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Does one size fit all? Drug resistance and standard treatments: results of six tuberculosis programmes in former Soviet countries

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SUMMARY

SETTING: After the collapse of the Soviet Union, countries in the region faced a dramatic increase in tuberculosis cases and the emergence of drug resistance.

OBJECTIVE: To discuss the relevance of the DOTS strategy in settings with a high prevalence of drug resistance.

DESIGN: Retrospective analysis of one-year treatment outcomes of short-course chemotherapy (SCC) and results of drug susceptibility testing (DST) surveys of six programmes located in the former Soviet Union: Kemerovo prison, Russia; Abkhasia, Georgia; Nagorno-Karabagh, Azerbaijan; Karakalpakstan, Uzbekistan; Dashoguz Velayat, Turkmenistan; and South Kazakhstan Oblast, Kazakhstan. Results are reported for new and previously treated smear-positive patients.

RESULTS: Treatment outcomes of 3090 patients and DST results of 1383 patients were collected. Treatment success rates ranged between 87% and 61%, in Nagorno-Karabagh and Kemerovo, respectively, and failure rates between 7% and 23%. Any drug resistance ranged between 66% and 31% in the same programmes. MDR rates ranged between 28% in Karakalpakstan and Kemerovo prison and 4% in Nagorno-Karabagh.

CONCLUSION: These results show the limits of SCC in settings with a high prevalence of drug resistance. They demonstrate that adapting treatment according to resistance patterns, access to reliable culture, DST and good quality second-line drugs are necessary.

KEY WORDS: tuberculosis; treatment outcomes; drug resistance; Eastern Europe

AFTER THE COLLAPSE of the Soviet Union, most countries in the region faced a dramatic increase in tuberculosis (TB) incidence.[1] The collapse of national TB programmes (NTPs) induced drug shortages, unreliable drug quality, over-the-counter medicines and poor treatment adherence. Facing what could be considered an epidemic, the World Health Organization (WHO) and the international community pushed the NTPs to implement the DOTS strategy. The approach of the NTPs was until then based on case detection and follow-up by radiography, long course individual chemotherapy and massive use of primary and secondary prophylaxis,[2] and policy makers were reluctant to accept a new strategy. After a pilot phase supported by international organisations, they slowly accepted DOTS.[3] However, unexpectedly high failure rates rapidly indicated potentially high levels of drug resistance. Previous drug resistance surveys conducted in DOTS pilot projects in Russia, the Baltic countries and Georgia showed rates of initial multidrug resistance (MDR) of between 9% and 20%.[4] No data were available for other countries in the former Soviet Union (FSU). Drug resistance is a major obstacle for NTPs to reach the WHO goal of 85% cure rate among new infectious TB cases.

The aim of the present study is to report new results on TB drug resistance and treatment outcomes from programmes in Russia, Uzbekistan, Turkmenistan, Kazakhstan, Georgia and Azerbaijan, and to discuss the limits of DOTS in settings with a high prevalence of drug resistance.

STUDY POPULATION AND METHODS

Setting

The non-governmental organisation Médecins Sans Frontières (MSF) supported six programmes in the

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FSU region. The first programme started in 1996 in Kemerovo Oblast, Russia, covering a population of 30 000 prisoners. Between 1998 and 2000, three projects started in Central Asia in the civilian population: in the semiautonomous Republic of Karakalpakstan, Uzbekistan (1.5 million); in Dashoguz Velayat, Turkmenistan (1.2 million), and in two districts of South Kazakhstan Oblast, Kazakhstan (140 000). Another two programmes were implemented in the autonomous regions of Nagorno-Karabagh, Azerbaijan (100 000) and Abkhasia, Georgia (250 000), in 1997 and 1999, both in a context of long-term conflict.

