CHAPTER 5

Discussion

5.1. Widal test.

Widal test is the oldest serodiagnosis for typhoid fever and right now it is still widely used, especially in developing countries where there are lack of equipment, money and knowledge.

Many studies were done to re-evaluate the value of Widal test in diagnosing typhoid fever. Some had good results, some were bad. It depended on each location and each country.

See the analysis of Widal test :

- Sensitivity is rather low 61.6%. With this sensitivity the ability of test for identification of typhoid fever is not high as expected diagnostic test. It will ignore many real typhoid fever cases. Thus it will influence a lot to the management of typhoid fever and making decision for treatment from physicians in case the blood culture negative or not available.
- Specificity is better than sensitivity (79%). Besides that the false negative result is high : 38.4%. Even the result of Widal test is negative the physicians need to carefully consider before making the treating decision.
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5.2. EIA (typhi dot test).

EIA is a new serodiagnostic test. It uses the 50 kDa of Salmonella typhi and provides a specific laboratory test to diagnose typhoid fever using a single serum specimen. Through the analysis of EIA , we can see that:

-The sensitivity is: 78.1%.with 95% CI= 78.1% $\pm$ 9.5%

-The specificity is: 81.1 % with 95% CI= 81.1% $\pm$ 4.3%

-The accuracy is : 78.0% - 80.6%

Some evaluations of EIA in other countries are:

In Pakistan : the study showed that: sensitivity and specificity of EIA was above 90% (Second international Biennial conference of Pakistan society for Microbiology Burban, Pakistan 1997). In the Philippines, M LuFong, Ac Ludan evaluated the EIA and conclusion were: sensitivity 100%, specificity 87.7% [14]. Another study in Malaysia concluded that the sensitivity was 90 % and specificity was 91%.[5]

Therefore, the results of EIA is not as high as expected and lower than some other studies. However when compare the EIA to Widal test we can see that sensitivity of EIA is better than Widal test with $P < 0.02$, CI 95%= 6.3% - 25.7% , and no difference of specificity, false positive of EIA and Widal tests (18.8% vs 21.1%), false negative of EIA and Widal tests (22% vs 38.4%), positive predictive value of EIA and Widal tests (48.3% vs 39.8%), negative predictive value of EIA and Widal test (94.2% vs 90.1%). In summary EIA is better than Widal test in diagnosing typhoid fever. Our conclusion is the same with some others studies that also compare

EIA with Widal test and their conclusion read: Diagnostic value of EIA is better than Widal test for diagnosis of typhoid fever (Papers from the first Asia-Pacific Symposium on typhoid fever. Kuala lumpur, Malaysia. Oct 1-3.1991).

One problem that can influence to the blood culture positive and results of EIA is antibiotics used. Normally the patients used antibiotics at the second or third days of fever with or without advice from doctors, so it affects to the bacteria. Hence it lead to the difficulty in catching organism in blood and also influence to antibody response. So that if we can control the use of antibiotics before admitting we think the results of EIA can be better.

In our study EIA were done only in inpatients, it is also interested to know the validity of EIA in diagnosis of typhoid fever in outpatients. As you see in inclusion criteria the admitted patients the study had fever >= 5 days, so for outpatients who came with fever has lasted >=5 day the results of EIA will be able as same as the study.

For a patients who came in the first to the fourth day of typhoid fever usually the clinical symptoms are very difficulty to distinguish from other diseases like some kind of viral diseases ..... Hence during this time it is not easy for doctor to diagnosis typhoid fever to odder the test and usually patients just stays at home with follow-up by private doctor. To answer exactly this question we should conduct a study with carring out the blood culture and EIA in patients in the first to fourth of fever. The results may be different, because it relates to the time for antibody producing.

Other more thing needed to be considered is that the location where the study was conducted is an endemic area , where the population frequently exposed with bacteria (Salmonella typhi), so some people has already low concentration of antibody (IgG), or previously have suffered from typhoid fever with IgG still maintained in the blood (IgG can remain in blood for 6.3 months[14]). Any time they catch the disease the antibody (IgG) will increase a lot and can compete with IgM when reactive with antigen, hence the reaction of IgM with antigen is not as strong as normal. It may lead to false negative interpretation. This problem may have happened for 4 cases of group 1 with IgM-, IgG + (table 4) and 1 case of group 2 (table 7). When we saw the results of EIA of these cases the color of IgG was much more intense than the control but the color of IgM was less than the control. We re-processed and got the same and concluded: the EIA of these cases were negative.

To prevent this phenomenon, we can use the typhi M dot test. Basically typhi M dot test with one added element is similar with typhi dot test. With this element IgG can be inactivated, so IgM will have chance to reactive with antibody as much as they can. But this test will take three hours to give a results and more expensive.

One more big problem needed to be discussed here is the results of group 2. The group that patients were accepted to be suffered from typhoid fever based on clinical feature. The reason why I put this group in this study is that: as we know the rate of blood culture positive is low (it is only 15 - 30%) . So in fact there are many truly typhoid fever that are ignored because of blood culture negative. I set up group 2 to see the positive rate of

serodiagnostic tests in it and saw the number of positive test between two groups (blood culture positive and blood culture negative but clinical feature suggested of typhoid fever). In group 2 the Typhi dot positive is 74.5% and the Widal test positive is 59% (table 6 and 8). Meanwhile in the blood culture positive group there is 78.1% positive with typhi dot and 61.6% with Widal test. The results in two groups seem a bit difference.

Also with the group 2 we have two situations for analysis of the validity of EIA and Widal tests:

- Based on group 1(typhoid) and 3 (non-typhoid)
- Based on group 1(typhoid) and 2,3 (non-typhoid).

Data were analyzed with two situations to see the difference of specificity between them. My aim here is to see the truly specificity, because we know that many real typhoid fever were accepted to be non-typhoid only due to negative blood culture (it can cause a lot of false negative). The results showed that: no significant difference of specificity between two situations.

As we saw here the number of patients in group 2 is too small (22) compared to number of patients in group 3 (323), so it can not clearly affect to the results of analysis. Some physicians said that: now few typhoid fever cases can meet the criteria of group 2 because of early used antibiotics. So we will still ignore many typhoid fever with negative blood culture. Some people suggest that other study should be conducted with criteria less specific as criteria in group2 to see the difference between two situations.

One more advantage of EIA is rapid. The whole process take only one hour unlike Widal test which needs an incubation period of at least 24 hours.

Another feature of the dot EIA is cost-effective.

EIA is rapid, no need special equipment and sensitivity is better than Widal test. Meanwhile the cost of EIA test is the same with the cost of Widal test (it is about 1.2 to 1.3 USD/test).

With these advantages EIA is easy to be used in the field and in many district hospitals where blood culture facilities may not be available, especially in poor, endemic area where test for diagnosis of typhoid fever needs to become routine test.