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Economic impact of the implementation of a fixed dose combination treatment for Tuberculosis in Mexico

Jorge González-Canudas[1]*; Jesús Felipe González-Roldán[2]; Martín Castellanos-Joya[3]; Yulia Romero-Antonio[4]; Aarón Molina-Pérez[4]; Juan Gabriel Gay-Molina[5]

[1]Internal Medicine Department, IMSS- Centro Médico Nacional Siglo XXI, Mexico City

[2]Board of Director, Sociedad Mexicana de Salud Pública, A.C, México City

[3]Department of Mycobacterium reference, CENAPRECE/ Secretaría de Salud, México City

[4]Research and Development Department, Laboratorios Silanes, S.A. de C.V, Mexico City

[5]Tecnología e Información para la Salud, Mexico City

***Corresponding Author(s): Jorge González-Canudas**

Head of Research and Development Department, Laboratorios Silanes, S.A. de C.V, USA

Tel: +52-5488-3761; email: jogonzalez@silanes.com.mx

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Abstract

Objective: To compare the cost-effectiveness of 2 treatment schemes for tuberculosis in Mexico, before and after the implementation of fixed-dose combination (FDC).

Material and methods: Model of economic evaluation based on information posted for 2014 cohort. The results and costs of drugs in both scenarios (1 = prior to 2006, single tablets; 2 = after to 2006, FDC) were evaluated using a decision tree model.

Results: The cost of first line treatment for scheme one was MX$ 15,112.00 and for scheme 2 was MX$ 9,418.00. The probability of failure with treatment for scheme 2 was 11.1% lower; additionally detected an increase in effectiveness with a survival increased (5%) for scheme 2.

Conclusions: The scheme of treatment for tuberculosis started from the year 2006 in Mexico, has economic advantages, of compliance, efficiency, and reduction of mortality from this cause.

Introduction

Tuberculosis is a challenge to Mexican Public Health System as well as other countries of the world. It is a multifactorial disease whose outcome is defined by: Social and economic situation, the chance of detection, opportunity of treatment and comorbid diseases, (viruses of the acquired immune deficiency, malnutrition, drug addiction, alcoholism, among others) of each subject [1].

Fundamental strategies for its control are focused on early diagnosis and effective treatment, in particular in patients with pulmonary tuberculosis that are contagious. The treatment of latent tuberculosis in vulnerable populations has the objective to break the chain of transmission in the shortest possible time. Free supervised treatment and prevention campaigns are an essential part of the strategies to prevent resistance to the

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drugs and its complications. The established treatment strategy includes a monthly clinical and bacteriological monitoring for six months; during the initial 2 months, the treatment consist of 6 days a week (resting 1 day) with rifampicin 600 mg/day, isoniazid 300 mg/day, pyrazinamide 1,600 mg/day and ethambutol 1,200 mg/day; the remaining 4 months the treatment is administered intemitently (Monday, Wednesday and Friday) rifampicin 300 mg/day and isoniazid 400 mg/day [1].

Mexico recorded the highest incidence of tuberculosis in 1997 with nearly 24 thousand cases and the highest mortality in 1990 with 7.6 deaths per 100 thousand inhabitants [2]. Prior to year 2000, the therapeutic success was less than 71%, which includes drop-out rates and reflected a failure of treatment above the internationally acceptable limit (< 5% and <2%, respectively) [3]. Control of this ancient disease has involved a gradual national effort.

In 2004 Mexican Ministry of Health (MMoH) managed a model of combined treatment which included the four basic drugs (rifampicin 150 mg, isoniazid 75 mg, pirazinamide 400 mg, ethambutol 300 mg) for an intensive phase of 10 weeks (~ 2 months) and rifampicin 150 mg and 300 mg / isoniazid 200 mg and 400 mg for the maintenance phase of 4 months in a single fixed dose tablet in order to improve therapeutic adherence, reduce failures and achieve better treatment success rates and fewer deaths, seeking thus to break the chain of transmission [1]. In 2006, the MMoH incorporated a fixed-dose combination, developed by the Mexican pharmaceutical laboratory (Laboratorios Silanes, S.A. de C.V.), to the antituberculosis program [1].

