For Best Practices in Health

CDBPS-H

Pour des Bonnes Pratiques en Santé

WORLD TUBERCULOSIS DAY

JOURNEE MONDIALE CONTRE LA TUBERCULOSE

24 Mars 2017

Pour la deuxième année consécutive, la journée mondiale de lutte contre la Tuberculose qui se tient le 24 Mars 2017 a pour thème: "S'unir pour mettre fin à la Tuberculose". Cette année l'Organisation Mondiale de la Santé mettra spécialement l'accent sur les efforts nécessaires pour ne laisser personne de côté, avec des actions visant à lutter contre la stigmatisation, la marginalisation et à supporter les obstacles empêchant l'accès aux soins.

Des progrès

49 millions de vies sauvées en 15 ans.

Résistances aux antituberculeux

480 000 nouveaux cas de tuberculose multirésistante en 2015.

Financement

Il manque 2 milliards de dollars (US $) pour financer les interventions nécessaires (OMS, 2017).

Dans le cadre de la célébration de la Journée mondiale de lutte contre la Tuberculose, le Centre pour le Développement des Bonnes Pratiques en Santé propose met à votre disposition des résumés simplifié de revues systématiques Cochrane portant sur la prévention et la prise en charge de la Tuberculose.

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2017 is the second year of a two-year "Unite to end TB" campaign for world TB day. This year, WHO places a special focus on uniting effort to "leave no one behind" including action to address stigma, discrimination, marginalization and overcome barriers to access care.

Progress

49 million lives were saved through effective diagnosis and treatment, 2000-2015

MDR – TB cases

480 000 people developed multidrug-resistant TB in the world in 2015.

Funding

2 billion US dollars per year needed to fill resource gap for implementing existing TB interventions.

As part of the celebration of World Tuberculosis Day, the Center for the Development of Best Practices in Health proposes below, simplified summaries of Cochrane's systematic reviews on tuberculosis prevention and management.

Table of content

1- What is tuberculous pleurisy and how might corticosteroids work?

Tuberculous pleurisy results from inflammation of the membrane that covers the lungs (the pleura) caused by exposure to Mycobacterium tuberculosis bacteria infecting the lungs. This results in a build up of fluid around the lung (pleural effusion) that causes pain and fever, impairs breathing, and may lead to impairment of lung function in the long term.
Some clinicians believe that corticosteroids used in combination with antituberculous drugs can speed up the recovery from TB pleurisy and help to prevent long-term complications.

What the evidence shows

We examined the available evidence up to 13 April 2016 and included six trials with 590 people, which evaluated prednisolone given with antituberculous treatment (ATT). One included trial was of high quality, while the rest had uncertainties regarding trial quality. All the included trials were in adults; one trial included only HIV-positive people, two included only HIV-negative people, and three did not report the HIV status of the participants.
Corticosteroids may reduce the time to resolution of the symptoms of TB pleurisy and the time to resolution of the pleural effusion on chest X-ray (low certainty evidence). Corticosteroids may also reduce the risk of having signs of pleural scarring on chest X-ray (pleural thickening and pleural adhesions) after the disease has resolved (low certainty evidence). There was not enough information about lung function to be sure whether or not corticosteroids reduce the risk of lung function impairment after TB pleurisy (very low certainty evidence).
Corticosteroids may increase the risk of adverse events leading to discontinuation of the trial drug (low certainty evidence). From one trial in people living with HIV, there was no detectable increase in HIV-related conditions with corticosteroids, although cases of Kaposi's sarcoma were only seen in the corticosteroid group and numbers of participants and events were too small to rule out an effect of corticosteroids (very low certainty evidence).
As the risk of disability and long-term illness after TB pleurisy is unclear, research looking at the association between TB pleurisy and lung function impairment would be useful to inform future research into corticosteroids for TB pleurisy.

