total	S-DOTS	V-DOTS	Mixed-DOTS	Hospitalized/ Nursing home	P-value (S- vs. V-)
	n=188(%)	n=130(%)	n=45(%)	n=2(%)	n=11(%)	
Sex						0.10
Male	132(70.2)	95(73.1)	27(60.0)	2(100)	8(72.7)	
Female	56(29.8)	35(26.9)	18(40.0)	0(0)	3(27.3)	
Age, yrs	50.6±17.2	52.5±16.6	40.5±14.7	59.0±7.1	67.9±14.0	0.04
<65	146(77.7)	100(76.9)	41(91.1)	2(100)	3(27.3)	
≥65	42(22.3)	30(23.1)	4(8.9)	0(0)	8(72.7)	
BMI	21.1±3.9	21.3±4.0	21.3±3.6	23.1±3.1	17.3±2.6	0.91
<18.5	41(21.8)	25(19.2)	9(20.0)	0(0)	7(63.6)	
≥18.5	147(78.2)	105(80.8)	36(80.0)	2(100)	4(36.4)	
TB history						0.42
New	104(55.3)	69(53.1)	27(60.0)	2(100)	6(54.5)	
Retreated	84(44.7)	61(46.9)	18(40.0)	0(0)	5(45.5)	
Sputum smear						0.87
Negative	90(48.1)	62(48.1)	21(46.7)	2(100)	5(45.5)	
Positive	97(51.9)	67(51.9)	24(53.3)	0(0)	6(54.5)	
Cavity lesion on CXR						0.88
Yes	65(34.6)	45(34.6)	15(33.3)	1(50.0)	4(36.4)	
No	123(65.4)	85(65.4)	30(66.7)	1(50.0)	7(63.6)	
HBsAg						0.44
Yes	21(11.1)	17(13.3)	4(8.9)	0(0)	0(0)	
No	165(87.8)	111(86.7)	41(91.1)	2(100)	11(100)	
Anti-HCV						0.24
Yes	18(9.7)	13(10.2)	2(4.4)	2(100)	1(9.1)	
No	168(90.3)	115(89.8)	43(95.6)	0(0)	10(90.9)	
Comorbidities						
DM	57(30.3)	44(33.8)	8(17.8)	0(0)	5(45.5)	0.04
Hypertension	43(22.9)	35(26.9)	5(11.1)	0(0)	3(27.3)	0.03
Heart disease	16(8.5)	14(10.8)	0(0)	0(0)	2(18.2)	0.02
Cancer	14(7.4)	11(8.5)	0(0)	0(0)	3(27.3)	0.04
CKD	10(5.3)	7(5.4)	2(4.4)	0(0)	1(9.1)	0.81
COPD	10(5.3)	9(6.9)	0(0)	0(0)	1(9.1)	0.07
Liver disease	9(4.8)	6(4.6)	1(2.2)	1(50.0)	1(9.1)	0.48
Drug Resistance						
Simple MDR	144(77.0)	102(78.5)	31(70.5)	2(100)	9(81.8)	0.46
Pre-XDRo	28(15.0)	18(13.8)	8(18.2)	0(0)	2(18.2)	
Pre-XDRi	13(7.0)	8(6.2)	5(11.4)	0(0)	0(0)	
XDR	2(1.1)	2(1.5)	0(0)	0(0)	0(0)	
Outcome*						0.19
Favorable	166(88.3)	117(90.0)	44(97.8)	2(100)	3(27.3)	
Unfavorable	22(11.7)	13(10.0)	1(2.2)	0(0)	8(72.7)	

Unfavorable outcome: Death: 14 (TB-related:1; Not-TB-related:13), Failure:3, Default:1, Transfer: 4 (refused DOTS, complete treatment)

Table 2. The characteristics and outcomes of MDR-TB patients: univariate analysis