Intervention

Diagnosis and treatment followed WHO and International Union Against Tuberculosis and Lung Disease (IUATLD) recommendations.[5] Case detection was passive for civilians and active for prisoners. Diagnosis was mainly based on sputum microscopy after Ziehl-Neelsen staining and on fluorescence microscopy in prison. New cases (NCs) were defined as patients who had never had treatment for TB or who had taken anti-tuberculosis drugs for <1 month. Previously treated cases (PTCs) were defined as patients who had previously received anti-tuberculosis drugs for a month or more. Patients were treated by standard short-course chemotherapy (SCC): NCs received a 6-month regimen, with 2 months of isoniazid (H, INH), rifampicin (R, RMP), ethambutol (E, EMB) and pyrazinamide (Z), followed by 4 months of HR (2HREZ/4HR); PTCs were given an 8-month regimen, with 2 months of streptomycin (S, SM) and HRZE, 1 month of HRZE, followed by 5 months of HRE (2SHRZE/1HRZE/5HRE). On the basis of preliminary results of drug susceptibility testing (DST), SM was not used for PTCs in Kemerovo. Treatment was given daily at the in-patient facility during the intensive phase, and three times a week in ambulatory health posts during the continuation phase. In prisons, treatment was given daily for the whole duration. Health care workers directly supervised drug intake in all projects. Since May 1999 in Nagorno-Karabagh and July 2001 in Abkhasia, patients with drug-resistant TB have been given adapted treatment including second-line drugs according to their individual DST results.[6–8]

Treatment follow-up was based on sputum microscopy. In prisons, supervision of sputum collection and drug intake were very strict to avoid cheating (spitting out drugs or sputum exchange between patients) by prisoners wanting to remain in the TB department where living conditions were better. Anti-tuberculosis drugs of guaranteed quality were provided by MSF. Quality control of the laboratories in each programme was performed on randomised samples of slides on a quarterly basis. TB notification rates were calculated in each programme by dividing the number of TB cases diagnosed by the population covered and expressed per 100 000 population.

Analysis of standard SCC outcomes

Definitions of treatment outcomes followed WHO/IUATLD recommendations: 1) cured: patient presenting a negative sputum smear in the last month of treatment and on at least one previous occasion; 2) failure: patient presenting a positive smear at 5 months or later during treatment; 3) death: patient who died from any reason during the course of treatment; 4) defaulted: patient who interrupted treatment for 2 or more consecutive months; 5) transfer out: patient transferred to another DOTS unit and for whom treatment outcome was not known; 6) treatment completed: patient who completed treatment but did not meet the criteria for cured or failure; 7) treatment success: patients declared either cured or treatment completed.[9] In Kemerovo prison, patients released before treatment completion were considered as defaulters, as no DOTS-based programme was in place in the civilian society during the study period.

Rates of different treatment outcomes were calculated by the ratio of the number of patients with one outcome divided by the total of patients enrolled in the programme for the period of the analysis. Treatment outcomes of all smear-positive patients treated with SCC in each programme were collected. Drug-resistant patients who received a treatment regimen adjusted to their DST during the study period were excluded from the analysis of the SCC. Results for 2001 were compiled for each programme for NCs and PTCs separately. Because of the small size of the programme, the results were compiled for 2 years (1999 and 2000) in Nagorno-Karabagh. Standard SCC outcomes were analysed according to the DST results for 2001 in Abkhasia and Kemerovo prison. In Kemerovo prison, culture was performed for patients who had fully susceptible strains on admission and were classified as failures at 5 months.

DST SURVEY

Each project conducted a DST survey, except for the programme in South Kazakhstan Oblast. Results from a survey performed in another region of Kazakhstan (Almaty region) are presented. Conventional cultures were performed on solid Lowenstein-Jensen media and DST for first-line drugs was based on the proportion method, with SM 8 μg/ml, INH 0.2 μg/ml, RMP 40.0 μg/ml and EMB 5.0 μg/ml.[10]

Consecutive positive sputum samples were collected at each diagnostic centre. Samples were sent directly to a Supranational Reference Laboratory (SRL): the National Mycobacterial Reference Laboratory, Borstel, Germany, for Karakalpakstan and Dashoguz Velayat; Istituto Superiore Di Sanita, Rome, Italy, for Abkhasia; and Institute of Tropical Medicine (ITM),

Table 1 Treatment outcomes of new cases for the Siberia, Uzbekistan, Turkmenistan, Abkhasia and Kazakhstan programmes for 2001 and for the Nagorno-Karabagh programme for 1999 and 2000