Citation: Ryan H, Yoo J, Darsini P. **Corticosteroids for tuberculous pleurisy**. Cochrane Database of Systematic Reviews 2017, Issue 3. Art. No.: CD001876. DOI: 10.1002/14651858.CD001876.pub3. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD001876.pub3/epdf

2- Antibiotic treatment for nontuberculous mycobacteria in people with cystic fibrosis

Nontuberculous mycobacteria are bacteria that are in the same family as tuberculosis and are commonly found in the soil and water. These bacteria can be found in the lungs of people with cystic fibrosis and can cause their lung function to worsen. Although there are guidelines on which antibiotics to use to treat lung infection due to these bacteria, these recommendations are not specific for people with cystic fibrosis. It is also not clear which are the most effective antibiotics. The main purpose of this review was to determine whether treatment with different antibiotic combinations for nontuberculous mycobacterial infection would improve lung function or decrease the frequency of chest infections in people with cystic fibrosis. We found one randomized controlled trial but it included both people with and without cystic fibrosis and we could not get the information specifically about individuals with cystic fibrosis so could not include the information

in this review. Until the time when such information is available, clinicians should follow the current guidelines for the diagnosis and treatment of lung infections due to nontuberculous mycobacteria in the general population.

Review question

We reviewed the evidence about using antibiotics to treat nontuberculous mycobacteria infection in people with cystic fibrosis.

Background

Nontuberculous mycobacteria are bacteria that are from the same family as tuberculosis and are commonly found in the soil and water. These bacteria can be found in the lungs of people with cystic fibrosis and may cause their lung function to worsen. Although there are guidelines on which antibiotics to use to treat lung infection due to these bacteria, these recommendations are not specifically for people with cystic fibrosis. It is also not clear which antibiotics work best. The main aim of this review was to show whether or not treating nontuberculous mycobacterial infection with different combinations of antibiotics improves lung function or decreases the frequency of chest infections in people with cystic fibrosis.

Search date

The evidence is current to: 02 September 2016.

Study characteristics

We found one randomized controlled trial but it included both people with and without cystic fibrosis and we could not get the information specifically about individuals with cystic fibrosis so could not include the information in this review.

Key results

Until the time when randomized controlled trial data is available for individuals with cystic fibrosis, clinicians should follow the current guidelines for the diagnosis and treatment of lung infections due to nontuberculous mycobacteria in the general population.

> **Citation**: Waters V, Ratjen F. **Antibiotic treatment for nontuberculous mycobacteria lung infection in people with cystic fibrosis**. Cochrane Database of Systematic Reviews 2016, Issue 12. Art. No.: CD010004. DOI: 10.1002/14651858.CD010004.pub4.
> http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010004.pub4/epdf

3- Effectiveness of EFV compared to NVP in the suppression of HIV infection when used as part of initial three-drug combination

Research question

For people living with HIV who have never received antiretroviral therapy (ART), which drug is more effective in suppressing HIV infection in combination with two nucleoside reverse transcriptase inhibitors (NRTI): efavirenz (EFV) or nevirapine (NVP)?

Background

The introduction of highly active ART as treatment for HIV infection has greatly reduced mortality and morbidity for adults and adolescents living with HIV around the world. The recommended initial treatments for HIV infection include two drugs from a class of drugs known as NRTI and one from a related class of drugs called non-nucleoside reverse transcriptase inhibitors (NNRTI). The two NNRTIs most commonly used are NVP and EFV. However, NVP can cause liver damage

and severe rash, both of which can be fatal. EFV may also cause a rash, impair mental function, and cause foetal malformations.