	Total (n=188)	Treatment outcome		p value
		Favorable (n=166, 88.3%)	*Unfavorable* (n=22, 11.7%)	
Sex				0.784
Male	132(70.2)	116(87.9)	16(12.1)	
Female	56(29.8)	50(89.3)	6(10.7)	
Age, yrs				
<65	146(77.7)	139(95.2)	7(4.8)	<0.001
≥65	42(22.3)	27(64.3)	15(35.7)	
BMI				
<18.5	41(21.8)	32(78.0)	9(22.0)	0.021
≥18.5	147(78.2)	134(91.2)	13(8.8)	
TB history				0.322
New	104(55.3)	94(90.4)	10(9.6)	
Retreated	84(44.7)	72(85.7)	12(14.3)	
Sputum Smear				0.471
Negative	90(48.1)	81(90.0)	9(10.0)	
Positive	97(51.9)	84(86.6)	13(13.4)	
Cavity lesion on CXR				0.851
Yes	65(34.6)	57(87.7)	8(12.3)	
No	123(65.4)	109(88.6)	14(11.4)	
Comorbidities				
DM				0.033
Yes	57(30.3)	46(80.7)	11(19.3)	
No	131(69.7)	120(91.6)	11(8.4)	
Hypertension				0.601
Yes	43(22.9)	37(86.0)	6(14.0)	
No	145(77.1)	129(89.0)	16(11.0)	
Heart Disease				0.195
Yes	16(8.7)	13(81.2)	3(18.8)	
No	172(91.3)	153(89.0)	19(11.0)	
CKD				1.000
Yes	10(5.3)	9(90.0)	1(10.0)	
No	178(94.7)	157(88.2)	21(11.8)	
COPD				0.097
Yes	10(5.3)	7(70.0)	3(30.0)	
No	178(94.7)	159(89.3)	19(10.7)	
Cancer				<0.001
Yes	14(7.4)	5(35.7)	9(64.3)	
No	174(92.6)	161(92.5)	13(7.5)	
Drug Resistance				0.267
Simple MDR	144(77.0)	125(86.8)	19(13.2)	
Pre-XDR and XDR-TB	43(23.0)	40(93.0)	3(7.0)	
DOTS-plus*				<0.001
S-DOTS	130(69.1)	117(90.0)	13(10.0)	
V-DOTS	45(23.9)	44(97.8)	1(2.2)	
Mixed-DOTS	2(1.1)	2(100)	0(0)	
Hospital/Nursing	11(5.9)	3(27.3)	8(72.7)	

*S-DOTS vs. V-DOTS: p=0.192

Table 3. The characteristics and outcomes of MDR-TB patients: multivariate analysis

Factors	Treatment outcome		Crude OR	95% CI	P- value	Adjusted OR	95% CI	P-value
	Favorable (%)	*Unfavorable* (%)						
Age, yrs					<0.001			<0.001
<65	139(95.2)	7 (4.8)	1			1		
≥65	27(64.3)	15 (35.7)	0.06	0.02-0.18		0.01	0.03-0.33	
BMI					0.025			0.073
<18.5	32(78.0)	9(22.0)	1			1		
≥18.5	134(91.2)	13(8.8)	3.35	1.22-9.17		3.13	0.90-10.85	
DM					0.037			0.031
Yes	46(80.7)	11 (19.3)	1			1		
No	120(91.6)	11 (8.4)	2.61	1.06-6.43		3.69	1.13-12.11	
Cancer					<0.001			<0.001
Yes	5(35.7)	9(64.3)	1			1		
No	161(92.5)	13(7.5)	22.29	6.51-76.32		14.18	3.44-58.45	

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CHINESE TAIPEI

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Molecular epidemiology of multidrug-resistant tuberculosis in three aboriginal villages of Hualien county in Eastern Chinese Taipei

Introduction

Multidrug-resistant tuberculosis (MDR-TB) is an important global public health issue. A high proportion of MDR-TB cases occurred among the aboriginal peoples of eastern Chinese Taipei.

Aims

Our aim was to investigate the transmission of MDR-TB in three aboriginal villages of Hualien county in eastern Chinese Taipei. The three aboriginal villages cover a total area of 3,281.7 km2 (9.15% of Chinese Taipei), but the population (28,183) accounts for only 0.12% of the total population in Chinese Taipei. (Fig 1)

Methods

All MDR-TB patients enrolled from January 2007 to December 2015 in three aboriginal villages of Hualien county were included. Spoligotyping and MIRU-VNTR were applied in identifying clustered pattern strains of MDR-TB.

Results

All MDR-TB patients (73) had isolates for genotyping. Spoligotyping identified the Beijing strain as the predominant genotype (n=47, 64%), followed by Haarlem H3 (n=19, 26%), T1 (n=1, 1%). Six (8%) isolates did not match any spoligotype in the spolDB4 data base. We have determined that 19 (26%) isolates were judged to have a unique pattern and 54 (74%) were clustered pattern strains (classifying into 6 clusters). (Fig 2)

The largest cluster (E cluster) belonged to the Beijing genotype and included 25 cases, 11 of whom lived in the same community (Shilin township) of 1,346 inhabitants with close contacts (relatives, neighbors or friends). (Fig 4)

The second largest cluster (F cluster) belonged to the Haarlem H3 genotype and comprised 19 patients, 18 of them lived in another community (Hechung township) of 470 inhabitants with close contacts (relatives, neighbors or friends). (Fig 3)

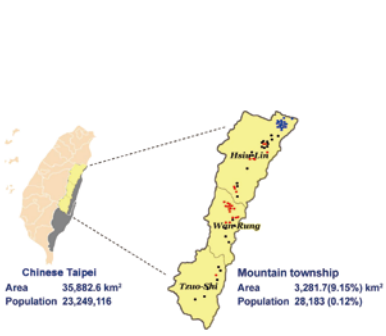

Fig.1 The map of three aboriginal villages of Hualien county in eastern Chinese Taipei and distribution of MDR-TB patients. E cluster – red dots. F cluster – blue dots.

