Comparison of safety and immunogenicity of a Vi polysaccharide typhoid vaccine with a whole-cell killed vaccine in Malaysian Air Force recruits

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Objective To carry out a comparative study of the safety and immunogenicity of Vi polysaccharide vaccine against whole-cell killed (WCK) typhoid vaccine.
Methods The study was carried out on young adult recruits (aged 18–25 years) of the Malaysian Air Force. A total of 125 subjects received the Vi polyssacharide vaccine and 114 received the WCK vaccine.
Findings The Vi vaccine was significantly less reactogenic than the WCK vaccine with regard to systemic and local reactions. Following administration of the Vi vaccine, seroconversion rates (defined as the percentage of subjects with a 4-fold rise of baseline antibody level) of 75.5% and 67% were observed at 2 weeks and 6 weeks, respectively, after immunization, compared with 25% and 31.3% among recipients of the WCK vaccine. Of the 110 Vi vaccinees with serological data, 21 (19%) had high, seroprotective, pre-immunization levels of anti-Vi antibodies ($\geqslant 1$ μg/ml). The majority of subjects in this group came from a region in Malaysia which is known to have high typhoid endemicity. Interestingly, these antibody levels were boosted considerably following administration of vaccine at a level that was 5-fold higher than in subjects with low pre-immunization levels. In contrast, the seroconversion rates in those receiving the Vi vaccine were higher in subjects with low pre-immunization levels of anti-Vi antibodies (76–84%), compared to those with protective levels of $\geqslant 1$ μg/ml prior to immunization (48–57%).
Conclusions The study reaffirms the safety and efficacy of the Vi polysaccharide vaccine and identifies a hitherto unrecognized advantage in its use, i.e. it is a potent immunogen that boosted considerably the protective antibody levels among a significant number of immunologically sensitized individuals living in typhoid-endemic regions.

Keywords Typhoid-paratyphoid vaccines/immunology/adverse effects; Polysaccharides, Bacterial/immunology/adverse effects; Vaccines, Inactivated/immunology/adverse effects; Military personnel; Randomized controlled trials; Comparative study; Malaysia (*source: MeSH*).

Mots clés Vaccin antityphoparatyphoïdique/immunologie/effets indésirables; Polyosides bactériens/immunologie/effets indésirables; Vaccin inactivé/immunologie/effets indésirables; Personnel militaire; Essai clinique randomisé; Etude comparative; Malaisie (*source: INSERM*).

Palabras clave Vacunas tifoide-paratifoide/inmunología/efectos adversos; Polisacáridos bacterianos/inmunología/efectos adversos; Vacunas inactivadas/inmunología/efectos adversos; Personal militar; Ensayos controlados aleatorios; Estudio comparativo; Malasia (*fuente: BIREME*).

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Voir page 816 le résumé en français. En la página 816 figura un resumen en español.

Introduction

In many developing countries, the problem posed by typhoid fever (*1–3*) has been exacerbated in recent years by the appearance of antibiotic-resistant strains of *Salmonella typhi*, and by rapid urbanization and problems associated with poor sanitation systems and lack of clean water. It has been estimated that

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globally over 16 million cases of typhoid fever occur annually with more than 600 000 deaths; however, it is believed that these estimates may be 5–10 times too low (*3*). Although effective vaccines against typhoid fever have been developed (*3*), notably the orally administered Ty21a (*4, 5*) and the purified Vi polysaccharide (*4, 6, 7*) vaccines, their use is not widespread and remains limited even in immunization programmes (*4*). The newer vaccines have provided alternatives to the efficacious but highly reactogenic whole-cell, heat-inactivated, phenol-preserved parenteral vaccine. The safety and efficacy of the Vi polysaccharide vaccine is now firmly established, and it maintains significant protective efficacy for a minimum of 3 years (*8, 9*) and may be protective even after 10 years (*10*). In a recent study, Klugman et al. (*9, 10*) were also able to define a serological correlate of protection following vaccination with Vi vaccine in an endemic area. However, and despite the clear advantages of the newer vaccines, the use of the whole-cell killed (WCK) vaccine (heat-inactivated, phenol-preserved) has remained popular in many developing countries because of its lower cost and perhaps also because of an inherent resistance to change. In Malaysia, for example, the armed forces still routinely use the WCK vaccine for the immunization of recruits and also of troops deployed to other endemic areas for peace-keeping duties. Local data on the safety and immunogenicity of the newer vaccines are required in order to support the choice of a safe and less reactogenic typhoid vaccine in the Malaysian Air Force. We therefore carried out a comparative safety and immunogenicity trial of the typhoid Vi polysaccharide vaccine versus the WCK typhoid vaccine among recent Malaysian Air Force recruits and report our findings in this article.

