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Evaluation of MGIT 960™ and the colorimetric-based method for tuberculosis drug susceptibility testing

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SUMMARY

SETTING: Dr Cetrángolo Hospital, Buenos Aires Province, Argentina.

OBJECTIVE: Evaluation of the BACTEC™ Mycobacteria Growth Indicator Tube (MGIT)™ 960 system and the colorimetric-based method (CMM) for first- and second-line drug susceptibility testing (FL-DST, SL-DST) against *Mycobacterium tuberculosis*.

DESIGN: FL-DST was studied using SIRE MGIT 960. Minimal inhibitory concentrations (MICs) for isoniazid (INH), streptomycin, rifampicin (RMP), ethambutol (EMB) and levofloxacin (LVX) were also determined by CMM using 3-(4,5-dimethylthiazolyl-2)-2,5-diphenyltetrazolium bromide (MTT). MICs for amikacin (AMK), kanamycin (KM), capreomycin (CPM), ethionamide (ETH), cycloserine, ofloxacin (OFX), linezolide (LZ) and moxifloxacin (MFX) were determined on 94 multidrug-resistant *M. tuberculosis* isolates by MGIT 960 and CMM. Statistical methods were applied to define drug-susceptible and drug-resistant isolates on the basis of the comparison between results obtained by gold standards.

RESULTS: A total of 1626 clinical isolates were studied. Critical drug concentrations could be defined in less than 10 days for both CMM and MGIT 960. CMM was cheaper but more laborious than MGIT 960. The highest performances of both methods were achieved for AMK, RMP, OFX, LZ and MFX, followed by INH, ETH, KM, CPM and LVX (tested only by CMM).

CONCLUSIONS: Both methods could be implemented as rapid diagnostic tools to detect drug-resistant isolates in clinical practice.

KEY WORDS: tuberculosis; drug susceptibility; MGIT 960; colorimetric methods

ABOUT 80% of the global burden of *Mycobacterium tuberculosis*, the main causative agent of tuberculosis (TB) in humans, occurs in low-income countries, and is mainly concentrated in 22 high-burden countries.[1,2] Resistance to commonly used anti-tuberculosis drugs is increasing worldwide, worsening the global TB situation.[3] Recently identified extensively drug-resistant strains (XDR-TB) have caused a deadly outbreak in a high-burden country.[4–6] The World Health Organization (WHO) estimates that about 500 000 cases of XDR-TB emerge annually.[3] National Tuberculosis Control Programmes (NTPs) therefore require effective strategies for the rapid detection of patients resistant to first- and second-line drugs to design appropriate anti-tuberculosis treatment regimens and prevent the dissemination and amplification of drug resistance.[6–8]

Guidelines for the treatment of multidrug-resistant TB (MDR-TB), such as the DOTS-Plus strategy and the Green Light Committee, have led to second-line drugs being made available at concessionary prices.[8,9] However, the best tool for detecting MDR- and XDR-TB in clinical laboratories in low-income countries still remains to be elucidated. The current drug susceptibility testing (DST) methods using solid media, such as the classical proportion method (PM), are slow and cumbersome, with limited worldwide spread and availability.[10] In contrast, alternative rapid and accurate methods for assessing in vitro drug susceptibility would permit the prompt detection and treatment of resistant cases, thereby reducing the transmission of MDR-TB and XDR-TB in the community.[8,11–13]

The Dr Cetrángolo Hospital is a reference centre for TB diagnosis and DST of *M. tuberculosis* isolates from patients receiving medical care in Buenos Aires Province, Argentina, where more than 4500 new TB cases (incidence rate 4.6 per 100 000 population) occur each year.[14] Argentina is considered a middle-income country; MDR-TB and XDR-TB cases are concentrated in the province of Buenos Aires and have been increasing over the last few years.[14] Rapid and accurate DST methods are therefore urgently needed.

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The present study reports on the evaluation of the BACTEC™ Mycobacteria Growth Indicator Tube (MGIT)™ 960 system (BD, Buenos Aires, Argentina) and the microplate colorimetric-based method (CMM) in comparison with gold standards for DST against first- and second-line anti-tuberculosis drugs (FL-DST, SL-DST) in clinical practice.