Fig.3 The map of 18 cases of F cluster lived in the Hechung township.

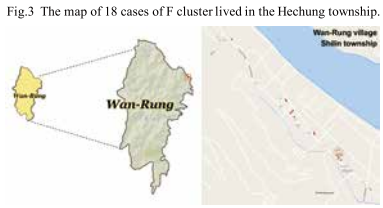

Fig.4 The map of 11 cases of E cluster lived in the Shilin township.

All 73 MDR-TB patients in three aboriginal villages were enrolled in the DOTS-Plus program. Six cases were still in treatment, and among 67 patients with final outcomes, 53 (79%) were treated successfully. The prevalence of MDR-TB patients improved dramatically over the last nine years. (Fig 5)

Conclusion

The proportion of MDR-TB patients with a clustered pattern strain in three aboriginal villages of Hualien county in eastern Chinese Taipei was very high.

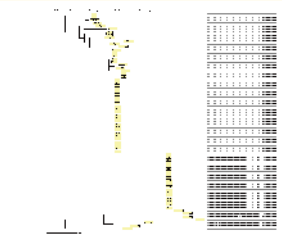

Fig.2 Dendrogram of 73 MDR-TB patients analyzed using spoligotyping and the MIRU-VNTR method.

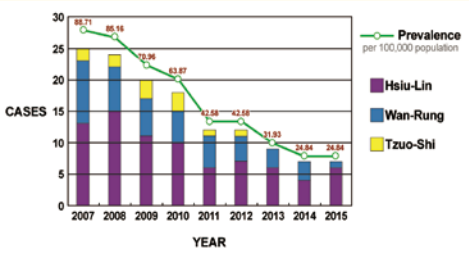

Fig.5 The prevalence of MDR-TB patients in three aboriginal villages in past nine years.

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Improved treatment outcome of MDR-TB in eastern Chinese Taipei: reducing default rate by DOTS-Plus

Introduction

Multidrug-resistant tuberculosis (MDR-TB) is an increasing global problem. Meta-analysis by Orenstein et al. of treatment outcome of MDR-TB worldwide was: 62% successful, 11% dead and 12% defaulted. Report by Chiang et al. about treatment without DOTS-Plus showed an outcome of 299 MDR-TB patients in Chinese Taipei as follows: 51.2% treatment success, 9.4% death, and 29.1% default.

Aims

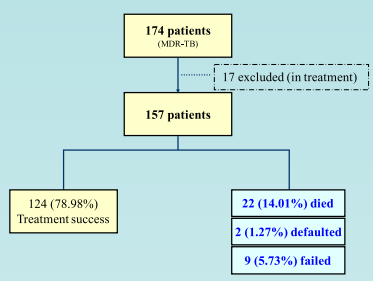
Our aim was to assess treatment outcome of MDR-TB patients after introduction of "DOTS-Plus strategy" in eastern Chinese Taipei, following WHO guidelines.

Methods

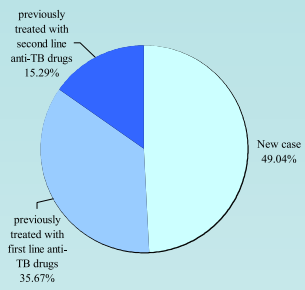
We reviewed all patients who began treatment with DOTS-Plus regimens for MDR-TB in eastern Chinese Taipei, between May 1st, 2007 and April 30th, 2016.

Results

Out of a total of 174 bacteriologically confirmed MDR-TB cases, 17 were still under treatment. Among 157 patients with final outcomes, 77 (49.04%) were new cases, 56 (35.67%) have been previously treated with first-line anti-TB drugs, 24 (15.29%) with second-line drugs. The mean age was 50.2 years (range of 12 to 93) and 114 (72.61%) were male. Six (3.82%) patients received surgical intervention. Finally, 113 (71.97%) patients were cured, 11 (7.01%) completed therapy, 22 (14.01%) died, 2 (1.27%) defaulted, treatment failed in 9 (5.73%) and treatment success was78.98%.



May 1st, 2007 ~April 30th, 2016



	Success	Death	Failed	Default	Transfer out	Total
Chinese Taipei [2] (Before DOTs-plus)	153 (51.20%)	28 (9.40%)	31 (10.40%)	87 (29.10%)	0 (0.00%)	299
Eastern Chinese Taipei (After DOTs-plus)	**124 (78.98%)**	**22 (14.01%)**	**9 (5.73%)**	**2 (1.27%)**	**0 (0.00%)**	**157**

Conclusion

Treatment success rate for MDR-TB patients in Eastern Chinese Taipei has improved since implementing "DOTS-Plus regimen" in May 2007 compared not only to Chinese Taipei´s prior rate but also to world-wide data. The default rate was reduced from 29.1% to 1.27% in Chinese Taipei, with world-wide data at 12%.

Treating MDR-TB patients under "DOTS-Plus regimen" can improve the treatment success rate in Eastern Chinese Taipei, and especially reduce default rate.