Main results

Cochrane researchers examined the available literature up to 12 August 2016 and identified 12 randomized controlled trials, with a total of 3278 people, that met the inclusion criteria of this review. None of the included trials included children. Four trials included people who were also receiving treatment for tuberculosis. There was little or no difference in suppression of HIV infection (*high quality evidence*), probably little or no difference in mortality, progression to AIDS, stopping treatment early and changes in blood cells affected by HIV (*moderate quality evidence*). There may be little or no difference in treatment failure (*low quality evidence*). We are uncertain whether there is a difference in side-effects (*very low quality evidence*). No studies were found that looked at sexual transmission of HIV. Development of drug resistance is probably slightly less in the EFV group (*moderate quality evidence*). When the side effects were examined individually, EFV probably caused more impaired mental function (6% in the EFV group and 2% in the NVP group; *moderate quality evidence*), while NVP probably caused more people to have a rash (3% in the EFV group and 6% in the NVP group; *moderate quality evidence*), caused more people to have reduced white blood cells (2% in the EFV group and 5% in the NVP group; *high quality evidence*), and signs of liver damage (6% in the EFV group and 11% in the NVP group; h*high quality evidence*). There was probably little or no difference in increases in liver enzymes and levels of cholesterol (*moderate quality evidence*). There may be little or no difference in digestive side-effects, fever, enzymes from the liver and pancreas, and fat in the blood (*low quality evidence*). People on NVP were probably more likely to die when given a once-daily regimen (2% in the EFV group and 4% in the NVP group; *moderate quality evidence*). In people who were taking treatment for tuberculosis compared to those who were not, there was probably little or no difference in suppression of HIV, deaths, progression to AIDS or stopping treatment early (*moderate to high quality evidence*).

Conclusion

EFV and NVP are similarly effective in viral suppression, preventing HIV progression and reducing mortality. EFV is more likely to affect mental function, while NVP is more likely to cause signs of liver damage, reduced white blood cells and rash.

Citation: Mbuagbaw L, Mursleen S, Irlam JH, Spaulding AB, Rutherford GW, Siegfried N. **Efavirenz or nevirapine in three-drug combination therapy with two nucleoside or nucleotide-reverse transcriptase inhibitors for initial treatment of HIV infection in antiretroviral-naïve individuals.** Cochrane Database of Systematic Reviews 2016, Issue 12. Art. No.: CD004246. DOI:10.1002/14651858.CD004246.pub4.
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD004246.pub4/epdf

4- Six-month therapy for people with abdominal tuberculosis

What is abdominal tuberculosis and why is duration of treatment important?

Abdominal tuberculosis (TB) is a type of TB that affects the gut, the peritoneum (the lining of the abdominal cavity), abdominal lymph nodes, and, more rarely, the solid organs in the abdomen

(liver, pancreas, and spleen). Abdominal TB leads to severe illness in adults and children, and can cause complications, such as bowel rupture, which can lead to death.

Most current guidelines recommend treating people that have abdominal TB with antituberculous treatment (ATT) for six months, but some clinicians treat for longer periods due to concerns that six months is not adequate to achieve cure and prevent relapse of the disease after the end of treatment. Longer ATT regimens have disadvantages: patients may find it more difficult to adhere to the tablets; patients are exposed to the risk of side effects of ATT for longer periods; and the cost to health systems and to patients is greater.

What the evidence shows

Cochrane researchers examined the available evidence up to the 2 September 2016. We included three trials with 328 participants that compared six-month ATT with nine-month ATT; two were from India and one was from South Korea. The trials were mostly of high quality, although two had concerns of risk of bias for detecting relapse of the disease. All the trials included HIV-negative adults with TB of the gut (gastrointestinal TB), and one also included TB of the peritoneum (peritoneal TB).

The results show that relapse was an uncommon event, but we are uncertain whether or not there is a difference between the six-month and nine-month groups as numbers of participants are small (*very low quality evidence*). Six-month and nine-month regimens are probably similarly effective in terms of the chances of achieving cure (*moderate quality evidence*). Death was uncommon in both groups, and all deaths occurred during the first four months of ATT, which suggests that duration of treatment did not have an effect on risk of death. Few people had poor treatment compliance, and few participants experienced side effects that led to their treatment being stopped or changed, and it was not possible to detect a difference between the groups.

Six-month regimens are probably as good as nine-month regimens in terms of numbers of people cured. We found no evidence to suggest that six-month regimens are less safe for gastrointestinal and peritoneal TB than nine-month regimens, but we still do not know whether there is a difference in risk of relapse between the two regimens. Further studies are needed to increase our confidence as to whether six-month regimens are as good as nine-month regimens for preventing relapse; and to provide information about treating abdominal TB in children and in people with HIV.

