

PULMONARY TB FACES IN THE NEW CONTEXT OF DRUG USERS

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Rezumat

Tuberculoza a căpătat o nouă față în contextul utilizării în creștere a drogurilor. Combinația de afecțiuni de tip infecție HIV, hepatită B sau C apărută la utilizatorii de droguri injectabile pune probleme serioase în spitale. Autorii analizează, în acest nou context, aspectele epidemiologice, factorii predispozanți, expresiile clinice și soluțiile terapeutice pentru aceste cazuri, dar și programele care trebuie adoptate pentru a permite controlul acestei noi provocări pe plan mondial.

Cuvinte cheie: tuberculoză, droguri, HIV, hepatita B și C.

Abstract

Tuberculosis has taken on a new face in the context of emergent drug use. The combination of conditions such as HIV infection, hepatitis B or C, arising from the use of injectable drugs create serious problems in hospitals. In this new context, the authors analyze epidemiological aspects, predisposing factors, clinical expressions and therapeutic solutions for these cases, but also the programs that must be adopted to allow the control of this new worldwide challenge.

Keywords: tuberculosis, drugs, HIV, hepatitis B and C.



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Introduction

Drug use and drug related diseases are two very important problems of all the services in charge for diagnosis and treatment of TB. People who inject drugs practice high-risk behaviors and utilization of screening services for infectious diseases for this cases is poor. Behaviors at risk are more usually generating: HIV infection, hepatitis, and other sexually transmitted infections (STIs). It is already known that tuberculosis (TB), human immunodeficiency virus (HIV), and hepatitis C virus (HCV) share a global presence and propensity to disproportionately affect marginalized populations. Once they are infected with one infectious disease, it is an increasing risk of another disease with progress of the pathogenesis of these connected illnesses. Vicious circle is created. One example is evident: HIV-positive people who inject drugs are at a high risk of tuberculosis. This happens more in countries with high prevalence of TB⁽²⁾. STIs increase also the risk of HIV infection⁽³⁾ and HIV infection accelerates the progress of viral hepatitis⁽⁴⁾. Needle-sharing behaviours are common among PWID (people who inject drugs). The percentage of those who share needles among PWID ranges is still very high (from 16 to 76 % in different countries)^(5,6). In this context there are new faces of tuberculosis

combined with other comorbidities in every part of the earth. There is a high prevalence of these infections among intravenous drug users (IDUs), with estimates of 30-60% for HCV and 1-30% for HIV^(7,8). Association of infectious diseases is very frequent. Among the European participants⁽⁸⁾ the researchers found: 71% TB, HCV, HBV, HIV, or STD infection, and 43% had two or more of these diseases concomitantly. The highest incidences of HCV and HIV were reported by participants in a poorer social and health situation. Drug addicts must cope not only with their addiction but also with the process of social exclusion they are immersed in⁽⁹⁾.

Epidemiological context-TB and other diseases

Changes of multiple TB faces depend on the analyzed period and the income / per inhabitant of different countries. One example is coming from USA. Since 2012 it was a declining of TB prevalence among US-born persons and no change among non-US-born persons. Overall, During 2014-2017 hospitalized patients for TB in this rich country had as features: older TB patients, more likely with combined pulmonary and extrapulmonary disease compared with exclusively extrapulmonary disease, nonwhite race, and less likely with human immunodeficiency virus-positive, or cavitary

pulmonary disease. After 2014 (2014-2017), the characteristics of the patients were: non-US-born persons with TB were more likely to have diabetes while the US-born were more likely to have smear positive TB and use noninjecting drugs⁽¹⁰⁾.

Every country has a prevalence of associated infectious diseases in HIV patients who inject drugs (IDU) very different but anchored to national prevalence of different diseases and rate of drug users. In India in HIV-infected IDUs the prevalence of hepatitis B and C infections were 11.9 and 94.1 percent, respectively and tuberculosis (33.9%), herpes zoster (9.3%) and herpes simplex (9.3%)⁽¹¹⁾. In the sample of participants with CD4+ <200 cells/ μ l, the prevalence of TB was 60 percent⁽¹¹⁾.