Default Rate		
kim et al	(Korea) [3]	32.20%
Chiang et al	(Chinese Taipei) [2]	29.10%
Brust et al	(South Africa) [4]	21.00%
Keshavjee et al	(Russia) [5]	20.00%
Palmero et al	(Argentina) [6]	19.90%
Mitnick et al	(Peru) [7]	19.00%
Singla et al	(India) [8]	18.00%
Malla et al	(Nepal) [9]	17.00%
Ferrara et al	(Italy) [10]	16.60%
Lin et al	**(this study)**	**1.27%**

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CHINESE TAIPEI

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Success in using bedaquiline, linezolid,clofazimine, and meropenem as part of treatment in extensively drug-resistant Mycobacterium tuberculosis (XDR-TB) cases

BACKGROUND

Current treatment for extensively drug-resistant mycobacterium tuberculosis (XDR-TB) is facing challenges with the development of second-line drug resistance. The adequate drugs are limited and with poor outcomes. We applied bedaquiline, linezolid, clofazimine, and meropenem as part of intensive treatment for XDR-TB or pre-XDR-TB patients.

METHODS

Patients with persistent positive sputa after a prolonged use of second line drugs and a lack of effective anti-TB drugs and/or treatment intolerance were included. A regimen of bedaquiline, linezolid, clofazimine ,and meropenem plus other anti-TB drugs was applied depending on the individual patient's drug susceptibility test and at least 7 effective drugs were used per patient. Intravenous drugs were given until the patient's sputa converted to negative for 6-9 months. Clinical, epidemiological and microbiological characteristics of subjects were collected. Drug tolerance, side effects and treatment outcomes were also recorded.

RESULTS

Five patients (3 XDR-TB and 2 pre-XDR-TB) were eligible and included in this study. The mean age of the subjects was 50. All patients had resistance to isoniazid, rifampin, ethambutol, streptomycin, levofloxacin, olfoxacin, and rifabutin. During the treatment, side effects inclulding dizziness, nausea, anemia, peripheral neuropathy, hypokalemia, poor appetite, rash, skin dark pigmentation, and thrombocytopenia were noticed, however, all of these were managed by supportive medication or cessation of all anti-TB medication for one to three days then rechallenging the regimen or reducing the linezolid dosage from 600mg to 300mg daily. The average sputum cultures converted was 55.6 days. All five patients were successfully treated.

CONCLUSIONS

The new treament based on bedaquiline, linezolid, clofazimine, and meropenem is a strong regimen with positive outcome. Adverse effect occurred during the treatment but it could be overcome by clinic management, 100% success rate was noted in our treatment. However, further study is required to investigate this new approach since the present study is limited by its small sample size.

KEYWORDS

extensively drug-resistant Mycobacterium tuberculosis (XDR-TB), bedaquiline, linezolid, meropenem

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Potential hypothyroidism secondary to oral second-line anti-tuberculosis drugs: An experience of Taichung Hospital.

Background:

Hypothyroidism is one of the common adverse effect in Multidrug resistant tuberculosis (MDR-TB) cases who received Prothionamide (TBN) and/or Para-aminosalicylic acid (PAS) during their treatment course. Our aim was to evaluate the incidence and risk factors associated with anti-tubercular agents related hypothyroidism among MDR-TB patients.

Methods:

From May 2007 to August 2015, 169 MDR-TB patients received individualized category IV anti-tubercular regimen and follow up above eight months at Taichung Hospital were enrolled in our study. After exclusion of HIV infection, XDR-TB, initial abnormal thyroid stimulating hormone (TSH) indicating hyper/ hypothyroidism and incomplete initial or follow up TSH data, do not use or intolerance to TBN and PAS, [Figure1] 96 cases included in our analysis. We used TSH level >5.0 mIU/L as suspicious indicator of potential hypothyroidism and conducted multivariate logistic regression to estimate the odds ratio (OR) of impact factors with 95% confidence intervals (95%CI). A *p* value less than 0.05 was considered statistical significant.

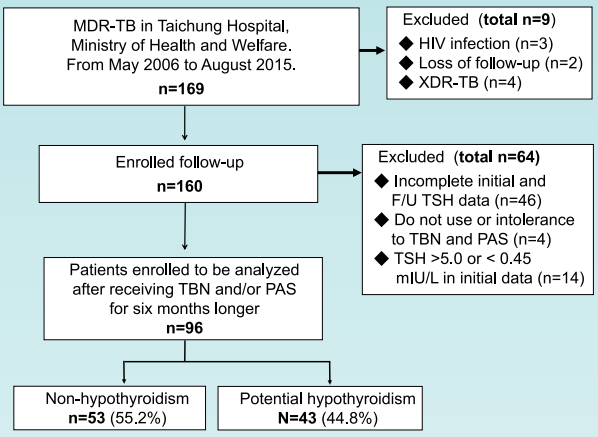


Figure 1. The flow chart of MDR-TB patients enrolled in our analysis

Results:

Among 96 MDR-TB patients who had received TBN and/or PAS for more than 6 months, elevation of TSH level happened in 43 (44.8%) patients with a mean time of 5.6 months (5.6±3.5), 13 (13.5%) patients TSH level>10 mIU/L, 31 (32.3%) patients had received Levothyroxine supplemental therapy (mean TSH 9.8±4.1). Alcoholism (p=0.049) and concomitant use of TBN and PAS (p<0.001) had higher rate and quicker events of potential hypothyroidism in univariate analysis. [Table1] In Multivariate logistic regression, age≧50 (OR=3.94; 95%CI=1.18-13.1; p=0.025), alcoholism (OR=4.53; 95%CI=1.17-17.6; p=0.029) and concomitant use of TBN and PAS (OR=11.4; 95%CI=3.54-36.6; p<0.001) were independent risk factors. [Table2]

Table 1. Comparison of clinical characteristics in group with/without potential hypothyroidism during MDR-TB treatment. (*n*=96)

Characteristic	*n* (%)	Hypothyroidism (TSH>5.0) Yes (*n*=43)	No (*n*=53)	*p*-value*
Sex	Male	32 (74.4)	40 (75.5)	0.906
Age	＜50	20 (46.5)	27 (50.9)	0.666
	≧50	23 (53.5)	26 (49.1)	
BMI	＜18.5	5 (11.6)	9 (17.0)	0.741
	18.5-24	25 (58.1)	30 (56.6)	
	≧24	13 (30.2)	14 (26.4)	
Aborigine	Yes	6 (14.0)	6 (11.3)	0.698
Smoking	Yes	19 (42.2)	19 (35.8)	0.406
Alcoholism	Yes	24 (55.8)	19 (35.8)	***0.049***
Diabetes	Yes	16 (37.2)	19 (35.8)	0.890
Cavitation	Yes	20 (46.5)	20 (37.7)	0.386
Previous TB	Yes	13 (30.2)	18 (34.0)	0.698
Regimen	TBN+PAS	27 (62.8)	12 (22.6)	***<0.001***
	TBN or PAS	16 (37.2)	41 (77.4)	

*p-value was count by χ^2 test or Fisher's exact test and less than 0.05 was considered statistically significant.

Table 2. Multivariate logistic regression analysis for impact factors of potential hypothyroidism during MDR-TB treatment. (*n*=96)

Characteristic		OR (95%CI)	*p*-value*
Sex	Male	0.65 (0.18-2.29)	0.508
	Female (reference)	1	
Age	≧50	3.94 (1.18-13.1)	***0.025***
	<50 (reference)	1	
BMI	<18.5	0.57 (0.12-2.71)	0.483
	≧24	0.69 (0.21-2.28)	0.552
	18.5-24 (reference)	1	
Aborigine	Yes	0.66 (0.15-2.93)	0.585
	No (reference)	1	
Smoking	Yes	0.55 (0.15-2.08)	0.379
	No (reference)	1	
Alcoholism	Yes	4.53 (1.17-17.6)	***0.029***
	No (reference)	1	
Diabetes	Yes	1.46 (0.49-4.34)	0.494
	No (reference)	1	
Cavitation	Yes	1.32 (0.45-3.88)	0.607
	No (reference)	1	
Previous TB	Yes	0.52 (0.17-1.63)	0.262
	No (reference)	1	
Regimen	TBN + PAS	11.4 (3.54-36.6)	***<0.001***
	PAS or TBN (reference)	1	

*p-value was count by binary logistic regression analysis and less than 0.05 was considered statistically significant.

Conclusions:

In our study, up to 44.8% patients had potential hypothyroidism with a mean time of 5.6 months after receiving an anti-tubercular regimen containing TBN and/or PAS. High caution should be delivered to patients with age≧50, alcoholism or combined use of TBN and PAS. Periodic thyroid function monitoring during treatment period in MDR-TB patients is recommended in integrated patient-centered care and prevention.

APEC CONFERENCE ON PREVENTION, CONTROL AND CARE FOR
MDR-TB AND SUPPLY OF 2nd-LINE ANTI-TB DRUG

CHINESE TAIPEI

Provided by
Shun-Tien Chien[1] , Ying-Shun Wu[2] , Ming-Chih LU[1] , Ray-Ming Huang[3]
Chest department[1] , Internal Medicine Department[2] Chest Hospital ,Ministry of Health and Welfare, Chinese Taipei; Hua-Lien Hospital[3] ,Ministry of Health and Welfare, Chinese Taipei

Side Effect of Linezolid in the Treatment of Multidrug Resistance Pulmonary Tuberculosis

Purpose

MDR-TB is very difficult to treat especially when fluoroquinolone was unavailable due to resistance or side effect. Group 5 drug like Linezolid was very effective In MDR/XDR treatment , but toxic adverse effect was very common when long term use. We will present the side effect of Linezolid used in MDR-TB/XDR treatment.