Citation: Jullien S, Jain S, Ryan H, Ahuja V. **Six-month therapy for abdominal tuberculosis.** Cochrane Database of Systematic Reviews 2016, Issue 11. Art. No.: CD012163. DOI: 10.1002/14651858.CD012163.pub2.
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD012163.pub2/epdf

5- The rapid test GenoType® MTBDRsl for testing resistance to second-line TB drugs

Background

Different drugs are available to treat tuberculosis (TB), but resistance to these drugs is a growing problem. People with drug-resistant TB require second-line TB drugs that, compared with first-line TB drugs, must be taken for longer and may be associated with more harms. Detecting TB drug resistance quickly is important for improving health, reducing deaths, and decreasing the spread of drug-resistant TB.

Definitions

Multidrug-resistant TB (MDR-TB) is caused by TB bacteria that are resistant to at least isoniazid and rifampicin, the two most potent TB drugs.

Extensively drug-resistant TB (XDR-TB) is a type of MDR-TB that is resistant to nearly all TB drugs.

What test is evaluated by this review?

GenoType® MTBDR*sl* (MTBDR*sl*) is a rapid test for detecting resistance to second-line TB drugs. In people with MDR-TB, MTBDR*sl* is used to detect additional drug resistance. The test may be performed on TB bacteria grown in culture from a patient specimen (indirect testing) or on a patient specimen (direct testing), which eliminates delays associated with culture. MTBDR*sl* version 1.0 requires a specimen to be smear-positive by microscopy, while version 2.0 (released in 2015) may use a smear-positive or -negative specimen.

What are the aims of the review?

We wanted to find out how accurate MTBDR*sl* is for detecting drug resistance; to compare indirect and direct testing; and to compare the two test versions.

How up-to-date is the review?

We searched for and used studies that had been published up to 21 September 2015.

What are the main results of the review?

We found 27 studies; 26 studies evaluated MTBDR*sl* version 1.0 and one study evaluated version 2.0.

Fluoroquinolone drugs

MTBDR*sl* version 1.0 (smear-positive specimen) detected 86% of people with fluoroquinolone resistance and rarely gave a positive result for people without resistance (*GRADE, moderate quality evidence)*.

Second-line injectable drugs

MTBDR*sl* version 1.0 (smear-positive specimen) detected 87% of people with second-line injectable drug resistance and rarely gave a positive result for people without resistance (*GRADE, low quality evidence)*.

XDR-TB

MTBDR*sl* version 1.0 (smear-positive specimen) detected 69% of people with XDR-TB and rarely gave a positive result for people without resistance (*GRADE*, *low quality evidence)*.

For MTBDR*sl* version 1.0, we found similar results for indirect and direct testing (smear-positive specimen).

As we identified only one study evaluating MTBDR*sl* version 2.0, we could not be sure of the diagnostic accuracy of version 2.0. Also, we could not compare accuracy of the two versions.

What is the methodological quality of the evidence?

We used the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool to assess study quality. Overall, we considered the included studies to be of high quality; however, we had concerns about how the reference standard (the benchmark against which MTBDR*sl* was measured) was applied.

What are the authors' conclusions?

MTBDR*sl* (smear-positive specimen) identified most of the patients with second-line drug resistance. When the test reports a negative result, conventional testing for drug resistance can still be used.

Citation: Theron G, Peter J, Richardson M, Warren R, Dheda K, Steingart KR. **GenoType ® MTBDRsl assay for resistance to second-line anti-tuberculosis drugs.** Cochrane Database of Systematic Reviews 2016, Issue 9. Art. No.: CD010705. DOI:10.1002/14651858.CD010705.pub
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010705.pub3/epdf

6- Nutritional supplements for people being treated for active tuberculosis

Cochrane researchers conducted a review of the effects of nutritional supplements for people being treated for tuberculosis. After searching for relevant studies up to 4 February 2016, they included 35 relevant studies with 8283 participants. Their findings are summarized below.

What is active tuberculosis and how might nutritional supplements work?

Tuberculosis is a bacterial infection which most commonly affects the lungs. Most people who get infected never develop symptoms as their immune system manages to control the bacteria. Active tuberculosis occurs when the infection is no longer contained by the immune system, and typical symptoms are cough, chest pain, fever, night sweats, weight loss, and sometimes coughing up blood. Treatment is with a combination of antibiotic drugs, which must be taken for at least six months.