	n	Cured *n* (%)	Treatment completed *n* (%)	Treatment success *n* (%)	Died *n* (%)	Failure *n* (%)	Defaulted *n* (%)	Transferred *n* (%)
Kemerovo prison	452	303 (67)	17 (3.8)	320 (70.8)	8 (1.8)	75 (16.6)	49 (10.8)	0
Karakalpakstan	396	183 (46.2)	86 (21.7)	269 (67.9)	21 (5.3)	64 (16.2)	35 (8.8)	7 (1.8)
Dashoguz Velayat	306	193 (63.1)	56 (18.3)	249 (81.4)	7 (2.3)	26 (8.5)	24 (7.8)	2 (0.1)
Abkhasia	76	38 (50)	28 (36.5)	66 (86.8)	2 (2.6)	2 (2.6)	5 (6.5)	1 (1.3)
Karabagh	57	28 (49)	25 (44)	53 (93)	1 (2)	1 (2)	2 (3.5)	0
South Kazakhstan Oblast	90	57 (63)	11 (12)	68 (76)	4 (4)	13 (14)	2 (2)	3 (3)

Antwerp, Belgium, for Nagorno-Karabagh and Almaty region. In Kemerovo prison, DST was performed locally in a laboratory supported by MSF and supervised by the ITM.

Results were collected separately for NCs and PTCs. 'Any resistance' was defined as resistance to at least one TB drug, monoresistance as resistance to only one drug, polydrug resistance (PDR) as resistance to more than one drug and MDR as resistance to at least INH and RMP.[4] The periods of surveys differed according to the stage and size of the project: 2001 in Kemerovo prison, July 2001 to January 2002 in Karakalpakstan and Dashoguz Velayat, September 2000 to August 2002 in Abkhasia, May 1997 to December 1998 in Almaty region and May 1999 to December 2002 in Nagorno-Karabagh. The proportions of different resistance profiles were calculated.

Statistical analyses

Univariate analysis was performed using Epi Info version 6.04d (Centers for Disease Control, Atlanta, GA, 2001). In Abkhasia and Kemorovo prison, negative outcomes were defined as the association of failures, defaulters and died, and positive outcomes as treatment success. Transferred patients were excluded from the analysis. Positive and negative outcomes were examined in groups of patients presenting a strain with 'any resistance,' MDR and monoresistance to INH (or INH + SM) and compared with those with fully susceptible strains. Crude odds ratios (OR) and 95% confidence intervals (CI) were used for the interpretation of univariate analysis. Fisher's exact test was used when the expected value of a cell was <5. P values <0.05 were considered significant.

RESULTS

TB case notification rates per 100 000 were 4600 in Kemerovo prison, 200 in Karakalpakstan, 100 in Dashoguz Velayat, 150 in Abkhasia, 86 in Nagorno-Karabagh and 250 in South Kazakhstan Oblast.

In Abkhazia and Nagorno-Karabagh, respectively 17 and 9 patients were excluded from analysis of the SCC outcome as their treatment was adjusted to individual DST. Standard SCC outcomes of 3088 smear-positive cases, including 1377 NCs and 1711 PTCs, are presented in Tables 1 and 2. Overall, SCC treatment success rates ranged between 87% in Nagorno-Karabagh and 63% in Siberia. Failure rates ranged between 23% in Kemerovo prison and 7% in Nagorno-Karabagh. Death rates ranged between 11% in Karakalpakstan and 2% in Nagorno-Karabagh.

Results of DST surveys are reported in Table 3 for a total of 1383 patients. The proportions of patients with TB resistant to INH were 54% in Kemerovo prison, 53% in Karakalpakstan, 31% in Dashoguz Velayat, 37% in Abkhasia, 28% in Nagorno-Karabagh and 59% in Almaty region. MDR rates ranged between 28% in Karakalpakstan and Kemerovo prison and 4% in Nagorno-Karabagh.

Treatment outcomes according to DST results are presented for 459 patients in Kemerovo prison and 163 patients in Abkhasia, in Tables 4 and 5. In Abkhasia, a negative outcome was observed in 60% of the 'any resistance' group, 95% of MDR, 46% of

Table 2 Treatment outcomes of previously treated cases for the Siberia, Uzbekistan, Turkmenistan, Abkhasia and Kazakhstan programmes for 2001 and for the Nagorno-Karabagh programme for 1999 and 2000