Material and Method

There were 310 MDR- TB patients treated in Chest hospital MDR-TB treatment alliance since June 2007. There were only 6 patients was treated with Linezolid-contained anti-MDR-TB regimen. The side effect and treatment outcome was described. All patients were followed CBC and DC and OPD visiting every month at least to monitor the side effect.

Result

The dosage of linezolid was 600mg QD for 5 patients and 1200mg QD for one patient. All patients developed anemia during treatment course. There were 80% (4/5) developed anemia in the first month. One patient developed anemia in the fourth month. 3 patients with anemia side effect was continued Linezolid treatment but should be discontinued in second month due to more severe anemia. 3 patients could restart Linezolid therapy with 600mg QOD without further anemia. Two patient developed severe peripheral neuropathy with pain , numbness and awkwardness in walking. One patient developed nausea and poor appetite. All patients became sputum AFB stain and culture conversion.

Conclusion

Linezolid 600mg QD or 1200mg QD will develop major side effect and patient cannot tolerate for more than 2 to 4 months. But patients could long term tolerate 600mg QOD. However , the effectiveness of Linezolid 600mg QOD should be investigated further.

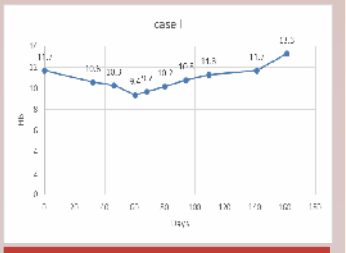


Fig 1. Linezoild 600mg QD initially , shift to Linezolid 600mg QOD when HB 9.4.

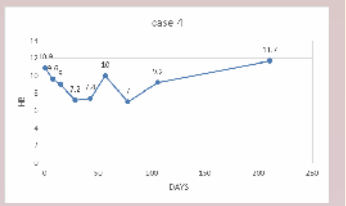


Fig 2. Linezolid 600mg initially , DC linezolid when HB 6.3 and blood transfusion was done. Linezolid 600mg QOD initiated when HB 11.

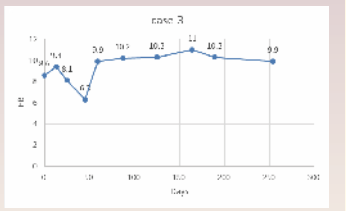


Fig 3. Linezolid 1200mg QD initially and discontinued when HB 7.2. Blood transfusion was done. Linezolid 600mg QD was given when HB 10 and discontinued when HB 7.

Case	AGE	BW	Sex	ADR	Comobidit ty	Category	DST
1	45	46	M	Anemia	NIL	MDR	HERZSm Km Pto PAS
2	32	56	F	Neuralgia , peripheral neuropathy	NIL	XDR	HERZSm Km Ofx Mfx Pto PAS RBT,
3	65	47	F	Anemia , poor appetite , nausea	DM	MDR	HER Ofx Lfx Mfx Pto PAS RBT,
4	58	35	F	Anemia	NIL	XDR	HERZSm Km Ofx Lfx Mfx PAS Cm RBT, Am
5	62	58	M	Anemia	DM	XDR	HERZSm Km Ofx Lfx Mfx Cm RBT, Am
6	52	63	M	Anemia ,peripheral neuropathy , pain , numbness	DM	MDR	HRSm Ofx Lfx Mfx RBT (PAS Pto side effect)

Table 1. Patient list.

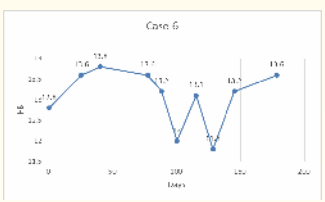


Fig 4. Linezolid 600mg QD and discontinued when HB 3.7. Patient refused to rechallenge. Blood transfusion was performed.

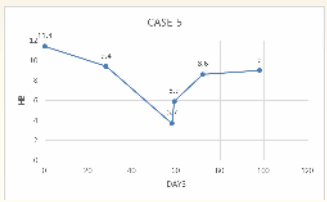


Fig 5. Linezolid 600mg QD initially and discontinued when HB 12. Linezolid 600mg was rechallenged when HB 13.1 and shitfed to linezolid 600mg QOD when HB 11.8.

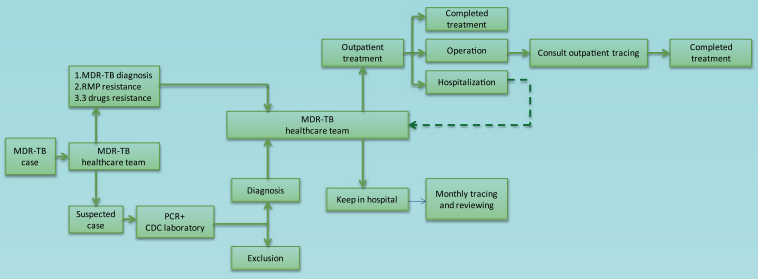
APEC CONFERENCE ON PREVENTION, CONTROL AND CARE FOR MDR-TB AND SUPPLY OF 2nd-LINE ANTI-TB DRUG

The Policy and Achievement of MDR-TB Treatment In South Chinese Taipei

Standardized Program of MDR-TB Care

MDR-TB patients will receive exclusive treatment, we strengthen the medical care and disease monitoring and management for patients to know well the states of each case whenever necessary.