People with tuberculosis are often malnourished, and malnourished people are at higher risk of developing tuberculosis as their immune system is weakened. Nutritional supplements could help people recover from the illness by strengthening their immune system, and by improving weight gain, and muscle strength, allowing them to return to an active life. Good nutrition requires a daily intake of macronutrients (carbohydrate, protein, and fat), and micronutrients (essential vitamins and minerals).

What the research says

Effect of providing nutritional supplements to people being treated for tuberculosis

We currently don't know if providing free food to tuberculosis patients, as hot meals or ration parcels, reduces death or improves cure (*very low quality evidence*). However, it probably does improve weight gain in some settings (*moderate quality evidence*), and may improve quality of life (*low quality evidence*).

Routinely providing multi-micronutrient supplements may have little or no effect on deaths in HIV-negative people with tuberculosis (*low quality evidence*), or HIV-positive people who are not taking anti-retroviral therapy (*moderate quality evidence*). We currently don't know if micronutrient supplements have any effect on tuberculosis treatment outcomes (*very low quality evidence*), but they may have no effect on weight gain (*low quality evidence*). No studies have assessed the effect on quality of life.

Plasma levels of vitamin A appear to increase after starting tuberculosis treatment regardless of supplementation. In contrast, supplementation probably does improve plasma levels of zinc, vitamin D, vitamin E, and selenium, but this has not been shown to have clinically important benefits. Despite multiple studies of vitamin D supplementation in different doses, statistically significant benefits on sputum conversion have not been demonstrated.

Authors' conclusions

Food or energy supplements may improve weight gain during recovery from tuberculosis in some settings, but there is currently no evidence that they improve tuberculosis treatment outcomes.

There is also currently no reliable evidence that routinely supplementing above recommended daily amounts has clinical benefits.

> **Citation**: Grobler L, Nagpal S, Sudarsanam TD, Sinclair D. **Nutritional supplements for people being treated for active tuberculosis.** Cochrane Database of Systematic Reviews 2016, Issue 6. Art. No.: CD006086. DOI: 10.1002/14651858.CD006086.pub4.
> http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD006086.pub4/epdf

7- Fixed-dose combinations for treating pulmonary tuberculosis

What are fixed-dose combinations and how might they improve care of people with tuberculosis

Tuberculosis (TB) is an important health problem, especially in developing countries. The treatment for pulmonary TB in new patients includes four oral medicines taken for six months, sometimes as fixed-dose combinations (FDCs) that are combined in one tablet, or taken separately as single-drug formulations. The World Health Organization recommends prescribers use fixed-dose combinations to reduce the number of tablets that people take. On the supply side, this might reduce prescribing errors and improve drug supply efficiency; on the patient's side, FDCS simplify treatment and improve adherence.

We conducted a review to assess the efficacy, safety, and acceptability of FDCs compared with single-drug formulations for treating people with newly diagnosed pulmonary TB.

What the research says

We searched for relevant trials up to 20 November 2015, and included 13 randomized controlled trials that enrolled 5824 people. Trials were published between 1987 and 2015 and included participants in treatment with newly diagnosed pulmonary TB in countries with high TB prevalence. Only two trials reported the HIV status of included participants.

There is probably little or no difference in FDCs compared to single-drug formulations for treatment failure (*moderate quality evidence*); relapse may be more frequent (*low quality evidence*); and the number of deaths were similar (*moderate quality evidence*).

There is little or no difference in sputum smear or culture conversion (*high quality evidence*), and no difference was shown for serious adverse events (*moderate quality evidence*) or adverse events that led to discontinuation of therapy (*low quality evidence*).

Authors' conclusions

We concluded that fixed-dose combinations have similar efficacy to single-drug formulations for treating people with newly diagnosed pulmonary TB.