	n	Cured *n* (%)	Treatment completed *n* (%)	Treatment success *n* (%)	Died *n* (%)	Failure *n* (%)	Defaulted *n* (%)	Transferred *n* (%)
Kemerovo prison	304	155 (51)	4 (1.3)	159 (52.3)	11 (3.6)	96 (31.6)	38 (12.5)	0
Karakalpakstan	645	253 (39.2)	104 (16.1)	257 (55.3)	90 (14)	98 (15.2)	91 (14.1)	9 (1.4)
Dashoguz Velayat	505	285 (56.4)	68 (13.5)	353 (69.9)	37 (12.1)	38 (12.4)	70 (13.9)	7 (1.3)
Abkhasia	112	39 (34.8)	26 (23.2)	65 (58)	9 (8)	8 (7.1)	26 (23.2)	4 (3.5)
Karabagh	30	18 (60)	5 (17)	23 (77)	1 (3)	5 (17)	1 (3)	0
South Kazakhstan Oblast	115	51 (44)	13 (11)	64 (56)	14 (12)	22 (19)	7 (6)	8 (7)

Table 3 Prevalence of TB drug resistance in the programmes in Siberia (2001), Uzbekistan (2001), Turkmenistan (2001), Abkhasia (September 2000–August 2002), Karabagh (May 1999–December 2002) and Kazakhstan (May 1997–December 1998)

	Kemerovo prison		Karakalpakstan		Dashoguz Veylat		Abkhasia		Karabagh		Almaty region	
	NC *n* (%)	PTC *n* (%)	NC *n* (%)	PTC *n* (%)	NC *n* (%)	PTC *n* (%)	NC *n* (%)	PTC *n* (%)	NC *n* (%)	PTC *n* (%)	NC *n* (%)	PTC *n* (%)
n	289	170	106	107	106	97	122	140	77	25	68	97
Fully susceptible	112 (38.8)	45 (26.5)	54 (50.9)	22 (20.6)	74 (69.8)	36 (37.1)	79 (64.8)	60 (43.2)	57 (74)	13 (52)	41 (60)	21 (21.6)
Any resistance	177 (61.2)	125 (73.5)	52 (49.1)	85 (79.4)	32 (30.2)	61 (62.9)	43 (35.2)	80 (57.6)	20 (26)	12 (48)	27 (40)	76 (78.4)
Monoresistance												
H	13 (4.5)	6 (3.5)	4 (3.8)	7 (6.5)	6 (5.7)	8 (8.2)	13 (10.7)	18 (12.9)	4 (5.2)	2 (8)	1 (1.5)	11 (11.3)
E	6 (2.1)	0	0	0	0	0	0	0	2 (2.6)	0	—	—
R	1 (0.3)	0	0	0	0	1 (1)	1 (0.8)	1 (0.7)	2 (2.6)	0	0	0
S	28 (9.7)	9 (5.3)	12 (11.3)	11 (10.3)	16 (15.1)	12 (12.4)	13 (10.6)	12 (8.6)	3 (3.9)	1 (4)	4 (5.9)	0
Polyresistance												
HS	36 (12.4)	30 (17.6)	13 (12.3)	15 (14)	5 (4.7)	10 (10.3)	9 (7.4)	17 (12.2)	9 (11.7)	0	12 (17.6)	10 (10.3)
HE±S	26 (9)	10 (5.9)	2 (1.9)	4 (3.7)	1 (0.9)	6 (6.2)	2 (1.6)	6 (4.3)	1 (1.3)	5 (20)	4 (5.9)	17 (17.5)
ES	7 (2.4)	1 (0.6)	0	0	0	0	0	0	0	0	—	—
RS	—	0	0	0	0	0	1 (0.8)	1 (0.7)	0	0	1 (1.5)	0
RE±S	0	1 (0.6)	0	0	0	0	0	0	0	0	—	—
MDR-TB	60 (20.8)	68 (40)	14 (13.2)	43 (40.2)	4 (3.8)	18 (18.6)	5 (4)	26 (18.7)	0	4 (16)	4 (5.9)	36 (37.1)
HR	0	1 (0.6)	0	1 (0.9)	0	0	0	2 (1.4)		0	0	1 (1)
HRS	24 (8.3)	11 (6.5)	4 (3.8)	10 (9.3)	3 (2.8)	7 (7.2)	3 (2.5)	5 (3.6)		0	0	3 (3)
HRE±S	36 (12.4)	56 (32.9)	6 (5.7)	19 (17.8)	1 (0.9)	6 (6.2)	2 (1.6)	19 (13.7)		4 (16)	4 (5.9)	32 (33)
Any resistance												
H	135 (52.3)	114 (67)	39 (36.8)	74 (69.2)	16 (15.1)	47 (48.5)	29 (23.8)	67 (47.9)	14 (18.2)	11 (44)	22 (32.4)	76 (78.4)
R	61 (23.6)	69 (40.6)	14 (13.2)	43 (40.2)	4 (3.8)	19 (19.6)	7 (5.7)	28 (20)	2 (2.6)	4 (16)	5 (7.4)	38 (37.1)
S	—	—	47 (44.3)	76 (71)	26 (24.5)	50 (51.5)	—	—	13 (16.9)	9 (36)	24 (35.3)	62 (63.9)

TB = tuberculosis; NC = new cases; PTC = previously treated cases; H = isoniazid; E = ethambutol; R = rifampicin; S = streptomycin.

