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# Adverse reactions among patients being treated for MDR-TB in Tomsk, Russia

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SUMMARY

**BACKGROUND AND SIGNIFICANCE:** Treatment of multidrug-resistant tuberculosis (MDR-TB) is challenging because of the toxicity of second-line medications. Little is known about whether adverse events impact treatment outcome.

**METHODS:** We conducted a retrospective case series of 244 MDR-TB patients enrolled in Tomsk between 10 September 2000 and 10 September 2002. Adverse reactions were determined by laboratory data and/or clinical criteria. A multiple logistic regression model was performed to determine whether the occurrence of adverse reactions was associated with poor treatment outcome.

**RESULTS:** In this cohort, 76.0% were cured, 6.6% failed, 4.9% died and 11.5% defaulted. Adverse events were observed in 73.3% of patients, occurring in 74.8% of patients who were adherent (taking at least 80% of prescribed doses) and 59.1% of non-adherent individuals ($P = 0.11$). The impact of adverse events on outcome was modified by non-adherence; among adherent patients, the occurrence of any adverse reaction was associated with treatment cure (adjusted odds ratio 3.24, 95% confidence interval 1.56–6.70).

**CONCLUSION:** Adverse reactions occurred frequently in MDR-TB patients in Tomsk, Russia, but did not negatively impact treatment outcome. The occurrence of adverse reactions among adherent patients was associated with treatment cure.

**KEY WORDS:** multidrug-resistant tuberculosis; DOTS-Plus; adverse reactions; Tomsk; Russia

TUBERCULOSIS (TB) is one of the leading infectious causes of global mortality, accounting for two to three million deaths annually. Multidrug-resistant tuberculosis (MDR-TB), defined as TB with isolates showing in vitro resistance to at least isoniazid and rifampicin, contributes to rising TB morbidity and mortality on a global level.[1,2] In Russia and other countries of the former Soviet Union, failure to adequately treat drug-resistant TB in the setting of major social and economic upheaval has contributed to poor outcomes.[3–7]

Between 1995 and 2002, the attitude of the international TB community towards the treatment of MDR-TB in resource-poor settings changed dramatically, enabling the creation of pilot treatment programs using low-cost second-line anti-tuberculosis drugs.[8] Using an approach termed 'DOTS-Plus', these programs build upon the framework of the treatment strategy of the World Health Organization (WHO) for drug-susceptible TB (DOTS) to provide MDR-TB treatment, termed 'DOTS-Plus'.[9–12] The expanded DOTS-Plus strategy relies on identification of drug-resistant strains through drug sensitivity testing (DST) and timely appropriate treatment. Despite the greater toxicity and lesser efficacy of second-line drugs compared with first-line treatment,[13,14] MDR-TB treatment programs have achieved cure rates of greater than 80% even in resource-poor settings.[15–17]

One of the major concerns about second-line anti-tuberculosis drugs is their potential to cause adverse effects. The experience of MDR-TB treatment pilot projects has contributed to greater knowledge about these adverse reactions in various populations.[18–25] However, more data on the characteristics and management of adverse reactions are needed to inform clinicians and program managers as MDR-TB treatment scale-up occurs in pilot sites and elsewhere. In

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addition, little is known about whether the occurrence of adverse reactions negatively impacts treatment outcome. The present study is a report on the adverse reactions encountered among patients receiving MDR-TB treatment in Tomsk, Russia.

## METHODS

This was a retrospective case series study performed among all 244 patients consecutively enrolled into the DOTS-Plus program in Tomsk, Russia, between 10 September 2000 and 10 September 2002. Patients were included in this cohort if they: 1) had active TB, as evidenced by positive culture or by previous treatment failure with clinical evidence of active disease, 2) had documented MDR-TB or suspected MDR-TB based on a history of previous treatment failures, and 3) agreed to MDR-TB treatment. There were no exclusion criteria based on clinical severity of disease or previous non-adherence. Patient management and treatment outcomes of this cohort have been reported elsewhere.[26] As part of programmatic requirements, physicians reported adverse reactions in real time using an adverse event reporting form. Criteria for prospective reporting were based on the physician's judgement. Management of reactions was based on protocols that were disseminated in training courses,[27] with modifications per clinical judgment.