> **Citation**: Gallardo CR, Rigau Comas D, Valderrama Rodríguez A, Roqué i Figuls M, Parker LA, Caylà J, Bonfill Cosp X. **Fixed-dose combinations of drugs versus single-drug formulations for treating pulmonary tuberculosis**. Cochrane Database of Systematic Reviews 2016, Issue 5. Art. No.: CD009913. DOI: 10.1002/14651858.CD009913.pub2.
> http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009913.pub2/epdf

8- The lateral flow urine lipoarabinomannan (LF-LAM) test for diagnosis of tuberculosis in people living with human immunodeficiency virus (HIV)

Background

Tuberculosis (TB) is a common cause of death in people with human immunodeficiency virus (HIV) infection, but diagnosis is difficult, and depends on testing for TB in the sputum and other sites, which may take weeks to give results. A rapid and accurate point-of-care test could reduce delays in diagnosis, allow treatment to start promptly, and improve linkage between diagnosis and treatment.

Test evaluated by this review

The lateral flow urine lipoarabinomannan assay (LF-LAM, Alere Determine™ TB LAM Ag, Alere Inc, Waltham, MA, USA) is a commercially available point-of-care test for active TB (pulmonary and extrapulmonary TB). The test detects lipoarabinomannan (LAM), a component of the bacterial cell walls, which is present in some people with active TB. The test is performed by placing urine on one end of a test strip, with results appearing as a line (that is, a band) on the strip if TB is present. The test is simple, requires no special equipment, and shows results in 25 minutes. During the period we conducted the review, the manufacturer issued new recommendations for defining a positive test. We collected data based on both the original and the new recommendations

Objectives

We aimed to see how accurately LF-LAM diagnosed TB in people living with HIV with TB symptoms, and how accurately LF-LAM diagnosed TB in people living with HIV being screened for TB whether or not they had TB symptoms.

Main results

We examined evidence up to 5 February 2015 and included 12 studies: six studies evaluated LF-LAM for TB diagnosis and six studies evaluated the test for TB screening. All studies were conducted in low- or middle-income countries.

Quality of the evidence

We assessed quality by describing how participants were selected for the studies, details of the test and reference standards (the benchmark test), and study flow and timing, using the standard QUADAS-2 approach. Few studies used multiple types of specimens for the reference standard (higher quality standard) and most relied on sputum culture alone (lower quality standard), which may have affected results.

What do the results mean?

In a population of 1000 HIV-positive individuals with TB symptoms, where 300 actually have TB, the test will correctly identify 135 people as having TB, but miss the remaining 165 people; for the 700 people who do not have TB, the test will correctly identify 644 people as not having TB, but will misclassify 56 as having TB.

The sensitivity of the test is higher in people living with HIV with low CD4 cell counts who are at risk of life-threatening illnesses. In patients with a CD4 ≤ 100 cells per µL, LF-LAM sensitivity was 56% (41% to 70%) versus 26% (16% to 46%) in patients with a CD4 count > 100 cells per µL.

If the test is used in screening HIV-positive people for TB, in a population of 1000 where 10 actually have TB, LF-LAM will correctly identify none of the 10, or up to four of the 10; on the other hand, the test will miss six to 10 people with TB; in the remaining 990 who do not have TB, the

test will correctly identify 931 to 941 people as not having TB while misclassifying 49 to 59 as having TB.

Limitations

The main limitations of the review were the use of a lower quality reference standard in most included studies, and small number of studies and participants included in the analyses. The results should, therefore, be interpreted with caution.

Conclusions

In this Cochrane review, we found that LF-LAM, whether the test is used for diagnosis or screening, has low sensitivity to detect TB. However, in HIV-positive people with low CD4 counts who are seriously ill, LF-LAM may help with the diagnosis of TB.

Citation: Shah M, Hanrahan C, Wang ZY, Dendukuri N, Lawn SD, Denkinger CM, Steingart KR. **Lateral flow urine lipoarabinomannan assay for detecting active tuberculosis in HIV-positive adults.** Cochrane Database of Systematic Reviews 2016, Issue 5. Art. No.: CD011420. DOI: 10.1002/14651858.CD011420.pub2.
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011420.pub2/epdf

9- Can smoking cessation interventions among adults with pulmonary tuberculosis improve their tuberculosis treatment outcomes?

Do treatments to help people with tuberculosis (TB) of the lungs to stop smoking also improve how they respond to treatment for their TB?