Table 4 Treatment outcomes by DST results for the Abkhasia programme for 2001

	n	Cured *n* (%)	Treatment completed *n* (%)	Treatment success *n* (%)	Died *n* (%)	Failure *n* (%)	Defaulted *n* (%)	Transferred *n* (%)
Fully susceptible	91	47 (51.6)	23 (25.3)	70 (76.9)	6 (6.6)	1 (1.1)	12 (13.2)	2 (2.2)
Any resistance	72	18 (25)	10 (13.9)	28 (38.9)	4 (5.5)	21 (29.2)	18 (25)	1 (1.3)
MDR	22	1 (4.5)	0	1 (4.5)	3 (13.6)	10 (45.4)	8 (36.4)	0
HR	1	0	0	0	0	0	1	0
HRS	5	1	0	0	0	3	1	0
HRE	0	0	0	0	0	0	0	0
HRES	16	0	0	0	3 (18.7)	7 (43.7)	6 (37.5)	0
RS	0	0	0	0	0	0	0	0
RES	0	0	0	0	0	0	0	0
HE	1	0	0	0	0	1	0	0
HS	12	4 (33.3)	2 (16.7)	6 (50)	0	4 (25)	2 (16.7)	0
ES	0	0	0	0	0	0	0	0
HES	4	1	0	1	1	2	0	0
H	23	9 (39.1)	4 (17.4)	13 (56.5)	0	4 (17.4)	6 (26.1)	0
R	2	0	1	1	0	0	1	0
E	0	0	0	0	0	0	0	0
S	8	3	3	6	0	0	1	1

DST = drug susceptibility testing; MDR = multidrug resistance; H = isoniazid; R = rifampicin; S = streptomycin; E = ethambutol.

patients resistant to INH (or INH + SM) and 21% in the group with fully susceptible TB. In Kemerovo prison, it was respectively 42%, 59%, 57% and 22%. In Kemerovo prison, culture and DST were available for 15 of 16 patients with fully susceptible strains on admission classified as failures: 9 were confirmed by culture, 8 had MDR strains and 6 had a negative culture. The risk of a negative outcome was significantly higher in patients with drug-resistant TB than in patients with fully susceptible TB in Abkhasia (OR 5.7; 95%CI 2.7–12.1, $P < 0.01$) and in Kemerovo prison (OR 2.6; 95%CI 1.6–4.2, $P < 0.01$). Resistance to INH or INH + SM was significantly associated with negative outcomes in both programmes (OR 3.1; 95%CI 1.2–7.8, $P < 0.01$ and OR 5.3; 95%CI 3.1–9.2, $P = 0.01$). MDR was strongly associated with negative outcomes in both programmes (OR 77.4; 95%CI 9.8–1664.3, $P < 0.01$ and OR 5.3; 95%CI 3.1–9.2, $P < 0.01$).

DISCUSSION

These programmes had a similar history and background of TB control, although the size and type of their target population, the level of implementation (district or regional) and the geopolitical contexts were different. The SCC outcomes in Nagorno-Karabagh and Kemerovo prison were similar to those reported at national level in Azerbaijan and Russia in 2000 (91% and 68% success rates for NCs and 3% and 13% failure rates, respectively).[4] In Karakalpakstan, Kemerovo prison and South Kazakhstan Oblast,