Retrospective data collection for this study included review of the entire patient chart, including adverse event reporting forms. All laboratory data related to adverse reactions were electronically exported from the civilian and prison TB databases to the study database.

All patients initiating TB treatment in Tomsk are routinely tested for human immunodeficiency virus (HIV) infection. Alcohol or illicit drug use during TB treatment was considered if documented by the treating physician in the patient chart. Hepatitis was defined as the documentation of hepatitis due to any cause at the time of treatment initiation and/or the presence of baseline transaminases that were higher than three times the upper normal limit. Other comorbid conditions, such as chronic renal insufficiency, diabetes mellitus or seizure disorder, were considered if documented in the patient chart by a physician. Low body mass index (BMI) was defined as $<18.5$ kg/m$^2$ for women and $<20$ for men.[28] Non-adherence was defined as missing $>20\%$ of the prescribed doses (a dose was defined as any single administration of all prescribed medications) during the entire treatment period due to patient preference. Final treatment outcome definitions proposed by the WHO MDR-TB Working Group were used for this study.[29]

As summarized in Table 1, for reactions not defined by laboratory criteria, an event was considered if the treating TB physician documented the reaction in the patient chart according to his/her clinical criteria. For reactions confirmed by laboratory testing, we chose to include any event reflected by at least one abnormal laboratory value, given that a single laboratory result might not be confirmed by a repeat test if the reaction were immediately corrected. Because adverse reactions were based upon retrospective chart reviews, the severity of adverse reactions was not graded. However, management of adverse reactions—ranging from no change in regimen to permanent discontinuation of an offending agent—was documented.

**Table 1** Adverse reaction definitions

| Term | Definition |
|---|---|
| Nausea and vomiting | Any documentation of nausea and/or vomiting by physician |
| Diarrhea | Any documentation of diarrhea by physician |
| Nephrotoxicity | Elevation of at least one creatinine value $>141$ mmol/l* |
| Hepatotoxicity | Elevation of either serum transaminase or serum bilirubin at least 3 times the upper limit of normal values* |
| Hypokalemia | At least one serum potassium value of $<3.0$ mEq/l* |
| Hypothyroidism | At least one measure of TSH $>10.0$ IU/ml* |
| Depression | As diagnosed by TB physician and/or as judged by a psychiatrist, based on ICD-10 criteria |
| Psychosis | As diagnosed by TB physician and/or as judged by a psychiatrist, based on ICD-10 criteria |
| Seizure | Witnessed or unwitnessed event consistent with seizure, e.g., tonic-clinic movement, bowel-bladder incontinence, post-ictal confusion, etc. |
| Ototoxicity | Hearing loss confirmed by physical examination or audiometry |
| Arthralgia | Pain of the joints as reported by patient and documented by physician, with or without the presence of arthritis |
| Rash | A dermatologic reaction felt to be related to anti-tuberculosis medications, as documented by physician |
| Neuropathy | Symptoms and findings consistent with neuropathy, e.g., pain or numbness of the distal extremities, as diagnosed by physician or by electromyography |

* Normal ranges: creatinine (44–100 mmol/l); AST (0.45–0.68 mmol/l); ALT (0.45–0.68 mmol/l); bilirubin (7.5–20.5 mmol/l); serum potassium (3.5–5.5 mEq/l); TSH (0–10.0 IU/ml).
TSH = thyroid-stimulating hormone; IU = international unit; TB = tuberculosis; ICD = International Classification of Diseases; AST = aspartate aminotransferase; ALT = alanine aminotransferase.