Materials and methods

Methodology

The study was an open, randomized comparative trial conducted at the Malaysian Air Force training camp in Ipoh, Malaysia, over the period October 1997 to April 1998. The cluster random sampling method was used. Subjects admitted to the study had no clinically known or detectable severe illness. Non-inclusion criteria included having received typhoid vaccines within the previous 3 years, having known immunodeficiency, having fever at the time of vaccination, and being currently included in other clinical trials. Signed, informed consent was obtained from all subjects before their assignment to one of the two vaccine groups. Eligibility criteria were similarly ascertained prior to such assignment. From a total of 300 subjects who were considered, 239 male recruits aged 18–25 years whose homes were in different parts of the country were included in the study; 114 received the whole WCK vaccine (Commonwealth Serum Laboratories, Melbourne, Australia, Batch No. 07-902, heat-inactivated, phenol-preserved *S. typhi*; two doses of 5×10^8 cells given two weeks apart intramuscularly, according to the routine schedule for immunization) and 125 received the Vi polysaccharide vaccine (Typhim Vi®, Lot N0308, Pasteur Mérieux Connaught, France; single dose of 25 µg intramuscularly). A total of 61 subjects (36 and 25 from the Vi and WCK groups, respectively) were not eligible because of a history of previous vaccination with typhoid vaccine, and were excluded from the study prior to taking a blood sample and receiving the first dose of vaccine. Subsequently a further 15 subjects from the Vi group dropped out. The single dose of Vi vaccine and the first dose of WCK vaccine were given immediately after the pre-vaccination blood sample was taken, while the second WCK dose was given two weeks later. Main outcome measures or evaluation criteria included systemic reactions (fever, headache and body ache) and local reactions (various degrees of pain at the injection site), as recorded on a questionnaire completed by all subjects during the 72 hours following injection. Fever was defined as a temperature of >37.2 °C, headache as uncomfortable and painful sensations/feelings in the head following vaccination, and body ache as the feeling of pain (aching) over the entire body after vaccination. With regard to assessment of local reactions, the researchers measured the size of the zone of redness (skin discoloration at and around the injection site) as well as the size of oedema (swelling/induration). Inability to lift the arm was indicated when the subject was unable to lift the arm because the vaccine provoked severe pain at the injection site. There was a potential bias in the reporting of symptoms because the WCK group had two opportunities to report symptoms, as opposed to a single opprtunity for the Vi group, but this was minimized because all subjects resided in a single location (the training camp) and, for all intents and purposes, had equal opportunities to report any symptoms without regard to the vaccination event. For the immunogenicity studies, blood samples were collected 2 weeks and 6 weeks after vaccine administration and processed at the site; the serum samples were stored at –20 °C until further testing.

Ethical approval for the study was obtained from the Malaysian Military Medical Ethical Committee.

Statistical methods

Calculation of the sample size was based on a Vi vaccine efficacy of 80% and WCK vaccine efficacy of 50%, an alpha significance level of 0.05, and a statistical power of 99%. The minimum number of subjects to be enrolled per group was 92.8. Safety data were described by the percentage of subjects presenting with at least one local reaction or systemic reaction. The proportion of subjects experiencing mild or moderate pain was also calculated. Levels of anti-Vi antibodies were summarized as geometric mean titres (GMT). Seroconversion rates ($\geqslant$4-fold increase of anti-Vi antibody titres over pre-immuni-

zation levels) were calculated and compared between the groups. Student's *t*-test and the goodness-of-fit method were used for statistical analysis.

