Causes and effects of tuberculosis

Tuberculosis is a chronic, infectious and deadly disease caused by Mycobacterium Tuberculosis. Tuberculosis often attacks lungs but it is also known for attacking other parts of the body (extrapulmonary tuberculosis). The infection site of extrapulmonary tuberculosis includes the central nervous system, the lymphatic system particularly in the neck, genitourinary system and bones and joints. People with active tuberculosis often show some of these symptoms:

Mycobacteria are found abundantly in habitats such as pond and soil. However, a few are intracellular pathogens to animals and humans. Tuberculosis is transmitted through aerosol route but the transmission can also occur via gastrointestinal route. Coughing, sneezing and spitting by people with active tuberculosis releases droplet nuclei containing the germ which is known as bacilli into the air. The droplet nuclei can remain suspended in the air for up to several hours. Infection only occurs when someone inhales the droplet nuclei. A person needs only to inhale a treated with existing drugs and medications. To make the condition even worse, new tuberculosis germ (XDR-TB) that is extremely resistant to drugs has been found in US. Now, the governments are focusing more on the preventive measure and at the same time, searching for a possible drug or vaccine that could eliminate the problem once and for all. So, to address this issue, I have focused my research on this question “ What are current available treatments for tuberculosis?”

Current Possible Solution

With the advancement of technology, mankind had the power in combating with deadly diseases. Tuberculosis, which had killed millions of people in the

nineteenth century, was brought under control by using vaccines and drugs. Drug treatments are used extensively in treating people with active tuberculosis. Latent tuberculosis, however, does not require intensive care but merely prescribed medication for several months. Vaccines, on the contrary, are used as preventive measures in areas of higher tuberculosis risk. Apart from that, vaccines are used by healthcare workers, newborns, and travelers who are at constant risk of getting infected by the disease. One of the most commonly used vaccine in prevention of tuberculosis, the BCG vaccine, is discussed below. But, first, I will discuss about the drug treatments.

Tuberculosis treated with drugs has a mortality rate of less than 5%. This shows that the current available drugs for tuberculosis are quite effective in treating the disease. Among the common drugs used in tuberculosis treatment are isoniazid, rifampicin, pyrazinamide, and ethambutol. These drugs aim at inhibiting the bacterial activity thus improving the patient’s conditions.

Anti-tuberculosis drugs are classified into three major categories. They are the first line drugs, the second line drugs and the third line drugs. These drugs are classified according to their effectiveness in treating the disease and their availability.

The first line drugs are as follows:

- Ethambutol-EMB or E,
- Isoniazid-INH or H,
- Pyrazinamide-PZA or Z,

- Rifampicin-RMP or R,
- Streptomycin-STM or S (802 words)

There are six classes of second line drugs. These drugs are classified second class because they may be less effective than first line drugs (p-aminosalicylic acid), they may have harmful side-effects (cycloserine) or they may not be available in the developing countries (fluoroquinolones).

- aminoglycosides: e. g.-amikacin(AMK), kanamycin(KM);
- polypeptides: e. g.-capreomycin, viomycin, enviomycin;
- fluoroquinolones: e. g.-ciprofloxacin(CIP), levofloxacin, moxifloxacin(MXF);
- thioamides: e. g.-ethionamide, prothionamide;
- cycloserine(the only antibiotic in its class);
- p-aminosalicylic acid(PAS or P).

Other drugs (third line drugs) that may be useful, but are not on the WHO list:

- rifabutin
- macrolides: e. g.-clarithromycin(CLR);
- linezolid(LZD);
- thioacetazone(T);
- thioridazine;
- arginine;
- vitamin D;
- R207910.

Tuberculosis treatments are often done as combination therapies (except for latent tuberculosis where only one type of drug is prescribed to the patient) because single drug therapy would result in rapid development of resistance which would lead to the failure of the treatment. Besides that, there are other reasons to support the combination therapy. Different drugs have different form of action. For example, PZA is a weak bactericidal but is very effective against bacteria located in acidic conditions. On the other hand, INH is very effective against replicating bacteria. RMP is a good bactericidal and at the same time, has sterilizing effects. This proves that, using combination therapy is effective to counter the disease and at the same time, it would prevent the mutation of the bacteria into drug resistant.

Upon infection, tuberculosis bacteria are taken up by the alveolar macrophages and are carried to the lymph nodes where it may be spread to other parts of the body (this is the basis of extrapulmonary tuberculosis). Two to eight weeks after infection, hypersensitivity and cell-mediated immunity develops and suppression of the infection will result in people with good, healthy immune system. People, who are immunocompromised, will develop inflammatory immune response which eventually leads to lung damage. These drugs functions by confining the bacteria and at the same time, since it has antibiotic effects, it will kill the bacteria, thus, improving the patient’s condition. It would usually take about six months or more for full

(1153 words)

recovery with 2-3% of relapse rate. Continuation of medication would be recommended by the physician to avoid the problem form reappearing. Isoniazid is one particular type of the drug which is commonly used due to its effectiveness in treating tuberculosis.