In case the sputum culture test revealed negative or patient is non- infectious and no physical discomfort after medical treatment, cases may back to community to be treated by DOTS- plus and consulting outpatient tracing regularly.



Union Hospital	WanQiao Branch,Taichung Veterans General Hopital ; Ministry of Health and Welfare Hopital(Chiayi ; Tainan ; Cishan ; Pingtung) ; National Cheng Kung University Hospital ; Kaohsiung Veterans General Hopital;Kaohsiung Municipal Minsheng Hospital
Department of Health	Yunlin County ; Chiayi County ; Chiayi City ; Tainan City ; Kaohsiung City ; Pingtung County ; Penghu County

MDR-TB 5 Core Value

Everyone's involvement
Patient-centered

Entire Journey Care
Enrolment & treatment、symptoms remission、conditions improve、early completed treatment

All year service DOTS-Plus
Directly observed treatment

Full supports
Physiology、spirit、community、religion

Full responsibility
Treating all of MDR-TB with any conclusion

Action Plan - C R M

Comfort
- Benefits of economic growth
- Assisting people with disability
- Shuttle bus for cases living in suburban district
- Ensure patient's privacy

Release
- Relieving side effects of patients
- Take care of other diseases
- Supports in interpersonal relationship
- Improving the patient experience

Make it Whole
- Enhancing the knowledge of health and ability of self-care
- Nutrition intervention and adjustment
- Remodeling patient's lifestyle
- Transforming the negative emotions of patients

Dynamic Policy

We formulate customized program for each case by data collection、evaluation、strategy making、intervention and results assessment.

Case Subsidy and Assistance

Each case will receive equitable subsidy and assistance.

Project grants	Subsidy
✓Medical expenses ✓Inpatient expenditures ✓Surgery costs	✓Transportations costs ✓Sentinel transportations costs ✓Caregiver costs
Living allowance	**Treatment & home visits**
✓Home nutrition allowance ✓Hospital care subsidy ✓Nutritional care	✓Accompanied visits ✓Home visits ✓Hospital visits

Effectiveness of Treatment

From 2011, not only MDR-TB patients, but also the cases who resistant to Rifampicin or at least three of first-line anti TB drugs (Type II) were admitted. From May 2007 to April 2016, there were 379 MDR-TB cases and 72 Type II cases were treated. Between 2010 and 2014, the treatment completed rate of MDR-TB(include Type II) increased by 68.1% to 75.8% ; default rate and death rate were unsteady but with decrease tendency these years.

MDR-TB	2010	2011	2012	2013	2014
Treatment completed rate(%)	68.1	72.5	73.9	74.2	75.8
Default rate (%)	2.0	1.5	5.6	5.7	2.2
Death rate(%)	12.2	9.1	19.4	7.5	8.9

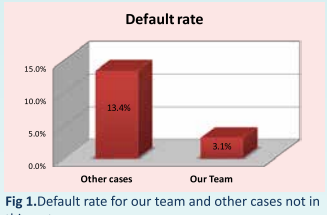


Fig 1. Default rate for our team and other cases not in this system.

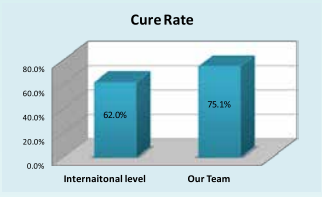


Fig 2. Cure rate for our team and international level.

Up to April 2016, 388 MDR-TB cases (include Type II) were cured , the default rate of our team is 10% lower than the rate of un-enrolled cases; and the cure rate is 10% higher than international level.

CHINESE TAIPEI

Provided by
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Specialized and Patient-Centered Care in Taoyuan General Hospital

Introduction

In 2004, being one of the designated regional hospitals to treat complicated TB patients, Taoyuan General Hospital (TYGH) first established its own TB center.

In 2007, the Centers for Disease Control of Chinese Taipei constructed a specific care system–Taiwan MDRTB Consortium (TMTC) in response to combat the increasing number of multidrug resistant TB (MDRTB) patients, and TYGH TB center has joined this consortium since then.

Over the past few years, we are dedicated to provide a treatment model that meets the WHO standard and is patient-friendly to boost our cure rate and also minimize the default rate. To date, we have enrolled 112 patients, and 100 patients have treatment outcomes in the fig. 1.