Background

Tuberculosis (TB) is a bacterial infection that can affect any organ of the human body. TB of the lungs can be transmitted from one person to another through the air when people who have TB cough, sneeze or spit. TB is a major cause of death in low- and middle-income countries. Smokers are twice as likely to become infected with TB as nonsmokers. Smoking is a common risk behaviour among people with TB. People who breathe in secondhand smoke are also more likely to be infected with TB. When people who smoke are infected with TB, they are more likely to have a more serious form of TB. They are also more likely to refuse or to stop their treatment and are less likely to respond to drug treatment.

Smoking can cause problems for the body's immune system (the system that protects a person from disease). However, research shows that most of these problems can be resolved after stopping smoking for six weeks. We therefore wanted to test whether quitting smoking can help people with TB by improving how they respond to treatment and reducing their infection levels.

Review methods

We searched various research databases that contain published and ongoing research on this topic up to the 29th of July 2015. We searched for studies written in any language, published and unpublished. We planned to include only studies that tested the success of a treatment to help someone with TB stop smoking, by comparing it to another treatment or to no treatment, using randomised controlled trials (RCTs). We considered treatments targeted at individuals (adults with TB and on TB treatment) or at whole populations. This included counselling or drug-based interventions for quitting smoking. We were interested in studies if they measured the number of people who completed the treatment for TB or the number of people cured of TB, or both.

Key results

We found no studies that met the eligibility criteria above. This is therefore an 'empty' review. However, there are studies that are currently being carried out, which may be reported in our next update of this review.

Quality of the evidence

There is as yet no high-quality evidence that can tell us whether treatments to help people with TB to stop smoking also help them to complete their TB treatment and to respond better to that treatment. There is therefore a need for good-quality research studies that test the usefulness of treatments to quit smoking in people with TB.

Citation: Jeyashree K, Kathirvel S, Shewade HD, Kaur H, Goel S. **Smoking cessation interventions for pulmonary tuberculosis treatment outcomes.** Cochrane Database of Systematic Reviews 2016, Issue 1. Art. No.: CD011125. DOI:10.1002/14651858.CD011125.pub2.
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011125.pub2/epdf

10- Incentives and enablers for improving patient adherence to tuberculosis diagnosis, prophylaxis, and treatment

Cochrane researchers conducted a review of the effects of material (economic) incentives or enablers on the adherence and outcomes of patients being tested or treated for latent or active tuberculosis (TB). After searching up to 5 June 2015 for relevant trials, they included 12 randomized controlled trials in this Cochrane review.

What are material incentives and enablers and how might they improve patient care?

Material incentives and enablers are economic interventions which may be given to patients to reward healthy behaviour (incentives) or remove economic barriers to accessing healthcare (enablers). Incentives and enablers may be given directly as cash or vouchers, or indirectly in the provision of a service for which the patient might otherwise have to pay (like transport to a health facility).

What the research says

Material incentives and enablers may have little or no effect in improving the outcomes of patients on treatment for active TB (*low quality evidence*), but further trials of alternative incentives and enablers are needed.

Material incentives and enablers may have some effects on completion of prophylaxis for latent TB in some circumstances but trial results were mixed, with one trial showing a large effect, and two trials showing no effect (*low quality evidence*).

One-off material incentives and enablers probably improve rates of return to a single clinic appointment for patients starting or continuing prophylaxis for TB (*moderate quality evidence*) and may improve the rate of return to the clinic for the reading of diagnostic tests for TB (*low quality evidence*).

Thus although material incentives and enablers may improve some patients' attendance at the clinic in the short term, more research is needed to determine if they have an important positive effect in patients on long term treatment for TB.

Citation: Lutge EE, Wiysonge CS, Knight SE, Sinclair D, Volmink J. **Incentives and enablers to improve adherence in tuberculosis.** Cochrane Database of Systematic Reviews 2015, Issue 9. Art. No.: CD007952. DOI: 10.1002/14651858.CD007952.pub3.
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD007952.pub3/epdf

11- Reminder systems to improve patient attendance at tuberculosis clinics

This Cochrane Review summarizes trials evaluating the effects of reminder systems on attendance at tuberculosis (TB) clinics and completion of TB treatment. After searching for relevant trials up to 29 August 2014, we included nine trials, including 4654 people.