MATERIALS

The first- and second-line drugs and the tested concentrations included in the different methods are listed in Table 1. FL-DST was performed by indirect PM, MGIT 960 and/or CMM on isolates obtained during the period 2004–2008 from both new and previously treated cases. Isolates underwent DST against second-line drugs at different times depending on the method used: CMM was carried out individually on MDR-TB isolates from either new or previously TB treated cases soon after they were detected, while SL-DST on MGIT 960 was performed on subcultured strains collected during the study period and in a single experiment.

Informed consent was obtained at the time of bacteriological TB diagnosis. Although this study did not affect treatment decisions or medical practice, approval was obtained from the Ethical Committee of Dr Cetrángolo Hospital at the time the study was designed.

DST against first- and second-line drugs

SIRE MGIT 960

The commercially available and fully automated BACTEC MGIT 960 SIRE kit (BD Argentina) was used to detect first-line drug resistance against streptomycin (S, SM), isoniazid (I, INH), rifampicin (R, RMP) and ethambutol (E, EMB) according to the manufacturer's protocol and previous reports.[15,16] SIRE results were automatically read and recorded using EpiCenter Microsoft (BD Argentina).

Second-line drugs in MGIT 960

The protocol provided by Siddiqi et al.[17] was followed, with modifications. Table 1 shows the drug concentrations used. A proper solvent drug dilution was added to all but one tube used as growth control.[17,18] Mycobacteria for DST were obtained from either solid media (Löwenstein-Jensen [LJ] or Stonebrink) or MGIT 960 cultures. All of the isolates were subcultured on Middlebrook 7H9 liquid medium. A bacterial suspension showing turbidity comparable to 0.5 MacFarland standard was prepared and 500 μl of a 1:5 bacterial suspension was inoculated onto both drug-containing and drug-free tubes.[17,18] Inoculated tubes were placed in the instrument, where they were incubated and monitored continuously for no more than 21 days. The isolated bacterium was considered resistant to a particular drug if a positive signal was flagged by the instrument within 3 days of the growth control tube giving a positive signal.

First- and second-line DST by the colorimetric-based method

A non-commercial microplate CMM using a tetrazolium salt was evaluated. 3-(4,5-dimethylthiazolyl-2)-2,5-diphenyltetrazolium bromide (MTT, ICN Biomedicals Inc, Cleveland, OH, USA) was used as a general indicator of cellular growth and viability. The oxidised yellow colour of MTT turns purple upon reduction to formazan by the dehydrogenase of live mycobacteria.[19,20] Briefly, a 96-well microtiter flat-bottomed,

Table 1 Drug concentrations used in the study and the gold standards ILJ and PM-M7H11

	Drug concentration, μg/ml			
Drug	CMM	MGIT 960	ILJ	PM–M7H11
First-line				
INH	1.00–0.03	0.10	0.20	
EMB	32.00–1.00	5.00	2.00	
LVX	4.00–0.13	—	4.00	
RMP	2.00–0.06	1.00	40.00	
SM	8.00–0.25	1.00	4.00	
Second-line				
AMK	8.00–0.25	8.00, 4.00, 2.00		5.00
CPM	10.00–0.65	10.00, 5.00, 2.50		30.00
CS	120.00–3.75	60.00, 30.00, 15.00		5.00
ETH	10.00–0.065	10.00, 5.00, 2.50		5.00
KM	10.00–0.65	10.00, 5.00, 2.50		5.00
LZ	2.00–0.06	2.00, 1.00, 0.50		1.00
MFX	1.00–0.03	10.00, 5.00, 2.50		0.50
OFX	4.00–0.13	2.00, 1.00, 0.50		2.00
PAS	8.00–0.25	—		1.00

ILJ = indirect proportion method using Löwenstein-Jensen; PM-M7H11 = indirect proportion method with Middlebrook 7H11 solid medium used as gold standard for second-line drug susceptibility testing; CMM = colorimetric-based method; MGIT = Mycobacteria Growth Indicator Tube; INH = isoniazid; EMB = ethambutol; LVX = levofloxacin; RMP = rifampicin; SM = streptomycin; AMK = amikacin; CPM = capreomycin; CS = cycloserine; ETH = ethionamide; KM = kanamycin; LZ = linezolid (Pharmacia); MFX = moxifloxacin; OFX = ofloxacin; PAS = p-aminosalicylic acid.