Based on data retrieved from the year books of morbidity of the Ministry of Health, the tuberculosis mortality rate in Mexico has decreased from 7.6 to 1.7 from 1984 to 2016, while the treatment success rate has increased 21 between 2000 and 2016 [2].

In Latin America, other countries have also changed from individual drugs to fixed dose (combined), including: Brazil, El Salvador, Paraguay, and Peru, which have also had an increase in success rate with percentage differences ranging from 0.2% to 9% [1,3-9].

This study is a economic evaluation which seeks to determine the differences in cost-effectiveness between the scheme of treatment for tuberculosis used in Mexico before the year 2005 and implemented subsequently with the presentation of fixed-dose combination. This latter strategy meant a decrease in the number of tablets per patient which is known to promote treatment adherence; the results of this strategy have a favorable impact for the National Public Health.

Material and methods

Economic evaluation model was performed in the software TreeAge® 2016. A comparison between tuberculosis morbi-mortality before 2006 and between 2007 and 2014 was made. The information of 2006 was excluded from the analysis because both treatments coexisted while the transition of drugs took place. The information included in the present analysis was published by the National Epidemiological Surveillance System (known in Spanish as SINAVE) in its Tuberculosis module for 2014 cohort and the National Center of epidemiological surveillance and Disease Control (known in Spanish as CENAVECE); such information reflects a steady increase in the percentage of patients who respond to treatment of tuberculosis since 2000, presenting the best successful treatment response rate from year 2007. Estimated percentages of treatment response average from 2000 to 2005 and the year 2007 to 2015. The year 2006 was excluded for the analysis because it was the year the treatment transitioned from (scheme 1; 4 single tablets) to the scheme of fixed-dose combination (scheme 2; 1 tablet) [1,10-11].

Each treatment group is facing a specific probability of success depending on the treatment period: scheme 1 (previous 2005, 4 single tablets) and scheme 2 (after 2007, fixed-dose combination tablet).

Our assumption was that 60% of patients with treatment failure repeat previous treatment and the rest (40%) were treated with second-line alternatives.

From the estimated averages we designed a model decision tree which compared the costs of purchase of drugs and therapeutic outcomes in both treatments schemes. The model assumed that in case of treatment failure, patients could receive a scheme with second-line drugs; the percentage of patients who received the same treatment again was defined based on the data published by the World Health Organization for Mexico at the periods mentioned [12].

In the model, patients with effective treatment response were exempt from mortality; to those with fail treatment was estimated a probability of dying 8.1 per each 100 patients, according to the data collected in the database of the World Health Organization for Mexico [12]. Figure 1 presents a summary of the probabilities used in the model.

The analysis included the costs of acquisition of drugs in first and second-line treatment.

Acquisition of first-line drugs prices were obtained from the consolidated bid of the Mexican Institute of Social Security and the Ministry of health of 2017. Prices of acquisition of second line drugs were obtained from the study of Arinaminpathy et al. published in the Bulletin of the WHO, which were updated with prices 2017 according to the inflation reported by Mexican Central Bank (known as BANXICO) [13-15].

Results

This economic evaluation analysis calculated a total average cost of MX$ 15,112.00 for patients treated with first line of scheme 1 (prior to 2005), while for scheme 2 (after 2007) estimated cost equivalent to $ 9,418.00.

The difference in units ingested per day between scheme 1 and scheme 2 was 43% for intensive phase (10 weeks, ~ 2 months) and 33% for continuation phase (4 months). The probability of failure to treatment in scheme 2 was 11.1% lower than that with the scheme 1, conditioning a decrease in total expenditure compared to scheme 1. In terms of effectiveness, patients treated in scheme 1, had a probability of survival of 0.989 while in scheme 2, this probability was 0.994; the above translates into an incremental effectiveness of 5% by greater survival for scheme 2. Figure 2 shows a summary of the results of the analysis of cost-effectiveness.