In Hungary, in Budapest, among injecting drug users (IDUs) some researchers⁽¹²⁾ found 0% HIV, 37% HCV, 24% HAV, and 14% past HBV infection. Infections with Herpes 1 or 2, tuberculosis, Chlamydia, syphilis, and gonorrhea were 79%, 12%, 7%, 4%, and 0%, respectively. They found that the ethnic Roma, and the homeless were more likely to have any hepatitis and a higher number of drug-related infections and the others (those who worked at least part time and those who were in treatment) were less likely to have drug-related infections. In crack cocaine users in Miami a gender difference was evident in the HIV seropositivity rates, with 25.7% of men and 32.2% of women testing positive for antibodies to HIV. One possible explanations concerning women is because they are more likely than men to trade sex for drugs and/or money⁽¹³⁾. TPHA reactivity and chest X-ray suggestive of tuberculosis were found to be higher in lower middle socio-economic class of the population among opiates ($p = 0.002$ and 0.027) and cannabinoids ($p = 0.000$ for both) abused as

well as with increasing age ($p = 0.000$) specially in poor countries⁽¹⁴⁾. Looking only to TB cases there are other important epidemiological reports. One example: almost one third of TB cases in a university hospital in Santiago, Chile occurred among immunosuppressed patients and 42% were extra-pulmonary forms. 28% had some type of immunosuppression at diagnosis: 11.7% HIV infection and 16.6% were using immunosuppressive drugs. In this group, a previous tuberculin skin test was done in only 12.2%. This means that it is necessary to make a regular screening for this cases on TB diagnosis and it's possible evolution⁽¹⁵⁾. Association of TB with infectious diseases continue to remain a challenging problem for many countries. In Argentina almost one in three participants (33.1 %) presented at least one infection in addition to TB and IDUs remains the main risk factor for HIV, HBV and HCV infections⁽¹⁶⁾. For another sample studied in Argentina infections with hepatitis B virus (HBV), HIV-1, hepatitis C virus (HCV), *Treponema pallidum* and human T-cell lymphotropic virus types I/II were present at 19.8%, 17.1%, 11.8%, 7.0% and respectively 2.2% patients. HIV genetic characterization showed the presence of subtypes Env subtype F in 54.2% and subtype B in 45.8%. Multiresistant TB was detected at high prevalence in Argentina during the 1990s and was particularly associated with AIDS patients attending some hospitals in large urban⁽¹⁷⁾. In India the prevalence of HIV infection among TB patients is 1.48% and that of HBsAg reactivity was found to be 2.96%. During 2007-2010, the HIV-positivity varied between 1.5% and 1.45% whereas HBV reactivity ranged between 2.4% and 3.63%. A substantial percentage of the TB patients attending the outpatient department had HIV and HBV infections,



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which otherwise would remain undiagnosed without serological screening⁽¹⁸⁾.

Another problem connected to multiple infections of TB patients remains the period of the time spent in prisons. A recent review of the global epidemiology of HIV, HCV, and TB in prisoners estimated that, of the roughly 10 million people detained worldwide on any given day, 3.8% are living with HIV, 15.1% with HCV, and 2.8% with active TB⁽¹⁹⁾; 56-90% of people who inject drugs are at risk to be incarcerated at some stage of their lives⁽²⁰⁾.

Moldavia another country with high prevalence of Tb has similar problems. In a sample of 321 cases with coinfection of HIV/TB during 2013-2014, 4.7% do not have stable place of life, 85% do not work, 84.4% (± 3.82) have a history or are present intravenous drug users. Only 2.6% (± 4.98) are on opioid substituent treatment during TB treatment, 53% are heavy drinkers, 33% had C hepatitis and 14% B hepatitis.