lidded plate was used to perform both FL- and SL-DST. All the wells except for those in the outside lines (A and H: 1 to 12, which contained sterile H_2O) were filled with 100 μl M7H9 medium. A total of 100 μl of four times the highest drug concentration of each of the drugs to be tested was placed in the upper wells of line B. Serial two-fold dilutions were performed for wells B to G. One column (B to G) was left drug-free to be used as growth controls.[21] All the wells except B and G were inoculated with 100 μl of a 1:25 dilution from a bacterial suspension with turbidity comparable to 0.5 MacFarland standard (original bacterial suspension). Well B, used as a sterile control without bacteria, and well G, used as 1:100 growth control, were inoculated with 100 μl of a 1:2500 dilution from the original bacterial suspension. The FL-DST plates were prepared with INH, SM, RMP, EMB (Sigma, St. Louis, USA) and levofloxacin (LVX; Janssen-Cilag, Buenos Aires, Argentina).[20–22] The SL-DST plates contained amikacin (AMK), capreomycin (CPM), cycloserine (CS), ethionamide (ETH), kanamycin (KM; Sigma), linezolid (Pharmacia, New York, NY, USA), moxifloxacin (MFX; Bayer, Buenos Aires, Argentina), ofloxacin (OFX) and para-aminosalicylic acid (Sigma).[23,24]

The plates were sealed with tape and placed in plastic bags for increased biosafety and incubated for 5 days at 37ºC and normal humidity. After the incubation period, 22 μl of an aqueous solution of 5% MTT were added to one growth control well and incubated for another 24 h. When the change in colour was verified, the dye was added to the other wells and incubated again for 24 h.[20,22,23]

Gold standards

Indirect PM on LJ medium (ILJ) and on Middlebrook 7H11 supplemented by OADC (oleic acid-albumin-dextrose-catalase) enrichment (M7H11; BD Argentina) were used as gold standards for FL-DST and SL-DST, respectively.[10,25,26]

Statistical analysis

MedCalc version 9.0.1 (MedCalc, Mariakerke, Belgium) Microsoft was used for statistical analysis. The following statistics were calculated: sample size, range, mean and medians, 95% confidence intervals, variance, standard deviation (SD), relative SD, standard error of the mean and correlation coefficients.

The receiver operating characteristic (ROC) curve method was used to calculate sensitivity, specificity, accuracy and the critical drug concentration at which the best distinction between drug-susceptible and drug-resistant isolates may be observed.[23,27] The ROC curve method applied to a particular isolate compares the results obtained for each one of the drugs by either CMM or MGIT 960 with those from the gold standard at the critical drug concentration for each method.[27] The ROC curve method also calculates the area under the curve, which represents the overall performance (as a measure of accuracy) of the test under evaluation compared with the gold standard and taking into account sensitivity and specificity values.[27] When it was not possible to apply the ROC curve method to the results of a particular drug, the mean value and SD (±2 SD) were used.[23]

RESULTS

Data on a total of 2242 bacteriologically confirmed TB cases were collected during the study period: 239 (10.7%) were co-infected with HIV, 309 (13.8%) were HIV-negative and 1694 (75.6%) were not investigated; 337 (15.0%) patients had been previously treated for TB and 111 (5.0%) had been categorised as 'contacts' by conventional contact tracing and/or molecular epidemiology studies (data not shown). Most of the cases (1910, 85.2%) had pulmonary disease, and 1284 of these (67.2%) were positive on acid-fast bacilli (AFB) microscopy. Only 156 (7.0%) were foreign-born. It was possible to perform DST on 1705 clinical isolates; of these, 1626 (95.4%) gave valid results. The fully drug-susceptible H37Rv ATCC (American Type Culture Collection) 29274 was used as reference strain for DST.