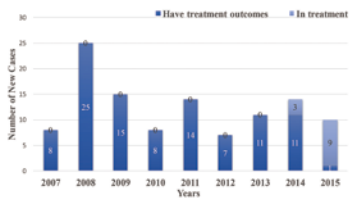


Fig. 1 New cases of MDRTB patients in TYGH from 2007 to 2015

Most of our MDRTB patients are new cases, which means that stopping the disease from spreading in the community is a key element in terms of prevention and control in the fig. 2. Also, nearly 27% of our patients are treated after relapse or default, which means they all have experiences in engaging with public health workers, and have a high risk of defaulting again.

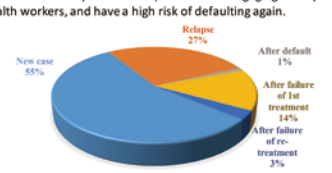


Fig. 2 Patient registry category of MDRTB patients with treatment outcome in TYGH from 2007 to 2015

One of the major factor that hinders MDRTB treatment outcome is co-morbid condition. Among our 100 patients, more than 63% have at least one co-morbid condition. On top of lists are diabetes mellitus (29%), alcohol abuse (26%) and psychiatric disorder (14%) as shown in the fig. 3. Patients with these medical conditions require continuous monitoring and care to promote their health and strengthen adherence.

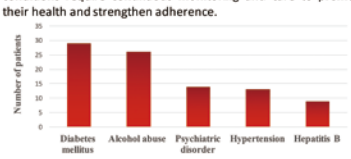


Fig. 3 Co-morbid conditions of MDRTB patients with treatment outcome in TYGH from 2007 to 2015

Management

The essence of TMTC care model is a "hospital-led treatment and directly-observed therapy (DOT)" program as illustrated in the fig. 4. By providing incentive and funding, most of the MDRTB patients are cared by TMTC group. The patients are encouraged to initiate their MDRTB treatment in hospital, in order to observe their side effects, provide counseling and education, and most important of all, establish rapport. When they are back to the community, our DOT workers can provide flexible DOT (by using car rental service to overcome time and distance factors) and health monitoring (nurse/DOT worker to evaluate their response on a daily basis). Any side effects or health issues can be addressed by reporting back to MDRTB center immediately and see if further hospitalization is required. The care physician will in charge of both hospital care and outpatient clinic.

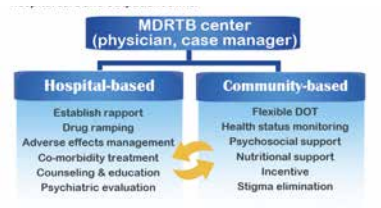


Fig. 4 MDRTB Care Model

Co-morbidity management

Top1 Diabetes mellitus

Our nurse/DOT worker can facilitate finger sugar monitoring and insulin injection. Also, by visiting the patient's home, they have a better idea about what the patient normally eats and, as a result, give a practical suggestion in terms of diet control and lifestyle modification.

Top2 Alcoholism

For those alcoholic patients, it is especially important to have them hospitalized in the initial phase of MDRTB treatment. It not only helps us establishing rapport with the patients, but also help us identifying the underlying cause of abuse.

Top3 Psychiatric disease

During the initial hospitalization period, every patient will receive routine psychiatric evaluation to see if any medication adjustment is needed. Also, psychiatrist can give the team members some valuable behavioral consultation to help us interact with our patients.

Others Hypertension / Asthma / COPD

Routine blood pressure and heart rate monitoring is provided by DOT worker. For patients with chronic airway diseases, we also facilitate regular inhaler drugs with spacer use to optimize disease control.

Common Problems

Nutritional support

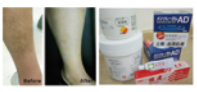
Malnutrition is a common problem encounter by the socio-economically deprived patients. We provide meal boxes and nutritional drinks to help them maintain better nutritional status.

Huge pill burden

Some patients will need jellos to help them swallow the pills. Others may need candies to cover the bitter or metallic aftertaste.

Skin condition

Severe scaling of skin, especially over the distal extremities, is a commonly encountered aesthetic problem following MDRTB treatment. Topical lotion/cream is provided as moisturizers.



Injection site pain

To help the patients endure the long duration of injectional drug use, we use PICC (peripherally inserted central catheter) as vascular access. For the intramuscular injection site pain, we use handheld massage device to ease the local pain and induration.

Result and Conclusion

Among the 100 patients with treatment outcomes, the overall treatment success rate is 84% as shown in the fig. 5. The mortality rate is around 14%. The major improvement observed in TMTC model is the marked decrease in default rate. It takes a strong relationship established between the care team member and the patients to retain them within the program, to design a patient-centered treatment plan, and above all, to have them adhere to the treatment till it ends.

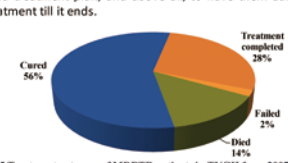


Fig. 5 Treatment outcome of MDRTB patients in TYGH from 2007 to 2015