Data were entered into an Electronic Medical Record, using a Microsoft SQL server 2000 (Microsoft Corporation, Seattle, WA, USA) and exported into an Access 2000 database (Microsoft). Analysis was conducted using SAS Version 9.1 (SAS Institute, Cary, NC, USA). Univariate and multiple logistic regression models were used to generate effect estimates of the association between the occurrence of adverse reactions and poor treatment outcome. Interaction between non-adherence and occurrence of adverse reactions was assessed. If effect modification was confirmed by a $P$ value for the interaction variable of $<0.05$, the interaction variable was included in the model. We also included clinically relevant variables (age, sex, sector, alcohol use and bilateral plus cavitary disease) in the

multivariable analysis, based on outcome analysis of this same cohort reported elsewhere.[26]

Informed consent was obtained for initiation of MDR-TB treatment. Study approval was obtained from the Ethics Committee of the Siberian State Medical University and the Institutional Review Board of the Harvard School of Public Health.

## RESULTS

All patients had final treatment outcomes at the time of analysis. These are represented in the Figure, by occurrence of adverse reaction and adherence. The median treatment duration was 18.5 months (range 1.0–42.4). The median duration of injectable drug use was 8.6 months (range 0–27.5). Table 2 describes the clinical and demographic characteristics of the cohort. Age, low BMI, treatment sector and non-adherence were not associated with the occurrence of adverse reactions. Treatment outcomes were significantly better among those who experienced an adverse reaction. Individualized regimens were variable, but generally included a parenteral agent (capreomycin or an aminoglycoside), a fluoroquinolone, para-aminosalicylic acid, prothionamide/ethionamide and cycloserine, as shown in Table 3. Routine laboratory monitoring—including liver function tests, creatinine and potassium—was performed monthly. Thyroid-stimulating hormone (TSH) was checked approximately every 2 months.

The majority of the cohort (73.3%) experienced at least one adverse event. Table 4 summarizes the incidence and characteristics of the adverse reactions assessed in this study. Mean presenting abnormal laboratory values (with standard deviations) were as follows: creatinine 156 ± 15.0 mmol/l, aspartate aminotransferase (AST) 3.3 ± 2.0 mmol/l, alanine aminotransferase (ALT) 3.1 ± 1.9 mmol/l, bilirubin 124.2 ± 86.1 mmol/l, potassium 2.6 ± 0.3 mEq/l, and TSH 25.0 ± 29 iU/l. Most adverse reactions occurred during the first 8 months of treatment. Every effort was made to avoid permanent discontinuation of any antituberculosis drug unless the adverse reaction was life threatening or could not be controlled otherwise.

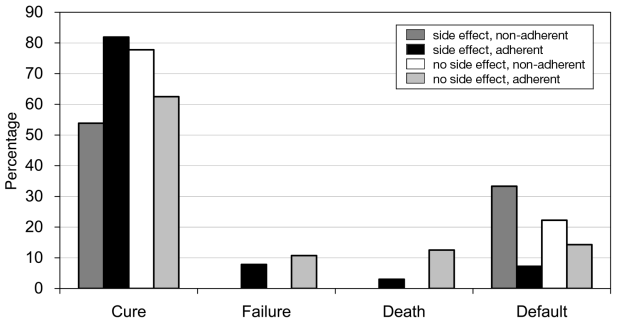


**Figure** Treatment outcome by occurrence of adverse events and non-adherence.

**Table 2** Clinical and treatment characteristics of patient cohort ($N = 244$)

| Characteristics | No adverse reaction ($n = 65$) $n$ (%) | Adverse reaction ($n = 179$) $n$ (%) |
|---|---|---|
| Age, mean years (range) | 31 (18–54) | 32.6 (17–65) |
| Male sex | 59 (90.8) | 152 (84.9) |
| Prison sector | 32 (49.2) | 78 (43.6) |
| Years with tuberculosis, mean (range) | 2.5 (0.1–28.3) | 3.5 (0.1–22.1) |
| Drugs to which they are resistant, mean (range) | 4.0 (3–9) | 5.0 (3–9) |
| Low baseline body mass index | 30 (46.2) | 72 (40.2) |
| Baseline comorbidity* | 21 (32.3) | 48 (26.8) |
| Substance abuse | | |
| Alcohol use† | 21 (32.3) | 56 (31.3) |
| Illicit drug use† | 4 (6.2) | 9 (5.0) |
| Treatment outcome | | |
| Cure‡ | 42 (64.6) | 145 (81.0) |
| Default | 10 (15.4) | 18 (10.1) |
| Failure | 5 (7.7) | 11 (6.2) |
| Death‡ | 7 (10.8) | 5 (2.8) |
| Non-adherent | 9 (13.9) | 13 (7.3) |