The overall results of resistance to first- and second-line drugs are summarised in Table 2. A total of 1532 isolates were *M. tuberculosis* complex and 94 (5.8%) were classified as non-tuberculous mycobacteria (NTM). Overall drug resistance—or resistance to one or more drugs—was detected in 362/1532 (23.6%) of isolates; 137 were categorised as MDR-TB (8.9%), seven (0.5%) of which met the criteria for XDR-TB, being resistant to KM + OFX ($n = 5$) and MFX + KM ($n = 2$), in addition to INH and RMP. A total of 1033 (67.4%) strains were fully drug-susceptible.

Table 2 Results of overall drug resistance to first- and second-line drugs

Drug resistance	*n/N* (%)*
INH	286/1532 (18.7)
EMB	71/1532 (4.6)
LVX	10/1532 (0.7)
RMP	156/1532 (10.2)
SM	195/1532 (12.7)
AMK	25/94 (26.6)
CPM	8/94 (8.5)
CS	19/94 (20.2)
ETH	25/94 (26.6)
KM	29/94 (30.9)
LZ	1/94 (1.1)
MFX	3/94 (3.2)
OFX	13/94 (13.8)
PAS	4/94 (4.3)

*Drug-resistant isolates/total number of samples for which DST was performed.
INH = isoniazid; EMB = ethambutol; LVX = levofloxacin; RMP = rifampicin; SM = streptomycin; AMK = amikacin; CPM = capreomycin; CS = cycloserine; ETH = ethionamide; KM = kanamycin; LZ = linezolid (Pharmacia); MFX = moxifloxacin; OFX = ofloxacin; PAS = p-aminosalicylic acid; DST = drug susceptibility testing.

The correlation between the percentages of first- and second-line drug-resistant strains found with ILJ or indirect PM with Middlebrook 7H11 solid medium used as gold standard for SL-DST (PM-M7H11) and those found with CMM and MGIT 960, respectively, are shown in Table 3. Correlation coefficients (*r*) for CMM with ILJ ranged between 0.92 and 0.99 for SM and LVX, respectively, with 0.97 the average *r* value. For MGIT 960 and ILJ, the *r* range was 0.90–1.00 (EMB and RMP, respectively, average $r = 0.97$). For the comparison of MGIT 960 with CMM, the range was 0.93–1.00 (SM and RMP, average $r = 0.96$).

Lower correlations were observed for ETH (0.90 and 0.94) and CS (0.70, 0.78 and 0.82) with both CMM and MGIT 960 in comparison with PM-M7H11 as gold standard. Statistical parameters and critical concentrations for each of the drugs tested are given in Table 4. Parameters were calculated by the ROC curve method by comparing the results obtained using either CMM or MGIT 960 and the gold standards. Satisfactory performance is defined as an accuracy of >0.90. With MGIT 960, accuracy was highest for AMK, RMP and OFX. Performance was also high for INH, ETH and KM, followed by CPM, EMB, CS and SM. With CMM, the highest accuracy was found for AMK, CPM, RMP, OFX and PAS, followed by INH, LVX and EMB. Neither CMM nor MGIT 960 gave good sensitivity values (MGIT 960 80.0% and CMM 87.5%) for CS, although both methods showed good specificity (MGIT 960 94.3%, CMM 93.5%) and general performance (MGIT 960 accuracy 0.94, CMM accuracy 0.95).

The time required by the methods for the detection of drug resistance is shown in the Figure. The overall performance of the methods showed that 8 days were necessary for detecting 50% of the drug-resistant isolates using MGIT 960 and 9 days for CMM (t 6.34, $P < 0.0001$). To obtain 95% of the drug-resistant results by PM (ILJ or PM-M7H11), CMM and MGIT 960, respectively 20, 11 and 10 days were required.