Table 5 Treatment outcomes by DST results for the Kemerovo prison programme for 2001

	n	Cured *n* (%)	Treatment completed *n* (%)	Treatment success *n* (%)	Died *n* (%)	Failure *n* (%)	Defaulted *n* (%)
Fully susceptible	157	92 (58.6)	31 (19.7)	123 (78.3)	2 (1.3)	16 (10.2)	16 (10.2)
Any resistance	302	115 (38.1)	60 (19.9)	175 (57.9)	11 (3.6)	98 (32.4)	18 (6)
MDR	128	31 (24.2)	21 (16.4)	52 (40.6)	9 (7)	58 (45.3)	9 (7)
HR	1	0	0	0	0	1	0
HRS	35	8 (22.5)	7 (20)	15 (42.9)	2 (5.7)	17 (48.6)	1 (2.9)
HRE	1	0	1	1	0	0	0
HRES	91	23 (25.3)	13 (14.3)	36 (39.6)	7 (7.7)	40 (44)	8 (8.8)
RS	0	0	0	0	0	0	0
RES	1	0	0	0	0	1	0
HE	3	1	1	2	0	1	0
HS	66	30 (45.5)	11 (16.8)	41 (65.1)	1 (1.5)	20 (30.3)	4 (6.1)
ES	8	4	2	6	0	2	0
HES	33	12 (36.4)	11 (33.3)	23 (69.7)	0	7 (21.2)	3 (9.1)
H	19	9 (47.4)	4 (21.1)	13 (68)	1 (5.3)	4 (21.1)	1 (5.3)
R	1	1	0	1	0	0	0
E	6	2	3	5	0	1	0
S	37	25 (67.6)	7 (18.9)	32 (86.5)	0	4 (10.8)	1 (2.7)

DST = drug susceptibility testing; MDR = multidrug resistance; H = isoniazid; R = rifampicin; S = streptomycin; E = ethambutol.

treatment outcomes were sub-optimal, with success rates for NCs far below the DOTS objective of 85%.[6] The high defaulter rate in Kemerovo prison was explained by the amnesty and release of patients before treatment completion and by the absence of a DOTS unit in the civilian community during the study period. The exclusion of patients with drug-resistant TB who received adapted treatment regimens in Abkhasia and Nagorno-Karabagh may have resulted in an overestimation of the treatment success rate and an underestimation of the failure and death rates.

The DST surveys confirm the importance of drug resistance, as suspected from the poor treatment outcomes. In Karakalpakstan and Almaty region, the MDR rates were equivalent to those reported in Latvia and Estonia, with 9% and 14% of MDR among NCs.[11] Coninx et al. reported similar results in an Azerbaijan prison to those in Kemerovo prison, with 27% of MDR among NCs.[12] Drug resistance was higher for INH and SM, which were prescribed intensively during the Soviet period for TB and other infectious diseases.[3]

The failure rate observed in Kemerovo prison in patients with fully susceptible strains was surprisingly high. Although occasional cheating cannot be totally excluded, the quality of the implementation of the programme can hardly explain these results, as all procedures were strictly supervised. Forty per cent of the failures (6/15) as defined by smear microscopy were not confirmed as such by culture. This could be explained by the presence of dead bacilli at 5 months in patients with large cavities. The high proportion of MDR (89%) among the failures confirmed by culture suggests that a more probable explanation was reinfection by more resistant strains in the TB wards.[13] Confirmation of this hypothesis would require DNA fingerprinting.[14,15] Some authors have reported mixed infection with different *Mycobacterium tuberculosis* strains that could explain inconsistent DST results.[15–17]

We found a significant association between drug resistance and unfavourable outcomes. MDR is known as an independent risk factor of treatment failure and death.[15,18–23] In Kemerovo prison, the 7% death rate observed in patients with MDR-TB was surprisingly low compared to the overall death rate (5%). The proportion of chronic cases among patients with MDR-TB and the impact of the systematic supply of high-energy food on treatment outcomes should be investigated. The success rate for patients with MDR-TB under SCC was low, as previously reported.[15,24–26] It was probably overestimated in our study, as treatment outcomes were defined by direct microscopy only.[7,27] A high recurrence rate would have been expected but could not be measured, as follow-up after treatment completion was not systematically recorded. A previous study in Russia reported 27% recurrence among patients with MDR-TB considered cured under SCC.[24] According to our study, administering a 6-month regimen to any NC would result in RMP monotherapy during the continuation phase for 20–50% of patients, resulting in an increased risk of resistance to RMP.[21,28] Adding SM to the PTC treatment regimen was ineffective in one third to two thirds of cases. INH prophylaxis would have been inappropriate for contact cases of 25–50% of the patients.

