A COMPARATIVE STUDY OF THE EFFECTIVENESS OF 'STANDARD' AND 'AFIP' TYPHOID VACCINES

M. I. Burney (National Health Laboratories, Islamabad.)
Ashfaq Ahmed (Armed Forces Medical College, Rawalpindi.)
K. A. Karamat (Armed Forces Institute of Pathology, Rawalpindi.)

Abstract

A typhoid vaccine, named 'AFIP' vaccine, was prepared with a local strain of S. typhi (strain 42\63) isolated at AFIP Rawalpindi. The initial batches also contained S. para A and B (both local strains) but later these were dropped as S. para A and B do not possess satisfactory antigenicity. Comprehensive laboratory investigations of the comparative effectiveness of 'AFIP' vaccine and the 'Standard' vaccine currently in use and foreign vaccines imported in Pakistan were carried out by one of the authors (M.I.B.) by the active and passive immunization of mice with subsequent challenge with saline and/or mucin suspended S. typhi and the production of agglutinin titre in rabbits. The 'Standard' and foreign vaccines which were both phenolized were superior to AFIP (alcoholized) vaccine in production of H-antibodies. AFIP vaccine was however, found to be more potent in production of Vi antibody. Field trials, however, provided the conclusive proof of much higher effectiveness of 'AFIP' vaccine as compared to Standard vaccine in preventing the incidence of typhoid fever. The trials were carried out among the recruits joining six selected Regimental Centres of Pakistan Army and were started in April 1975 and continued till April 1979.

Both vaccines at the time of field trials were phenolized and were similar in all respects except for the strains of the organisms used in their preparation. Three thousand seven hundred and eighty recruits were inoculated with 'Standard' vaccine while 2757 were given vaccine. The two vaccines were given to alternate batches of recruits in each regimental centre. Each inoculated recruit was followed for one year for the development of typhoid fever. A total of 98 cases of enteric fever were reported from recruits immunized with 'Standard' vaccine giving a case incidence rate of 2.59% while 31 cases of typhoid fever occurred among those immunized with 'AFIP' vaccine showing the incidence rate of 1.34% only. The incidence of typhoid cases among those immunized with AFIP vaccine was almost half than among those immunized with standard vaccine. The difference of 1.25% was found to be statistically significant at level of 'P' less than 0.111.

It is recommended that the currently used Standard vaccine prepared with S. typical Ty 2 strain be replaced by AFIP vaccine for use in the country (JPMA 30:67, 1980).

Introduction

A new vaccine, named the 'AFIP' vaccine, was prepared using three strains of S. typhi II 42\63, S. para A 81\63, S. \para B 60\63, isolated at Armed Forces Institute of Pathology (AFIP) from among the Pakistani patients. Later batches of AFIP vaccine contained only S. typhi. The 'Standard' vaccine currently used in Pakistan is prepared with S. typhi Ty-2 strain and is also heat killed and phenolized. The earlier batches of vaccine contained S. para A and B but the vaccine now contains S. typhi only as S. para A and B do not possess good antigenic property. Both types of vaccines are prepared at the Division of Biological production of National Health Laboratories, Islamabad. In addition, foreign vaccines have also been imported in Pakistan and used in the country.

A laboratory study of the 3 types of vaccines - "Standard" "AFIP" and "foreign" - by active and passive immunization of mice followed by challenge by saline and/or mucin suspended S. typhi organism;
agglutinin production in rabbits after graded doses of various vaccines and other related aspects was
carried out by one of the authors (M.I.B.) At the time of experimental study the AFIP vaccine was
alcoholized while the other two types were phenolized.
A controlled field trial of the 'Standard' and 'AFIP' vaccine was organized by the Department of
Experimental Research, Armed Forces Medical College, Rawalpindi among the recruits joining six
selected regimental centres of Pakistan Army. The two vaccines at the time of field trials were
phenolized and were exactly similar except for the strains of organism used in their preparation.
The present report gives the comparative findings of the field trials of 'Standard' and 'AFIP' vaccines.

Material and Method

The 'Standard' and AFIP' vaccines made in National Health Laboratories, Islamabad were used in the
study. Recruits joining the Baluch, Frontier Force, Army Services Corps, Artillery and Engineers were
enlisted for field trials of the two types of vaccines. The recruitment to these centres is on all Pakistan
basis.
The field trials to determine the relative efficiency of the standard ana AFIP vaccine was started in
April 1975. Inoculation by the two types of vaccine was carried out for 3 years after immunization.
Those inoculated between April 1977 and April 1978 were followed till April 1979.
A visit was made to the regimental centres at the beginning of the trial to elicit the co-operation of the
administrative authorities, paramedical and medical staff working there. It was ensured that each
regimental centre indent half of the requirement of vaccine of the two types. The officers
Commanding of the supporting hospitals were also briefed in this regard.
Every alternate batch of recruit tobe inoculated on enlistment was vaccinated with either of the two
types of the vaccines. The nominal roll of recruits with their regimental numbers and batch number and
type of vaccine was received every month in the Deptt. of Experimental Research. Enteric fever is a
notifiable disease in the army. A copy of the notification form is received by the Deptt* of
Experimental Research. Each notification of typhoid case was checked with the nominal roll of the
recruits enlisted in the trials. In case of the typhoid fever occurring among the enlisted recruits the type
of vaccine used to vaccinate him was noted and a record kept. A counter check was done with the
record of notified typhoid cases maintained at General Headquarters and that of the hospitals.
A total of 6537 recruits were enlisted in the study, 3780 were immunized with standard vaccine while
2757 were immunized with AFIP vaccine. Cases of typhoid fever in the two series within one year of
inoculation were found to be 98 and 37 respectively giving the typhoid incidence rate of 2.59% and
1.34% respectively. Recruits immunized with AFIP vaccine, therefore, showed almost exactly half the
incidence rate of typhoid fever than those immunized with standard vaccine. The figures are given in
the table below:-
The difference between the case incidence of typhoid fever among recruits with the two vaccines was highly significant. The field trials conclusively proved that the AFIP vaccine is almost twice as effective in preventing typhoid fever as the Standard vaccine.

**Discussion**

Antigenic stimuli indigenous to one's country have a prime facie reason to be more protective than the stimuli provided by foreign antigens. Phage typing of bacteria has shown that each phage type is responsible for its own immunological pattern. Antibodies against one antigen may be protective against homologous type but not as against others even though the agglutinin production may be the same for the different phage type.

It was reasonable therefore that attempt should have been made to phage type the locally prevalent organisms and to use them in making vaccine for use in the country. The laboratory tests were suggestive of the superiority of vaccine produced out of the locally isolated strains. However, the results of large scale trials carried out in Yugoslavia (Yugoslav Typhoid Commission, 1957) proved that...
mice and men cannot be compared regarding the protection which a vaccine affords. The final verdict regarding the efficacy of any type of vaccine can only be provided by extended field trials among human populations. Army recruits provided an ideal population for carrying out controlled trials and following them up for the given period of time.

Conclusion

The AFIP vaccine was thoroughly tested initially through laboratory study which showed the slight superiority of AFIP vaccine over the standard vaccine. Controlled field trials extending over a period of 4 years, however, proved the AFIP vaccine to be almost twice as effective in preventing typhoid fever as the standard vaccine.
The authors recommend that the currently used "Standard" vaccine be replaced by 'AFIP' vaccine for use in the country. This promises to reduce the incidence of typhoid fever among immunized population by half.