“ This medication is best taken on an empty stomach 1 hour before or 2 hours after meals. But it may be taken with food or milk if stomach upset occurs. Take as directed. Do not stop taking this medication without your doctor’s approval. Stopping therapy early may result in ineffective treatment and the infection could recur. Vitamin B6 (pyridoxine) supplements may be prescribed in addition to this medication to prevent numbness and tingling.” Extracted from MedicineNet. com- Isoniazid ORAL (Niazid) side effects, medical uses and drug interaction.

Figure 1 Fgure4- Effect of aspirin or ibuprofen administered in combination with isoniazid on lung(a) and spleen(b) log10 CFU in murine tuberculosis. ASP only, aspirin(20 mg/kg of body weight); IBU only, ibuprofen(20 mg/kg); INH only, isoniazid(25 mg/kg); ASP+INH, aspirin and isoniazid(20 and 25 mg/kg, respectively); IBU+INH, ibuprofen and isoniazid(20 and 25 mg/kg, respectively).

There is reliable and concrete evidence that isoniazid is effective in curbing the disease. The graph shows clearly that when isoniazid is administered to a patient with murine tuberculosis, it effectively inhibits the progress of the disease. This can be seen when there is zero tuberculous bacterium count when INH is administered. The drug acts in the same way in both liver and spleen. Other drugs, such as ibuprofen and aspirin are used to compare the

relative effectiveness of each individual drug. Ibuprofen seems not to interfere with the INH mechanism while aspirin reduces the effectiveness of INH. So, aspirin should be avoided when using drug regime containing INH to prevent it from interfering with INH mechanism. (1447 words)

Benefits and Risks of Drug Treatment

As with all forms of medications, tuberculosis drugs also pose some side-effects which may cause uneasiness to the patient. The benefits of tuberculosis drug treatments are well known. It effectively reduces symptoms of the disease upon the administration of the medication and in most cases; the drug cures the disease with 2-3% of relapse rate. Drug treatment also decreases the mortality rate significantly; reducing it to less than 5%. This means number of people dying from tuberculosis or tuberculosis related diseases is falling every year.

On the other hand, the risks of drug treatments are severe but only in remote cases. This is usually due to the aggravation of the side-effects by the risk factors such as alcohol abuse, history of hepatitis, diabetes mellitus and HIV infection. Increasing age is also a risk factor for the noncompliance to the treatment. The severe forms of side-effects are drug-induced hepatitis, arthralgia, central nervous system toxicity and exanthema. The drug treatments also pose some rather common adverse-effects. These include nausea, abdominal pain, fever, diarrhea and fluid (saliva, tears and urine) discolouration.

Table1-Number of side-effects due to isoniazid,

rifampin or pyrazinamide followed by final termination of one of the drugs (n= 519)

Side-effect Isoniazid Rifampin Pyrazinamide Total

Hepatotoxicity 19(4) 8(1. 5) 28(5) 55(11)

Arthralgia 1(0. 2) 12(2) 13(2)

Exanthema 6(1. 2) 27(5) 33(6)

CNS toxicity* 8(1. 5) 8(1. 5)

Nausea 5(0. 9) 5(0. 9)

Others# 7(1. 4) 7(1. 4)

Total 34(7) 8(1. 5) 79(15) 121(23)

Values are present as absolute number, and percentage in parenthesis. *: including peripheral neuropathy(n= 6) and seizure(n= 2); #: including leucopenia(n= 1), fever(n= 3) and severe hyperuricaemia(n= 3). CNS: central nervous system.

After evaluating both pros and cons of the drug treatment, I feel that the benefits of drug treatment outweigh the risks. Therefore, the risks should not discourage the patient from continuing the medication. The completion of the medication is vital for the full recovery from the disease.

Social and Economic Implications of the Disease

Tuberculosis is the world’s largest endemic with one third of world population being infected with the disease. And tuberculosis remains the greatest terror in developing nations. This is because the disease causes unbearable social and economic implications to the one infected with the disease.

“ The substantial non-treatment costs of TB are borne by the patients and their families. These are often greater than the costs of treatment to the health sector.

The largest indirect cost of TB for a patient is income lost by being too sick to work.

Studies suggest that on average three to four months of work time are lost, resulting in average lost potential earnings of 20% to 30% of annual household income.

For the families of those that die from the disease, there is the further loss of about 15 years of income because of the premature death of the TB sufferer.”

Extracted from the Stop Tb Initiative by WHO

It is very clear that tuberculosis, left untreated, would result in loss in terms of financial support. Therefore, it is vital for the authority to provide necessary treatment to the patients and, at the same time, they should also work on preventive measures such as awareness campaigns and vaccinations to prevent the spread of the disease.

The World Health Organization (WHO) have cited TB treatment as one of the most cost-effective health interventions accessible – at a cost of only $10 for every year of life gained.