What are reminder systems and how might they help?

Effective treatment for TB requires people to take multiple drugs daily for at least six months. Consequently, once they start to feel well again, some patients stop attending clinics and stop taking their medication which can lead to the illness returning and the development of drug resistance. One strategy the World Health Organization recommends is that an appointed person (a health worker or volunteer) watches the person take their medication everyday (called direct observation). Other strategies include reminder systems to prompt patients to attend for appointments on time, or to re-engage people who have missed or defaulted on a scheduled appointment. These prompts may be in the form of telephone calls or letters before the next scheduled appointment ("pre-appointment reminders"), or phone calls, letters, or home visits after a missed appointment ("default reminders").

What the research says:

For people being treated for active TB:

- More people attended the clinic and completed TB treatment with pre-appointment reminder phone-calls (*low quality evidence*).
- More people attended the clinic and completed TB treatment with a policy of default reminders (*low and moderate quality evidence respectively*).

For people on TB prophylaxis:

- More people attended the clinic with pre-appointment phone-calls, and the number attending the final clinic was higher with three-monthly phone-calls or nurse home visits.

For people undergoing screening for TB:

- Similar numbers of people attended clinic for skin test reading with and without pre-appointment phone-calls (*low quality evidence*).
- Similar numbers of people attended clinic for skin test reading with and without take home reminder cards.

Systèmes de rappel pour améliorer l'assiduité des patients dans les centres de traitement de la tuberculose

Cette revue Cochrane résume des essais évaluant les effets des systèmes de rappel sur la fréquentation des centres de traitement de la tuberculose et sur l'exécution du traitement de la tuberculose. Après avoir recherché les essais pertinents jusqu'au 29 août 2014, nous avons inclus 9 essais portant sur 4 654 sujets.

Que sont les systèmes de rappel et en quoi peuvent-ils être utiles?

Pour être efficace, le traitement de la tuberculose oblige à prendre plusieurs médicaments par jour pendant au moins six mois. De ce fait, certains patients cessent de se présenter en consultation et de prendre leurs médicaments quand ils commencent à se sentir mieux, ce qui peut entraîner une récidive de la maladie et le développement de résistances aux médicaments. L'une des stratégies préconisées par l'Organisation mondiale de la Santé consiste en ce qu'une personne désignée (professionnel de santé ou bénévole) regarde le patient prendre des médicaments chaque jour (méthode dite d'observation directe). Il existe aussi des systèmes de rappel qui incitent les patients à se présenter à leurs rendez-vous à l'heure ou relancent les patients qui ont manqué un rendez-vous ou y sont venus en retard. Ces messages peuvent prendre la forme d'appels téléphoniques ou de lettres avant le rendez-vous suivant (« rappels avant rendez-vous ») ou encore d'appels téléphoniques, de lettres ou de visites à domicile après un rendez-vous manqué (« rappels après absence »).

Que dit la recherche?

Pour les personnes traitées pour une tuberculose active:

- Un plus grand nombre de personnes se sont présentées au centre et ont mené à terme le traitement de la tuberculose avec des appels téléphoniques avant les rendez-vous (preuves de faible qualité).

- Un plus grand nombre de personnes se sont présentées au centre et ont mené à terme le traitement de la tuberculose avec une politique de rappels après absence (preuves de qualité faible et modérée, respectivement).

Pour les personnes suivant une prophylaxie de la tuberculose:

- Un plus grand nombre de personnes se sont présentées au centre avec des appels téléphoniques avant rendez-vous, et le nombre de personnes venues à la consultation finale a été plus élevé avec des appels téléphoniques ou des visites à domicile de personnel infirmier tous les trois mois.

Pour les personnes faisant l'objet d'un dépistage de la tuberculose:

- Un nombre comparable de personnes se sont présentées au centre pour la vérification des tests cutanés avec et sans appels téléphoniques avant les rendez-vous (preuves de faible qualité).

- Un nombre comparable de personnes ayant et n'ayant pas emporté chez elles des cartes de rappel se sont présentées au centre pour la vérification des tests cutanés.

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