For all of this patients a social vulnerability is obvious⁽²¹⁾. The overall prevalence of HBV and HIV infections is also high in TB patients in Brazil; in a study it was 25.6% and 27.6%, respectively. A higher HBV infection rate was found among HIV-infected patients (36.9%) compared to patients infected with TB only (20.0%)⁽²²⁾. There are also important signals from Kazakhstan: in a screening of HIV patients 27%, 8%, 2%, and 5% were coinfecting with, respectively, HCV, TB, HBV,

and STI (sexual transmitted infections); they also found a long list of triple or quadruple infections of HCV/TB (12%), TB/STI (0.8%), HCV/STI (2%), HCV/HBV (1%), HBV/TB (0.4%), HBV/STI (0.2%), HBV/HCV/TB (0.4%), HBV/HCV/STI (0.2%), or HCV/TB/STI (0.2%)⁽²³⁾.

Premature mortality attributable to socioeconomic inequality

Is another cause related to all the new faces of TB. One example is coming from England. The authors start with the definition of this parameter: socioeconomic position was defined using deciles of the Index of Multiple Deprivation: a measure of neighborhood income, employment, education levels, crime, health, availability of services, and local environment. 35,6% of premature deaths were attributable to socioeconomic inequality.

The biggest contributors were well known diseases like ischemic heart disease, respiratory cancers and chronic obstructive pulmonary disease. In the same time the most unequal causes of death were deaths due to tuberculosis, opioid use, HIV, psychoactive drugs use, viral hepatitis, and obesity, each with more than two-thirds attributable to inequality⁽²⁴⁾. Mycobacterium tuberculosis causes approximately 10.4 million new cases of tuberculosis and 1.5 million deaths annually, with an additional

0.4 million deaths in individuals co-infected with human immunodeficiency virus (HIV)⁽²⁵⁾. Despite existing very successful HIV and methadone program, like the one from Vietnam, the mortality remains high among PWID, and is largely due to curable infectious diseases such as tuberculosis and viral hepatitis⁽²⁶⁾.

In the HIV-positive cohort, in which 81% of participants had undetectable viral load, the two main causes of death were tuberculosis and HIV-related diseases; at the opposite in the HIV-negative cohort, the two main causes of death were liver-related diseases and overdose. Low socio-economic status including poor housing, poor nutritional status, very frequent smoking, and frequent indoor gathering for sharing drugs likely contributed to this excess risk of TB. Cure rate is very low for patients with tuberculosis and HIV; 67.3% were cured of tuberculosis and 15.7% died in poor country like Cameroon⁽²⁷⁾. Hepatitis B, absence of cotrimoxazole prophylaxis, poor treatment adherence, and a CD4 count <50 were combined risk factors for mortality.

Covid 19, drugs and all these disease

It was an important impact of viral pandemic evolution on harm reduction services and also on TB problems. In Spain for example the average number of service users across all centers decreased by 22% in comparison to the same period in the previous year and the average needle distribution decreased by 40% in comparison to 2019. This was connected with a decrease in infectious disease testing rates (hepatitis B and C viruses, human immunodeficiency virus, and tuberculosis) for March, April, and May in 2020 and an increase in overdose deaths immediately after finalization of the state of

alarm⁽²⁸⁾. Another consequence for PWUD living with HIV, HCV or TB are the disruptions in access to antiretroviral therapy (ART), and direct-acting antivirals (DAAs) for HCV and TB treatment, which could drive drug resistance and/or treatment failure. In the COVID period opioid maintenance treatment, needle/syringe programs and antiretroviral treatment /hepatitis C treatment continued but many problems appears like: important reductions and operational changes, increases in overdoses, widespread difficulties with food and hygiene needs, disruptions in drug supply, and increased homelessness⁽²⁹⁾.

Screening of disease starting from healthcare administrative datasets could be used to monitor programs providing prevention and treatment services to people who inject drugs (PWID). The British Columbia Hepatitis Testers Cohort (BC-HTC) including 1.7 million individuals tested for HCV/HIV or reported HBV/HCV/HIV/tuberculosis cases in BC from 1990 to 2015, datasets were analyzed including physician visit, hospitalization, and prescription drug records.