Table 3 Correlation between percentages of first- and second-line drug-resistant strains identified by the gold standards and study methods

Method/ drug	DST method, reference methods			
	ILJ		MGIT 960_1	
	n	*R*	*n*	*R*
CMM_1	717 (2)*	0.97	368 (3)†	0.96
INH		0.98		0.96
SM		0.92		0.93
RMP		0.99		1.00
EMB		0.95		0.96
LVX		0.99		—
MGIT 960_1	1052 (4)‡	0.97		
INH		0.98	—	—
SM		0.99		
RMP		1.00		
EMB		0.90		
	PM-M7H11		MGIT 960_2	
	n	*R*	*n*	*R*
CMM_2	94	0.96	94	0.94
AMK		1.00		1.00
CPM		1.00		1.00
CS		0.78		0.70
ETH		0.94		0.90
KM		0.96		0.95
LZ		1.00		1.00
MFX		1.00		1.00
OFX		1.00		1.00
PAS		1.00		—
MGIT 960_2	94	0.97	—	—
AMK		1.00		
CPM		1.00		
CS		0.82		
ETH		0.94		
KM		0.96		
LZ		1.00		
MFX		1.00		
OFX		1.00		

*Number of strains tested by ILJ and CMM_1.
†Number of strains tested by MGIT 960_1 and CMM_1.
‡Number of strains tested by MGIT 960_1 and ILJ.
CMM_1, MGIT 960_1 = methods for testing first-line drugs; CMM_2, MGIT 960_2 = methods for testing second-line drugs; DST = drug susceptibility testing; ILJ = indirect Löwenstein-Jensen proportion method; MGIT = Mycobacteria Growth Indicator Tube; CMM = colorimetric-based method; INH = isoniazid; SM = streptomycin; RMP = rifampicin; EMB = ethambutol; LVX = levofloxacin; PM-M7H11 = indirect proportion method with Middlebrook 7H11 solid medium used as gold standard for second-line DST; AMK = amikacin; CPM = capreomycin; CS = cycloserine; ETH = ethionamide; KM = kanamycin; LZ = linezolid (Pharmacia); MFX = moxifloxacin; OFX = ofloxacin; PAS = p-aminosalicylic acid.

DISCUSSION

TB control efforts have been relatively successful over the last few decades, but human immunodeficiency virus (HIV) co-infection and the emergence of MDR-TB and XDR-TB are compromising progress towards full TB control. Worldwide surveillance reveals that drug-resistant strains are becoming widespread and reaching alarming levels in several countries.[3,28] To reinforce laboratory capacity, the WHO recommends using liquid cultures for the diagnosis of TB cases by primary isolation of *M. tuberculosis* and also for DST.[29]

In Argentina, several MDR-TB outbreaks comprising both HIV-co-infected and non-co-infected individuals have been reported in the last decade.[30,31] The country still has a paradoxical TB situation in which the total number of cases notified to the NTP is almost stable while the number of MDR-TB cases is increasing each year, with more than 30 XDR-TB cases recorded since 2000.[14] As usual, MDR- and XDR-TB cases are concentrated in big cities with overcrowded populations, with a high risk of dissemination. For this reason, clinical laboratories in big cities should be prepared to deal with MDR- and XDR-TB by detecting resistant mycobacteria as rapidly as possible. To prevent therapeutic mistakes and amplification of MDR-TB, FL- and SL-DST should be implemented in clinical laboratories and used to aid clinicians to adapt antituberculosis treatment regimens accordingly.[7,13,32]

Table 4 Statistical parameters obtained for the different drugs by the methods under evaluation

	Sensitivity, %		Specificity, %		Area under the ROC curve		Critical concentration µg/ml*	
Drug	MGIT 960	CMM	MGIT 960	CMM	MGIT 960	CMM	MGIT 960	CMM
INH	100.0	94.8	98.2	97.3	0.99	0.97	0.10	0.25
EMB	95.2	80.0	96.2	90.0	0.96	0.96	5.00	4.00
LVX	ND	100.0	ND	98.0	ND	0.98	ND	1.00
RMP	100.0	100.0	100.0	99.7	1.00	1.00	1.00	0.50
SM	93.0	83.3	96.7	96.6	0.91	0.92	1.00	2.00
AMK	100.0	100.0	100.0	100.0	1.0	1.0	4.00	4.00
CPM	100.0	100.0	95.0	100.0	0.95	1.0	5.00	2.00
CS	80.0	87.5	94.3	93.5	0.94	0.95	30.00	15.00
ETH	91.7	90.0	90.5	95.7	0.98	0.91	5.00	2.00
KM	90.0	100.0	100.0	99.0	0.97	0.99	5.00	2.00
LZ	100.0	100.0	100.0	100.0	ND†	ND†	1.00	1.00
MFX	ND	100.0	ND	100.0	ND	ND†	ND	0.50
OFX	100.0	100.0	100.0	100.0	1.00	1.00	2.00	1.00
PAS	ND	100.0	ND	100.0	ND	1.00	ND	1.00