* Any of the following: diabetes mellitus, renal insufficiency, hepatic dysfunction, cardiovascular disorder, seizure diagnosis, gastritis/ulcer, psychiatric disorder.
† Alcohol or illicit drug use during DOTS-Plus treatment as per physician report.
‡ $P < 0.05$.

Seventy patients (28.7%) required permanent discontinuation of an offending agent due to an adverse event. No adverse reaction led to indefinite suspension of complete MDR-TB treatment. The incidence of adverse events and the rate of drug discontinuation due to adverse events did not differ significantly among adherent versus non-adherent individuals ($P = 0.11$ and $P = 0.63$, respectively).

In general, adverse reactions were managed symptomatically. Offending agents were either reduced in dose or temporarily suspended. Re-introduction of the

**Table 3** Anti-tuberculosis medications received in individualized treatment regimens ($N = 244$)

| Medication, daily doses, unless specified | $n$ (%) |
|---|---|
| INH, 300 mg, 900 mg biweekly | 5 (2.05) |
| RMP, 600 mg | 0 |
| EMB, 15–20 mg/kg | 63 (25.82) |
| PZA, 20–30 mg/kg | 178 (72.95) |
| SM, 1000 mg, 15 mg/kg | 0 |
| KM, 1000 mg, 15 mg/kg | 114 (46.72) |
| CM, 1000 mg, 15 mg/kg | 154 (63.11) |
| AMK, 1000 mg, 15 mg/kg | 2 (0.82) |
| CS, 500–1000 mg | 241 (98.77) |
| Fluoroquinolone: CPX 1500 mg, OFX 800 mg, LFX 500 mg* | 243 (99.59) |
| Ethionamide/prothionamide, 500–1000 mg | 184 (75.41) |
| PAS, 8 mg | 217 (88.93) |
| Amoxacillin-clavulanate, 1500–2000 mg | 20 (8.20) |
| Rifabutin, 300 mg | 4 (1.64) |

* Most patients received OFX as their fluoroquinolone.
INH = isoniazid; RMP = rifampicin; EMB = ethambutol; PZA = pyrazinamide; SM = streptomycin; KM = kanamycin; CM = capreomycin; AMK = amikacin; CS = cycloserine; CPX = ciprofloxacin; OFX = ofloxacin; LFX = levofloxacin; PAS = para-aminosalicylic acid.