These results underline the need for more DST surveys to better understand anti-tuberculosis drug resistance in FSU.[29,30] They also highlight the need for culture for patient follow-up rather than relying only on sputum microscopy.[31] In settings where there is a high prevalence of drug resistance, adapting treatment according to DST results is necessary. Both standard and individual MDR treatment strategies have been proposed in different settings.[8,32] Considering the frequency of other forms of resistance (H, HS, HE) and the fact that some second-line drugs (mainly ethionamide and kanamycin) were widely used during the Soviet period, individually adapted treatment is probably advisable in this region. This was initiated during the study period and progressively implemented in Nagorno-Karabagh and Abkhazia, and has been used since 2003 in Karakalpastan. To date about 300 patients with drug-resistant TB have received adapted treatment in these programmes.

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RÉSUMÉ

CONTEXTE : Après l'effondrement de l'URSS, les pays de la région ont déploré une augmentation importante des cas de tuberculose et de l'émergence de la résistance aux antituberculeux.

OBJECTIFS : Discuter la pertinence de la stratégie DOTS dans les régions avec une haute prévalence de résistance.

SCHÉMA : Analyse rétrospective des résultats de la chimiothérapie à courte durée (SCC) pendant un an et des enquêtes de résistance dans six programmes en ex-URSS : Kemerovo prison (Russie), Abkhasie (Géorgie), Nagorno-Karabagh (Azerbaïdjan), Karakalpakstan (Ouzbékistan), Dashoguz-Velayat (Turkmenistan) et South Kazakhstan Oblast (Kazakhstan). Les résultats sont reportés pour les patients à frottis positif nouveaux et déjà traités.

RÉSULTATS : Les résultats de traitement de 3090 patients et les profils de résistance de 1383 patients ont été collectés. Les taux de succès variaient entre 87% au Nagorno-Karabagh et 61% à Kemerovo et les taux d'échec entre 7% et 23%. Entre 66% des patients à Kemerovo et 31% au Nagorno-Karabagh étaient résistants à au moins un antituberculeux. Entre 28% au Karakalpakstan et à Kemerovo et 4% au Nagorno-Karabagh étaient multirésistants.

CONCLUSION : Ces résultats montrent les limites du SCC dans les régions à haute prévalence de résistance aux antituberculeux. L'adaptation thérapeutique en fonction de la résistance, l'utilisation de la culture plus antibiogramme et l'accès à des antituberculeux de 2nde ligne de bonne qualité sont nécessaires.

RESUMEN

MARCO DE REFERENCIA: Después del colapso de la Unión Soviética, los países de la región confrontan un grave aumento de los casos de tuberculosis y la aparición de resistencia a los medicamentos.

OBJETIVO: Analizar la pertinencia de la estrategia DOTS en ambientes con alta prevalencia de resistencia a los medicamentos antituberculosos.

MÉTODO: Análisis retrospectivo del desenlace del tratamiento de un año, con el protocolo acortado (SCC) y de los resultados de estudios de sensibilidad a los medicamentos, de seis programas ubicados en la antigua Unión Soviética: la prisión de Kemerovo (Rusia), Abkhasia (Georgia), Nagorno-Karabagh (Azerbaiján), Karakalpakstán (Uzbekistán), Dashoguz Velayat (Turkmenistán) y Oblast Kazajstán del sur (Kazajstán). Los resultados del tratamiento de casos con baciloscopia positiva se agrupan por pacientes nuevos y pacientes con antecedente de tratamiento previo.

RESULTADOS: Se estudió el desenlace del tratamiento de 3090 pacientes y el resultado de 1383 pruebas de sensibilidad a los medicamentos. Las tasas de tratamiento exitoso oscilaron entre el 87% en Nagorno-Karabagh y el 61% en Kemerovo, y las tasas de fracaso entre el 7% y el 23%. En estos mismos programas, se encontró algún tipo de resistencia a los medicamentos en el 66% y el 31% de los casos, respectivamente. Se observaron tasas de multidrogorresistencia entre el 28% en Karakalpakstán y la prisión de Kemerovo y el 4% en Nagorno-Karabagh.

CONCLUSIÓN: Los resultados pusieron en evidencia los límites del SCC en ambientes con alta prevalencia de resistencia a los medicamentos. Demostraron también la necesidad de adaptar el tratamiento al tipo de resistencia y de tener acceso a un cultivo fiable, a las pruebas de sensibilidad y a medicamentos de segunda línea de buena calidad.