The authors from British Columbia assessed the performance of IDU (injecting drug use) algorithms through calculation of sensitivity, specificity, positive predictive, and negative predictive values versus IRI (injecting related infections).

They found that sensitivity was highest (90-94%), and specificity was lowest (42-73%) for algorithms based either on IDU or IRI and drug misuse codes. An optimal sensitivity and specificity combination was found with two medical visits or a single hospitalization for injectable drugs with (83%/82%) and without OST (opioid substitution therapy) (78%/83%), respectively. There conclusion is that



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algorithms for identifying PWID using diagnostic codes in linked administrative data could be used for tracking the progress of programming aimed at PWID and this is another modality to estimate PWID population size⁽³⁰⁾. Prevalence of HIV (43.9%), HCV (22.6%) and HBV (5.9%) was higher among PWID in screening done in Mozambique first drop-in-center⁽³¹⁾. This highlights the importance of targeted integrated care services for the sample of population with high risk and PWID. HCV prevalence was most common among MDR-TB patients in Eastern Europe and was also high in several countries outside of Eastern Europe: Kazakhstan, Pakistan and Myanmar; HCV prevalence was generally much higher than HBV prevalence and also higher than previously reported estimates in the general population. HBV prevalence exceeded even 20%⁽³²⁾ (ex. Myanmar). That's why it's important to integrate a routine HBV and HCV screening into national MDR-TB treatment protocols in high prevalence countries.

Romanian data

Romanian data are not very different if we are looking to information's coming from other countries. The introduction of new psychoactive substances on the Romanian market in 2008 was associated with high risk behavior for HIV acquisition compared to

opioid abuse, which resulted in an increased number of new HIV infections among injecting drug users (IDU). 1/5 of new diagnosed HIV patients in 2015 (21% patients were IDUs out of a total of 698 newly)⁽³³⁾. The majority of IDUs were young men, with HIV/HCV coinfection. They found tuberculosis in 27% HIV infected vs 7% HIV non-infected patients. Rifampicin resistance - based on genotypic (MTB/RIF Xpert) and routine phenotypic methods (microscopy, Lowenstein-Jensen cultivation) was detected in a high proportion of HIV/tuberculosis coinfecting patients from a tertiary level infectious diseases hospital (18.5%), with a positivity rate of 35% for pulmonary samples and 21% for non-pulmonary samples⁽³⁴⁾. In another retrospective study of HIV and TB cases, a quarter (23.8%) of coinfecting patients were IDUs.

Comparing HIV positive and HIV negative samples the researchers observed that pulmonary TB (PTB) was found in 54% versus 50%, extra-pulmonary TB (EPTB) in 27% versus 38% and PTB associated with EPTB were found 19% versus 12% of cases⁽³⁵⁾. In a screening study (on almost 10000 patients) of association HIV with hepatitis B and C the authors found 5,4% positive for HBsAg, 2,7% for anti-HCV, and 0.1% positive on ELISA tests for HIV infection⁽³⁶⁾.

It is a demonstration of underdiagnosed viral infections for Romania. Concerning Tb and

HIV in Romania there are two important signals already announced in 2016: more than half of newly diagnosed TB patients were HIV-coinfected. (HIV/TB patients were younger, without any differences versus HIV negative patients concerning localization) and a high rate of rifampicin resistance is present mainly in HIV-infected patient population.

Clinical and paraclinical data

As it was described in a Thai referral center in new infected patients with HIV and Tb versus Tb patients there are no differences in the frequency of pyrexia, dyspnea, cough or haemoptysis and cavitory lesions and upper zone infiltrates were observed significantly less often in the HIV-infected group ($p = 0.02$ and 0.01 , respectively)⁽³⁷⁾. On a Russian study, another country with problems concerning TB the authors divided in 2 groups their patients: Group 1 - with primary HIV infection and TB developing at any stage of HIV infection and Group 2 with primary TB and HIV infections joining different forms of TB at any stage.