**Table 4** Incidence and characteristics of adverse reactions ($N = 244$)

| Adverse reaction | Incidence *n* (%) | Months treatment at presentation median (range) | Any change in DOTS-Plus MDR-TB regimen among those with specific adverse reactions % | Permanent interruption of any drug associated with reaction among those with specific adverse reactions % | Drugs permanently discontinued due to specific adverse reactions (*n* of patients) |
|---|---|---|---|---|---|
| Nausea and vomiting | 184 (75.4) | 1.8 (0.03–24.6) | 47.3 | 14.6 | INH (1), KM (3), CM (3), OFX (2), CS (2), PAS (9), ETH (5), PZA (8), EMB (4), AMX-CLV (1) |
| Diarrhea | 113 (46.3) | 2.3 (0.03–20.9) | 23.9 | 5.3 | CM (4), OFX (1), PAS (3), ETH (1) |
| Nephrotoxicity | 24 (9.8) | 4.8 (0.20–18.4) | 25.0 | 0 | None |
| Hepatotoxicity | 41 (16.8) | 5.8 (0.13–20.0) | 26.8 | 9.8 | PZA (3), EMB (1), ETH (3), PAS (3) |
| Hypokalemia | 81 (33.2) | 4.8 (0.10–20.9) | 28.4 | 7.4 | CM (6) |
| Hypothyroidism | 42 (17.2) | 6.0 (0.95–16.7) | 19.0 | 7.1 | PAS (2) |
| Depression | 21 (8.6) | 7.3 (1.4–20.8) | 38.1 | 14.3 | OFX (2), CS (1), ETH (1), EMB (1) |
| Psychosis | 29 (11.9) | 3.3 (0.16–18.1) | 79.3 | 17.2 | CS (4) |
| Seizure | 28 (11.5) | 5.4 (0.43–39.0) | 57.1 | 10.7 | CM (1), CS (1) |
| Ototoxicity | 38 (15.6) | 6.6 (0.62–26.0) | 44.7 | 34.2 | CM (1), KM (12) |
| Arthralgia | 115 (47.1) | 3.7 (0.39–19.0) | 19.1 | 9.6 | CM (2), PAS (1), ETH (1), PZA (6), EMB (1), AMX-CLV (1) |
| Rash | 39 (16.0) | 4.7 (0.07, 18.6) | 15.4 | 7.7 | ETH (2), PZA (1) |
| Neuropathy | 10 (4.1) | 14.0 (4.9, 29.7) | 30.0 | 0 | None |

MDR-TB = multidrug-resistant tuberculosis; INH = isoniazid; KM = kanamycin; CM = capreomycin; OFX = ofloxacin; CS = cycloserine; PAS = para-aminosalicylic acid; ETH = ethionamide; PZA = pyrazinamide; EMB = ethambutol; AMX-CLV = amoxacillin-clavulanate.

agent was generally attempted after symptoms improved. Because patients usually received all drugs to which their isolate was susceptible, adding an alternative drug to replace the offending agent was rarely an option. Whereas the incidence of adverse reactions and adherence did not differ between civilian and prison cohorts ($P = 0.43$ and $P = 0.35$, respectively), the discontinuation of at least one drug due to an adverse event occurred more frequently in the prison sector, compared with the civilian sector, among both adherent and non-adherent patients (35.5% vs. 23.1%, $P = 0.03$).

We assessed whether the occurrence of an adverse reaction was associated with unfavorable treatment outcome (defined as death, default, or treatment failure). On univariate analysis, the occurrence of an adverse reaction was negatively associated with unfavorable outcome, with an odds ratio (OR) of 0.46 (95% confidence interval [CI] 0.24–0.87). Likewise, the occurrence of an adverse reaction requiring discontinuation of a medication was negatively associated with poor treatment outcome (OR 0.21, 95%CI 0.09–0.52). We postulated that non-adherence to treatment could have an interactive effect on this negative association; we therefore assessed for effect modification between non-adherence and adverse events on treatment outcome. An interaction between the occurrence of adverse reactions and non-adherence was observed with the magnitude of association between the occurrence of an adverse reaction and poor treatment outcome differing by adherence status (Table 5). Among non-adherent individuals, there was an increase in the risk of poor outcome among those who experienced an adverse reaction, although this association was not statistically significant (OR 3.00, 95%CI 0.44–20.3). Among those who were adherent, the occurrence of an adverse reaction was significantly associated with poor treatment outcome (OR 0.37, 95%CI 0.18–0.72). This modifying effect of non-adherence on the association between adverse reactions and treatment outcome was relatively unchanged after adjusting for all confounding factors.

**Table 5** Interaction between occurrence of adverse reactions and non-adherence on treatment cure ($n = 244$)*

| | Treatment cure | |
|---|---|---|
| | Unadjusted OR (95%CI) | Adjusted OR (95%CI) |
| Occurrence of adverse reactions | | |
| Among non-adherents | 0.33 (0.05–2.26) | 0.24 (0.03–1.89) |
| Among adherents | 2.72 (1.39–5.32) | 3.24 (1.56–6.70) |

* Controlling for sector (prison vs. civilian), sex, age, alcohol use, advanced baseline clinical status, both bilateral and cavitary disease.
OR = odds ratio; CI = confidence interval.