“ Effectively treating TB will not solve the worldwide AIDS crisis, but it will significantly reduce its burden”

Dr Piot, Executive Director, Joint United Nations Program on HIV/AIDS

On the other hand, a person with tuberculosis would have to live as an “ outcast”. This is very true in the poorer nations of the world where the people do not have enough knowledge about the disease thus exiling the patient from their community. This would result in the patient losing moral support and faith which may ultimately lead to suicide.

(2093 words)

Alternative Solution

Ayurvedic treatment

Ayurveda, traditional Indian medication, is also proven to be effective in combating against tuberculosis. Current tuberculosis drug treatments induce unfavourable side-effects such as decreased appetite and liver inflammation. On the long run, it could lead to permanent liver damage. Therefore, combined with ayuvedic medication such as Kutki (Picrorrhiza kurroa), Guduchi (Tinospora cordifolia), Sharapunkha (Tephrosia purpurea) and Kalmegh (Andrographis paniculata) would prevent any damage to the liver and would result in increased efficiency in treating the disease. Tuberculosis of the lymph glands also could cause serious problems. Ayurvedic medicines

like Kancnnaar (Bauhinia variegata), Kanchnaar Guggulu and Triphala Guggulu can increase the body's immune response towards the disease. These ayurvedic medicines when combined with correct drug regimes would effectively fight off the disease and prevent it from relapsing. Ayurvedic medicines are known to increase immune response significantly, thus, making the body to be able to fight the infection.

Prevention Methods

Vaccination

Besides drug treatments, there is another practical approach to eradicate the endemic worldwide. This solution aims at preventing the disease. Vaccination is the best, available solution for most of the contagious disease. For tuberculosis, Bacillus Calmette Guerin (BCG) is the current available vaccine. This vaccine is actually an attenuated strain of live mycobacterium bovis which has lost its virulence after being carefully cultured artificially for many years. This vaccine works by providing natural passive immunity in which the infection with bovine tuberculosis would protect against infection with human tuberculosis. This is the result of memory cells in our body being able to recognize the same type of infection and providing instant protection against the disease. BCG is found to be very effective in giving protection primarily in children aged 3 and below and teenagers aged 14-20. Efficiency of BCG also differs according to geography.

The first large scale trial evaluating the efficacy of BCG was conducted from 1956 to 1963 and involved almost 60, 000 school children who received BCG at the age of 14 or 15; this study showed an efficacy of 84% up to 6 years after immunization. However, a US Public Health Service trial of BCG in

Georgia and Alabama published in 1966 showed an efficacy of only 14%, and did much to convince the US that it did not want to implement mass immunization with BCG. A further trial conducted in South India and published in 1979 (the “ Chingleput trial”), showed no protective effect. Extracted from Bacillus_Calmette-Guerin_Wikipedia-the_free_encyclopedia.

Reducing exposure

Tuberculosis is directly dependent on the degree of exposure. The more a person comes into contact with the disease, the higher is the chance to suffer from active tuberculosis. Generally, inhalation of minute amount of the bacilli would result in the immune response which immediately inactivates the disease thus preventing it from progressing. However, a direct exposure to a relatively high amount of the bacilli would result in the immune system to be unable to wall off the disease fast enough. This would result in the person developing active tuberculosis although he may not have the history of the disease before. Therefore, visit to places with a high incidence of tuberculosis should be avoided. Furthermore, we should also avoid close contact with people infected by the disease. Apart from that, personal hygiene, and the practice of wearing mask should be cultured in the society to prevent the spread of the disease. On top of that, self-quarantine should be practiced by individuals if they are suspected to carry the infection.

Evaluation

For the research on this issue, I have used a number of sources ranging from websites to newspaper articles and books. The World Health Organisation official webpage; http://www. who. int/en/ is one of the sources that I have used in my research. I find that this website provides loads of information

regarding tuberculosis. This source is definitely trustable as it is the official webpage of a world-recognized organization which is committed to the welfare of the people. The facts and information obtained from this website is valid and reliable under any circumstances because they are up to date. Moreover, WHO have also organized research on this issue and the findings have been reviewed by experts from all over the world. One such research is the ‘ Economic Impacts of Tuberculosis’. On top of that, I found that a lot of other websites such as http://en. wikipedia. org/wiki/Tuberculosis, http://www. plospathogens. org/article/info: doi%2F10. 1371%2Fjournal. ppat. 1000600 and http://www. wrongdiagnosis. com/t/tuberculosis/stats. htm have cited WHO in their websites. This proves that WHO is a reliable source of information for this issue.

Furthermore, I have evaluated another source http://www. mayoclinic. com/health/tuberculosis/DS00372/DSECTION= treatments-and-drugs and found that there are similarities in terms of facts presented in the website with other renowned websites such as http://en. wikipedia. org/wiki/Tuberculosis_treatment, http://familydoctor. org/online/famdocen/home/common/infections/common/bacterial/120. html, and http://www. nlm. nih. gov/medlineplus/tuberculosis. html. Similar information was also found in the journal ‘ Risk factors for side-effects of isoniazid, rifampin and pyrazinamide in patients hospitalized for pulmonary tuberculosis’ from the European Respiratory Journal. This source, therefore, is trustable because it has a lot of correspondence with other sources.