The social problems are huge: they found 50% unemployed, 26,5% homeless persons. Comparing both groups, they found in Group 1 more employees and pupils and fewer homeless persons, associated with younger age of patients and greater social security. In Group 1, it was a predominance of primary tuberculosis with lesion of intrathoracic and peripheral lymph nodes (12.8%), acutely progressive disseminated and miliary tuberculosis of the lung and extrapulmonary systems and organs (49%). Multidrug resistance tends to increase: 2% in 2001, 3.4% in 2002, 4.6% in 2003, and 8.9% in 2004. The patients with TB/HIV infection had a concomitance of 3 infectious diseases: HIV

infection, TB, and, in 74% of the patients, sexually transmitted infections (syphilis, chlamydiosis, gonorrhea) and the proportion of TB/HIV patients with drug abuse (65%), hepatitis B and C (47%), and nervous and mental diseases was extremely high⁽³⁸⁾. Active screening in methadone consumers another possibility to act, discovered 11% of this patients with one or more TB symptoms and a prevalence of 4% new TB cases⁽³⁹⁾.

Factors associated with ever being screened for tuberculosis among participants

People who inject drugs were more likely to have ever been screened for tuberculosis when they had education levels higher than primary⁽³⁹⁾. In the same time jobless patients, belonging to a minor ethnicity, with a low education, had a greater tendency toward needle-sharing behaviors and in the same time this predisposed to HIV infections and TB⁽⁴⁰⁾. These patients with PWID who are HIV seropositive will be an ideal target group for harm reduction programs.

Another source of combined diseases with Tb remains the imprisoned patients. In 2016, one-sixth of people living in prison in Europe were incarcerated for drug offences⁽⁴¹⁾. Incarceration moment represent further increase of the risk of developing drug-related problems⁽⁴²⁾, including acquisition and transmission of human immunodeficiency virus (HIV), hepatitis B and C virus (HBV, HCV).

Estimation on coverage range of TB testing, in a recent study were available only in 7 countries, 4 countries reporting full coverage, one country reporting high coverage, while 2 countries only medium coverage⁽⁴³⁾. Testing upon release remains another major problem. It is only available sporadically, 2



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countries reporting to provide testing upon release for HIV and only 1 country provides testing for HBV, HCV and TB⁽⁴³⁾. For harm reduction measures that are well established in the community, authors described significant delays in their introduction in prisons. The level of 5 type of infections with TB, HIV, syphilis, hepatitis B and hepatitis C virus are connected also to the socioeconomic level of the countries. In Pakistan prisons prevalence of tuberculosis was 2.2%, HIV infected 2.0%, with confirmed syphilis in 8.9%, hepatitis B virus in 5.9%, and hepatitis C virus in 15.2%. 59.0% had used any illicit drugs, among whom 11.8% had injected drugs⁽⁴⁴⁾.

The higher risk of tuberculosis observed in people who inject illicit drugs is usually the result of associated HIV infection; in other people who use illicit drugs without injecting this higher risk is primarily attributable to the sharing of drug equipment, such as marijuana water pipes, and to living in cramped conditions or in dwellings with poor ventilation⁽⁴⁵⁾. The risk of becoming infected with the tuberculosis bacillus and the risk of developing active tuberculosis are 26 and 23 times higher, respectively, among prisoners than among members of the general population if there are no preventive measures in place and illicit drug use and drug equipment sharing are common among prisoners.

Therapy problems

Many problems are generating by the therapeutical agents. The efficiency of treatment for TB and HIV infection in Russia is satisfactory. Continuous therapy for 4 months or more provides positive clinical and X-ray changes in most patients; bacterial isolation ceases in 75%, and decay cavities close in 44% of cases. Mortality rates in patients with TB and HIV infection are gradually on the rise and equal to 11.2% of the treated patients in 2001, 5% in 2002, 15.2% in 2003, and 19.6% in 2004. In patients with HIV/TB, the rates are higher than those in patients with TB/HIV and are 19.2 and 14.5%, respectively. Acutely progressive pulmonary TB and miliary TB of the lung and extrapulmonary organs and systems are a cause of death in most (76%) patients with TB/HIV⁽⁴⁶⁾. Shared use of needles or syringes was significantly lower among PWID who received an estimated ≥ 7 syringes per week than those who did not (2.9% versus 35.1%)⁽⁴⁷⁾.