*Critical drug concentration was defined as the lowest MIC value of a drug showing the best discriminatory power in differentiating drug-resistant from drug-susceptible isolates.
†Insufficient data for ROC curve analysis. LVX, MFX and PAS were not tested using MGIT 960.
ROC = receiver operating characteristic; MGIT = Mycobacteria Growth Indicator Tube; CMM = colorimetric-based method; INH = isoniazid; EMB = ethambutol; LVX = levofloxacin; ND = not done; RMP = rifampicin; SM = streptomycin; AMK = amikacin; CPM = capreomycin; CS = cycloserine; ETH = ethionamide; KM = kanamycin; LZ = linezolid (Pharmacia); MFX = moxifloxacin; OFX = ofloxacin; PAS = p-aminosalicylic acid; MIC = minimum inhibitory concentration.

The results of this study show that DST results from pure culture can be obtained in 8–9 days by both MGIT 960 and CMM. This means savings of approximately 40 days in diagnosing MDR- or XDR-TB from the clinical sample compared with primary culture and DST using solid media and conventional PM on LJ. MGIT 960 was faster but more expensive than CMM. However, CMM was more laborious and required more biosafety precautions than MGIT 960, which uses plastic screw-cap tubes that remain inside the instrument during the entire period of incubation.[15] CMM needs to be removed from the incubator and is handled until the dye addition is completed and the plate can be read.

On the whole, our study results are in line with those published by other authors, and allowed us to define the critical concentrations of first-line drugs to be tested by CMM and of second-line drugs to be tested by both CMM and MGIT 960.[18,33,34] The following drug concentrations (µg/ml) are recommended for testing in MGIT and CMM: AMK 4.0, CPM, ETH and KM 5.0 and 2.0, CS 30.0 and 15.0, LZ 1.0, OFX 2.0 and 1.0. For MFX and PAS, tested only by CMM, the concentrations are 0.5 and 1.0, respectively.

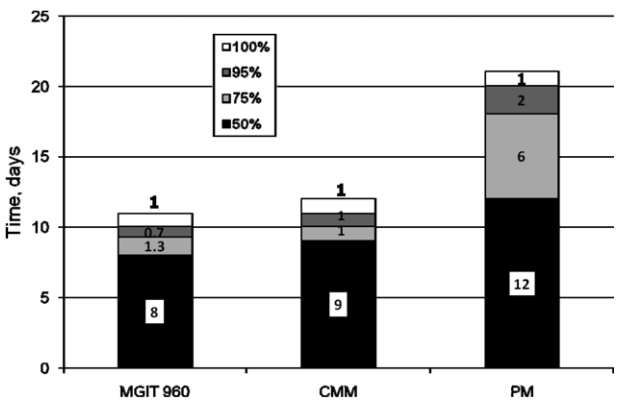

Figure Time to detection of drug resistance for each of the methods evaluated. MGIT = Mycobacteria Growth Indicator Tube; CMM = colorimetric-based method; PM = proportion method.

Our study had the following limitations: statistical analysis was not always performed by the ROC curve method, as no discrepancies between the method under study and the gold standard were found for CPM, LVX, LZ, MFX and OFX. For SL-DST, isolates were tested individually using CMM shortly after culture results were obtained. For MGIT 960, isolates were collected during the study period and tested in a single experiment.

CONCLUSION

CMM is an in-house method that does not require any special apparatus. It uses a very versatile platform, and is an effective, low-cost tool for screening isolates suspected of being MDR- or XDR-TB. However, the MGIT 960 system for SL-DST can be adapted to automatically detect growing strains (using TB eXIST™, BD EpiCenter), with the important added benefit of reducing transcription errors by fully automated readings and DST interpretation.[35]

We conclude that both methods could be implemented in clinical laboratories as rapid diagnostic tools for detecting MDR- and XDR-TB. However, financial resources and the availability of reagents and supplies need to be taken into account by decision makers, particularly in low- or middle-income settings.