## DISCUSSION

In this cohort of young MDR-TB patients with excellent adherence and high rates of substance abuse, adverse

reactions to MDR-TB treatment occurred frequently but were managed with minimal treatment interruption. Although there have been concerns that complicated adverse reactions would prove difficult to manage and lead to default and treatment failure, this has not been borne out in our experience. No patient in this cohort required permanent discontinuation of MDR-TB treatment due to drug toxicity. This is similar to the experience in other DOTS-Plus pilot projects, where toxicity-related discontinuation of treatment is rare (0–8.2%).[18]

There are several findings of interest in this study. First, gastrointestinal side effects were common and often resulted in changes in TB treatment. In addition, neuro-psychiatric toxicities required frequent changes in DOTS-Plus regimens, usually involving the temporary suspension of the culprit drug (cycloserine in the case of depression, psychosis, seizure; a parenteral agent in the case of ototoxicity). Interestingly, the three most potentially life-threatening adverse reactions—hepatotoxicity, hypokalemia and nephrotoxicity—required changes in MDR-TB regimens less than 30% of the time. Mild transient alterations in transaminases, serum potassium and serum creatinine levels could often be managed through close monitoring and prompt correction of contributing factors, such as dehydration, gastrointestinal electrolyte loss and alcohol consumption. Management principles were generally supportive therapy, discontinuation of the offending drug only when necessary and replacement of an alternative effect drug (when available). There were some differences in management practice between the civilian and prison sectors which may be due to clinical style, severity of events and/or patient preference.

Finally, we found that treatment non-adherence influenced the relationship between the occurrence of an adverse reaction and treatment outcome. The occurrence of an adverse reaction was protective against a poor treatment outcome among individuals who were adherent to therapy. We offer several explanations. Symptomatic toxicity may be observed more frequently among individuals achieving higher drug serum levels.[30,31] Patients who have side effects and are adherent to treatment may be followed more closely by TB providers, thus increasing the likelihood of a favorable treatment outcome. Because testing of serum drug levels is not available in Tomsk, we are unable to prove this hypothesis. Alternatively, a patient who experienced early default would be less likely to experience some of the adverse reactions presenting later during treatment. Whereas non-adherent individuals who experienced adverse reactions appeared more likely to do poorly, this relationship was not significant. The limited number of non-adherent patients makes it difficult to draw further conclusions from this finding.

There are several potential limitations to this study. First, data were collected retrospectively through chart review. Under-reporting or over-reporting as well as reporting bias are all possible, especially for reactions not defined by laboratory criteria. Of note, we compared prospective and retrospective reporting of adverse reactions in a subgroup of this Tomsk cohort and found that prospective physician reporting actually under-estimated the incidence of reactions compared with retrospective chart review.[32] Because few individuals in this cohort were non-adherent, we were unable to assess whether the occurrence of an adverse event among non-adherent individuals was associated with poor outcomes. Finally, given the characteristics of our population—those measured, such as recorded alcohol use, and those unmeasured, such as local diet—our findings may not be applicable to other populations with MDR-TB. Nevertheless, this is one of the largest cohorts of MDR-TB patients undergoing treatment in Russia and it thus adds useful information to our understanding.

MDR-TB treatment is associated with a complicated spectrum of potential adverse reactions. Adverse reactions occurred frequently in MDR-TB patients in Tomsk, but did not negatively impact treatment outcome among individuals who were adherent to treatment. Successful management can be attributed to aggressive supportive care and correction of other contributing factors while avoiding regimen compromise.