Tolerance of treatment in HIV patients with Tb is another problem. Human immunodeficiency virus status and alcohol consumption constitutes aggravating factors for the occurrence of hepatic toxicity. In addition, the consumption of antioxidant foods simultaneously with TB drugs help in reducing the hepatotoxic effects of these drugs⁽⁴⁸⁾. The development of hepatotoxicity due to TB drugs

is significantly associated with a decrease in nutritional status to all this category of patients⁽⁴⁹⁾. The relative risk of developing drug-induced hepatitis remains high if the patient was hepatitis C or HIV positive. It was fivefold and fourfold, respectively. In patient with both hepatitis C and HIV the relative risk of developing antituberculous drug-induced hepatitis (DIH) was 14.4-fold⁽⁵⁰⁾. The only treatment of hepatitis C with alpha-interferon, available in 1998-2000, allowed the reintroduction of anti-TB agents in those who previously developed DIH when exposed to these drugs.

Of course, the new therapies for hepatitis C changed the evolution of this kind of association. In other papers it is described hepatitis as the most common drug-induced serious adverse event associated with anti-tuberculosis treatment, occurring in 20% of HIV-infected patients⁽⁵¹⁾. In cases of meningeal TB international guidelines cautiously recommend dexamethasone for HIV-associated TBM because it is a paucity of evidence⁽⁵²⁾. More data coming from trials are needed.

Anergic HIV-infected patients are at high risk for development of tuberculosis. Anergic HIV-infected patients, in addition to HIV-infected patients with positive results of PPD tests, should be offered preventive therapy if they live in areas with a high prevalence of tuberculosis, at least when the CD4 count decreases to less than 500 CD4 cells/mm³⁽²⁾.

All the prophylactic measures depend on the harm reduction programmes. In 2014, 17 countries in Asia provide needle and syringe programmes (NSP) provision and 15 opioid substitution therapy (OST). Between 60 and 90 % of people who use drugs in Asia have HCV; there are many problems due to cost barriers, TB screening testing and availability of treatment services. What is very clear is

that nearly 15 % of the global burden of new cases of HIV-TB co-infection are attributed to southeast Asia but only 18% of the total number of people living with HIV are eligible for antiretroviral treatment in this region. Only Malaysia and Indonesia provide OST in prison, with no NSP provision in prisons in the region⁽⁵³⁾.

Solutions

The World Health Organization recommends and repeat this recommendation of routine voluntary HIV testing and counseling, screening of STIs, hepatitis B/C, and tuberculosis to all key populations including people who inject drugs⁽⁵⁴⁾.

It's important also for lung physicians to focus on marginalized (Roma or homeless) IDUs and address not only injecting and sex risk, but also hygienic living and injecting conditions.

There are also other important modalities of corrections among disadvantaged, marginalized, mostly minority populations, but only with the help of the system like: structural interventions to increase social integration (working or being in treatment) with the possibility to improve the welfare and physicians should maintain a high index of suspicion for tuberculosis among HIV-seropositive patients for short-course chemotherapy to be promptly instituted a concomitant decreasing of drug use and infection risk tied to drug use/injection, especially in countries with high prevalence of both diseases. It is crucial in low and middle income countries specially to increase the coverage of screening services for IDUs and strengthen the counseling of safer sexual practices..

Active screening in users of methadone is also important. TB control can identify this



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new hidden cases. One example is coming from the same low income countries. TB prevalence in a population of PWID in Tanzania is 23 times that of the general Tanzanian TB prevalence of 0.2%⁽³⁹⁾.