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RÉSUMÉ

CONTEXTE : Hôpital Dr Cetrángolo, Province de Buenos Aires, Argentine.

OBJECTIF : Evaluation du système BACTEC™ Mycobacteria Growth Indicator Tube (MGIT)™ 960 et de la méthode basée sur la colorimétrie (CMM) pour les tests de sensibilité de *Mycobacterium tuberculosis* à l'égard des médicaments de première ligne (FL-DST) et de deuxième ligne (SL-DST).

SCHÉMA : FL-DST a été étudié par le SIRE MGIT 960. Les concentrations minimales inhibitrices (MIC) utilisées pour l'isoniazide (INH), la streptomycine (SM), la rifampicine (RMP), l'éthambutol (EMB) et la lévofloxacine (LVX) ont été également déterminées par la CMM utilisant le MTT (bromure de 3-(4,5-diméthylthiazolyl-2)-2,5-diphényltétrazolium). Les MIC pour l'amikacine (AMK), la kanamycine (KM), la capréomycine (CPM), l'éthionamide (ETH), la cyclosérine, l'ofloxacine (OFX), le linezolide (LZ) et la moxifloxacine (MFX) ont été déterminées sur 94 isolats multirésistants de *M. tuberculosis* à la fois par MGIT 960 et par CMM. Des méthodes statistiques ont été utilisées pour définir les isolats sensibles ou résistants aux médicaments sur la base de la comparaison avec les résultats obtenus par les gold standards.

RÉSULTATS : On a étudié au total 1626 isolats cliniques. Les concentrations critiques ont pu être déterminées en moins de 10 jours à la fois par CMM et MGIT 960. CMM est moins coûteux, mais demande plus de travail que MGIT 960. Les performances les meilleures des deux méthodes ont été obtenues pour AMK, RMP, OFX, LZ et MFX, suivis par INH, ETH, KM, CPM et LVX (testé uniquement par CMM).

CONCLUSIONS : La mise en œuvre des deux méthodes pourrait être prometteuse en pratique clinique comme outils de diagnostic rapide pour la détection des isolats résistants aux médicaments.

RESUMEN

MARCO DE REFERENCIA: Hospital Dr Cetrángolo, Buenos Aires, Argentina.

OBJETIVOS: Evaluación de un micrométodo colorimétrico (CMM) y BACTEC™ Mycobacteria Growth Indicator Tube (MGIT)™ 960 para la determinación de la sensibilidad de *Mycobacterium tuberculosis* a drogas de primera y segunda línea (FL-DST, SL-DST).

MÉTODO: La FL-DST fue determinada empleando SIRE MGIT 960. Con el CMM adicionado con bromuro de 3-(4,5-dimethylthiazolyl-2)-2,5-diphenyltetrazolio, se determinó la concentración inhibitoria minima (MIC) para isoniacida (INH), estreptomicina, rifampicina (RMP), etambutol (EMB) y levofloxacina (LVX). Sobre 94 aislamientos multidrogorresistentes (TB-MDR) se determinaron las MIC de amicacina (AMK), kanamicina (KM), capreomicina (CPM), etionamida (ETH), cycloserina, ofloxacina (OFX), linezolid (LZ) y moxifloxacina (MFX) en MGIT 960 y CMM. Métodos estadísticos permitieron diferenciar aislamientos resistentes de sensibles a las drogas comparando los resultados con los obtenidos por métodos de referencia.

RESULTADOS: Fueron incluidos 1626 aislamientos clínicos. Las concentraciones críticas fueron definidas en aproximadamente 10 días para MGIT 960 y CMM, más barato pero más laborioso que MGIT 960. Los mejores rendimientos de ambos métodos fueron obtenidos para AMK, RMP, OFX, LZ y MFX seguidos de INH, ETH, KM, CPM y LVX (sólo por CMM).

CONCLUSIONES: Estos métodos podrían ser promisoriamente implementados en la práctica clínica como herramientas de diagnóstico rápido de TB-MDR.