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**RÉSUMÉ**

**CONTEXTE ET PORTEE : Le traitement de la tuberculose à germes multirésistants (TB-MDR) est un défi en raison de la toxicité des médicaments de deuxième ligne. Un plus grand nombre de données est nécessaire concernant l'incidence et la prise en charge des effets indésirables. De plus, on connaît peu la mesure dans laquelle les effets indésirables ont un impact sur l'adhésion thérapeutique et le résultat du traitement. Nous faisons état dans ce travail des effets indésirables chez les patients atteints de TB-MDR à Tomsk en Russie.**

**MÉTHODES : Nous avons mené à Tomsk une étude rétrospective d'une série de 244 patients atteints de TB-MDR enrôlés entre le 10 septembre 2000 et le 10 septembre 2002. Les effets indésirables ont été déterminés par les données de laboratoire et/ou par des critères cliniques. Nous avons recouru à un modèle de régression logistique multiple pour déterminer dans quelle mesure la survenue d'effets indésirables était en association avec un résultat médiocre du traitement.**

**RÉSULTATS : Dans la cohorte, la guérison a été acquise chez 76,0% ; il y a eu 7,8% d'échecs, 4,9% de décès et 11,5% d'abandons. Les effets indésirables les plus fréquents ont été nausées/vomissements, arthralgies, diarrhée et hypokaliémie. Ce sont les effets neuropsychiatriques qui ont exigé les modifications de régime les plus fréquentes. On a observés des effets indésirables chez 173 patients (73,4%) : ils sont survenus chez 74,8% de patients dont l'adhésion au traitement était bonne (prise d'au moins 84% des doses prescrites) et chez 59,1% des individus non-adhérents ($P$ = 0,11). L'impact des effets**

indésirables sur le résultat du traitement est influencé par l'absence d'adhésion au point que la survenue de n'importe quel effet indésirable chez les patients adhérents est en association négative avec un médiocre résultat (odds ratio ajusté 0,30 ; IC95% 0,14–0,62).
CONCLUSION : Les effets indésirables surviennent fréquemment chez les patients atteints de TB-MDR à Tomsk, mais n'ont pas d'impact négatif sur le résultat du traitement. La survenue d'effets indésirables chez les patients adhérents est en association avec une guérison après traitement.

## RESUMEN

MARCO DE REFERENCIA Y SIGNIFICACIÓN : El tratamiento de la tuberculosis multidrogorresistente (TB-MDR) representa un desafío, a causa de la toxicidad de los medicamentos de segunda línea. Se precisa información complementaria sobre la incidencia y el tratamiento de las diferentes reacciones adversas. Asimismo, se conoce poco a cerca de la repercusión de estas reacciones adversas sobre el cumplimiento y el desenlace terapéuticos. En el presente artículo se comunican las reacciones adversas observadas en pacientes con TB-MDR en Tomsk, República de Rusia.
MÉTODOS : Se llevó a cabo un estudio retrospectivo de 244 pacientes con TB-MDR, registrados en Tomsk entre el 10 septiembre 2000 y el 10 septiembre 2002. Las reacciones adversas se definieron mediante datos de laboratorio, criterios clínicos o ambos. Se aplicó un modelo de regresión logística múltiple, con el fin de determinar si la aparición de reacciones adversas se asociaba con un desenlace terapéutico deficiente.
RESULTADOS : Se obtuvo la curación en el 76,0% de la cohorte, hubo 7,8% de fracasos, 4,9% de fallecimientos y 11,5% de abandonos. Las reacciones más frecuentes fueron náusea y vómito, artralgias, diarrea e hipopotasemia. Las reacciones neuropsiquiátricas originaron la mayor parte de modificaciones del esquema terapéutico. Se observaron reacciones adversas en 173 pacientes (73,4%), de los cuales 74,8% cumplían con el tratamiento (ingestión, como mínimo, del 80% de las dosis formuladas) y 59,1% no lo hacían ($P$=0,11). El incumplimiento terapéutico modificó la repercusión de las reacciones adversas sobre el desenlace, de tal manera que la aparición de cualquier reacción adversa en los pacientes cumplidos presentó una asociación negativa con un desenlace terapéutico deficiente (aOR 0,30 ; IC95% 0,14–0,62).
CONCLUSIÓN : Las reacciones adversas fueron frecuentes en los pacientes con TB-MDR en Tomsk, Rusia, pero esto no tuvo una repercusión negativa sobre el desenlace terapéutico. La aparición de una reacción adversa en pacientes con buena observancia terapéutica se asoció con la curación de la TB.