We conducted a sensitivity analysis that identified the second-line treatmentas the most sensitive variable in the model , followed by the cost of acquisition of first-line drugs of both schemes, meaning that the cost savings identified in the FDC

treatment are composed of mainly direct acquisition cost and indirect savings due to a reduces need of second line antituberculosis treatment

Discussion

Treatment compliance is particularly important in the management of tuberculosis around the world and in Mexico, during year 2006 changed the scheme of 7 tablets to 1 tablet per day; from 2007 there is a consistent trend of increase in success rate in patients under treatment of tuberculosis in Mexico, which is directly related with the incorporation of fixed dose combination tablet.

The difference in number of tablets between schemes could be translates into various benefits by reducing the number of daily tablets to ingest for patient: Greater treatment compliance, reduced rates of drop-outs, prevention of drug resistance, simpler management of the treatment and to facilitate supervision by health personnel.

The increase in the success rate is also related to a decrease in the cost of treatment per patient, consequence of a smaller number of patients who require second-line treatment for full compliance of first-line treatment.

The additional cost of the acquisition of the treatment with rifampicin 150 mg / isoniazid 75 mg / 400 mg pyrazinamide / ethambutol 300 mg in a single tablet for intensive phase (10 weeks, ~2 months) and rifampicin 150 mg and 300 mg / isoniazid 200 mg and 400 mg in a single tablet for continuation phase (4 months), is offset and surpassed by the savings associated with the decrease in patients who require a second line of treatment in addition to the reduction in overall mortality.

Further research will be needed to confirm the causal relationship between fixed-dose treatment and improvement in treatment outcomes in Mexican population.

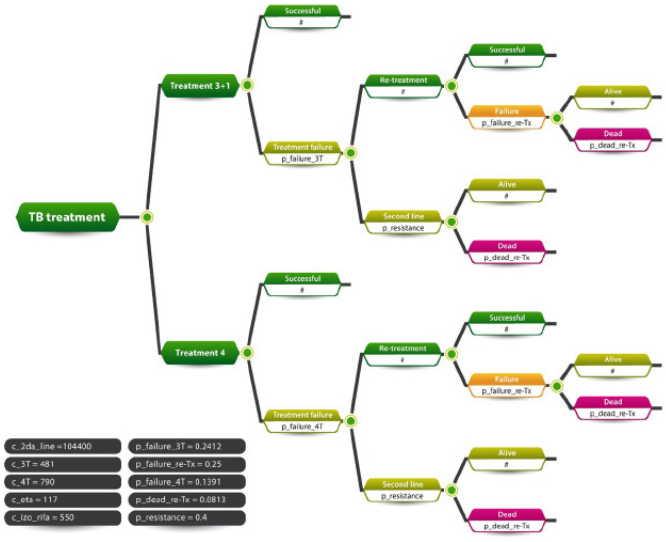

Figure 1: Economic model diagram

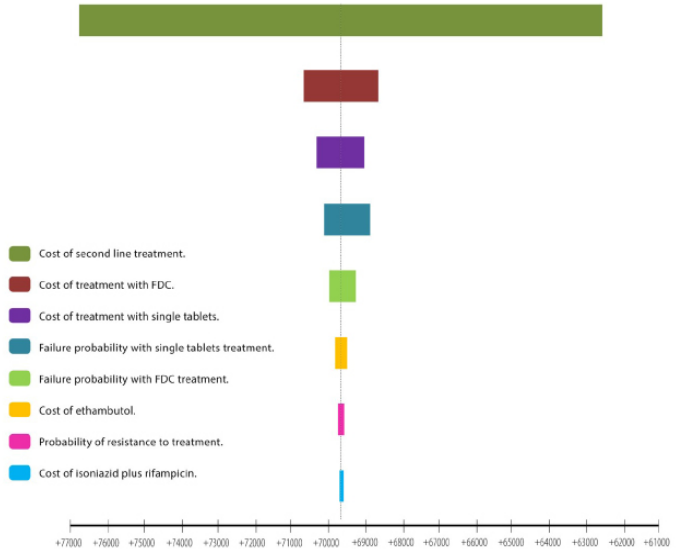

Figure 2: Twister analysis diagram

Conclusions

The fixed dose combination scheme for tuberculosis treatment started in Mexico in 2006 represents an economic advantage, effectiveness and reduction of mortality from this cause.

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