For prisons it's important to improve prison system's documentation of responses to health harms and to increase the comparability of information and data; in the same time it's vital to inform persons in charge for programmed planning and policy plans at national and international level for establishing common strategies. Prisons remains excellent venues for infectious disease screening and intervention given conditions of poverty and drug addiction and it's vital as models of collaboration with community-based health providers for post-discharge planning⁽⁴⁴⁾.

Another possible solution is coming from the new medications discovered for TB, HIV, HCV for this category of patients, drug users also. We know the risk of resistance to treatment induced by treatment interruptions. If we are looking to the new medications discovered in the last years we observe some connected problems; there are many disparities concerning research and development landscapes for treatment of TB, HIV, and HCV, Since 1987, 33 new chemical entities (NCEs) have been developed and approved for HIV⁽⁵⁵⁾ with many benefits on efficacy, safety and mortality; mortality declined from over 1.2

million acquired immunodeficiency syndrome (AIDS) - related deaths in 2010 to 690,000 in 2019⁽⁵⁶⁾. Since 1989, when HCV was first isolated, 20 NCEs have been granted regulatory approval for the treatment of HCV⁽⁵⁷⁾. The message for this type of infection is optimistic. With current HCV treatments, over 90% of people with chronic HCV can achieve cure in 2-3 months⁽⁵⁸⁾. If we are looking to TB over the last 40 years, the message is not so optimistic; only five NCEs (rifabutin, rifapentine, bedaquiline, delamanid, pretomanid) have been approved⁽⁵⁹⁾. HIV coinfection is another factor reducing the probability of treatment success to below 60% in the Americas, Eastern Mediterranean, and Europe countries⁽⁶⁰⁾. Another important problem concerning TB and new medications is the duration of trial and approval (for for Bedaquiline and Pretomanid - 8.0 and respectively 19.2 years) and fewer included participants in the studies. Concerning the use of antiretroviral therapy and treatment of Mycobacterium tuberculosis infection Rifampin appears to be safe and as effective as isoniazid across many populations with health conditions, including HIV in a regime of 4 months⁽⁶¹⁾.

Collaboration between TB and HIV programmes seems to be the best approach to decrease the incidence of these diseases, especially in high-prevalence HIV settings⁽¹⁶⁾. In prisons, starting from the WHO's Model List

of Essential Medicines including morphine, methadone, and buprenorphine, drugs commonly used to treat opioid dependence, classified as “controlled substances” (under the international drug conventions), all these are often with limited availability. That's why this model list must be adopted by all the countries⁽⁶²⁾.

The authorities must solved a long list of multiple problems concerning the right to non-discrimination and equivalence of care, to essential medicine, to medical care and treatment, to preventive health services, including harm reduction and to the underlying determinants of health⁽⁶³⁾.

Decreasing the incarceration rate in people who inject drugs and providing opioid agonist therapy it's important because this could reduce the burden of HIV in this population (example Hungary)⁽¹²⁾. The prevalence of HIV, HCV, HBV, and tuberculosis is and remains higher in prison populations than in the general population, mainly because of the criminalization of drug use and the detention of people who use drugs.

Recommended measures

These are very well synthetized by Getahun⁽⁶⁴⁾. The recommendations combined:

1. punitive drug policies and laws in fueling the tuberculosis epidemic among people who use illicit drugs
2. the programmatic management of tuberculosis, HIV infection, hepatitis, illicit drug use and prison health services in a vertical or silo fashion needs to be minimized
3. the prevention, diagnosis and treatment of tuberculosis among people who use illicit drugs require effective models of integrated delivery of HIV, hepatitis and harm reduction services that respect human rights.

4. quantifying the global, regional and national burdens of tuberculosis among people who use illicit drugs is important

5. clinical and programmatic research surrounding the use of illicit drugs must be addressed through a multidisciplinary approach involving medical and social science researchers as well as policy-makers and other key stakeholders.

Conclusions

Tb has new faces induced by the other types of coinfections. The practitioner must adapt the therapies to these new problems appeared in the last century. It is also very important to act for treating a TB case in a multidisciplinary team with other specialist in infection diseases, addictologist, etc.

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