Assay of anti-Vi antibodies

As mentioned above, a total of 15 subjects in the Vi group dropped out of the study or had to be excluded for technical reasons. For the group receiving the WCK vaccine, a random sample of 33 sera (every third sample was selected from the group of 114 sera) was selected for practical and technical reasons related to transportation of the samples to Pasteur Mérieux Connaught, Val de Reuil, France, for testing using standard radioimmunoassay procedures (*7, 11*). Thus serum specimens from 110 (out of 125) and 33 (out of 114) subjects receiving the Vi vaccine and the WCK vaccine, respectively, were assayed for anti-Vi antibody levels. The seroconversion rate was defined as the proportion of subjects who showed a $\geqslant$4-fold increase over pre-immunization anti-Vi antibody levels. A seroprotection level was defined as the proportion of subjects with anti-Vi titres of $\geqslant$1 μg/ml (*9*). Sera from both groups were tested simultaneously by technicians who were blinded to the type of vaccine received by the subjects being studied.

Results

Safety

Based on the presence of at least one sign or symptom, a systemic adverse event following vaccination was defined as one involving a subject reporting fever, body ache or headache, while a local adverse event was defined as the presence of mild pain (redness <10 cm, oedema/induration <5 cm), moderate pain (redness 10–20 cm, oedema/induration 5–10 cm, inability to lift the arm), or severe pain (redness >20 cm, oedema/induration >10 cm, functional incapacity to perform any activity) at the injection site. The response rate to filling the questionnaire to evaluate these events was 100%. It was observed that 1% of the subjects who received the Vi vaccine reported systemic complaints, compared with 28% among those who received the WCK vaccine (P <0.001) (Table 1). With regard to local reactions (i.e. pain at the injection site), 28% of the subjects who received the Vi vaccine complained of mild pain, compared with 48% among those who received the WCK vaccine (P <0.01) (Table 1). Among the subjects who reported local reactions, moderate pain (i.e. inability to lift the arm) was noted among 4% of those who received Vi vaccine and 42% of WCK vaccinees (P <0.001) (Table 1).

Table 1. **Systemic and local reactions after administration of Vi polysaccharide vaccine or whole-cell killed (WCK) typhoid vaccine in 239 young adults in Malaysia**

Event[a]	Vi vaccine	WCK vaccine
No. vaccinated	125	114
Systemic complaints (%)	1[b] (1/125)	28 (32/114)
Mild pain at injection site (%)	28[c] (35/125)	48 (55/114)
Moderate pain at injection site (%)	4[b] (5/125)	42 (48/114)

[a] Systemic complaints observed for 3 days after vaccination included fever, body ache and headache (at least one symptom). Mild pain at the injection site also included erythema (<10 cm) and oedema/induration (<5 cm). Moderate pain at the injection site refers to inability to lift the arm and also redness (10–20 cm) and oedema/induration (5–10 cm).

[b] Significantly different from those receiving WCK vaccine (P <0.001) by Student's *t*-test.

[c] Significantly different from those receiving WCK vaccine (P <0.01) by Student's *t*-test.

Immunogenicity

Subjects who received the Vi vaccine showed a 7–9-fold rise in serum anti-Vi antibody levels, with GMT values of 4.71 μg/ml and 3.64 μg/ml at 2 weeks and 6 weeks, respectively, after immunization (P <0.0001, compared with the pre-immunization level) (Table 2). In contrast, subjects receiving the WCK vaccine showed only a 2-fold rise in titre, with corresponding GMT values of 0.733 μg/ml and 0.796 μg/ml at 2 weeks and 6 weeks, respectively, after vaccination (P <0.05, compared with the pre-immunization level) (Table 2). Seroconversion rates

Table 2. **Geometric mean titres (GMT) of anti-Vi antibodies and seroconversion rates following one injection of Vi polysaccharide vaccine or 2 doses of whole-cell killed (WCK) typhoid vaccine in young male adults in Malaysia**

Type of vaccine[a]	*n*	Geometric mean titre of anti-Vi antibody (mg/ml)			Magnitude of increase
		Pre-immunization	2 weeks	6 weeks	
Vi	110	0.505 (0.07–11.0)[b]	4.71[c] (0.66–97) *75.5%*[d]	3.64[c] (0.22–85) *67.0%*	7–9-fold
WCK	33	0.356 (0.12–5.77)	0.733[e] (0.15–15) *25%*	0.796[e] (0.1–10) *31.3%*	2-fold

[a] Statistical analysis was carried out on 108/110 evaluable subjects for the Vi vaccine group and on 32/33 evaluable subjects for the WCK group.

[b] Figures in parentheses are 95% confidence intervals.

[c] Significantly different from pre-immunization level (P <0.0001) by Student's *t*-test.

[d] Figures in italics refer to percent seroconversion ($\geqslant$4-fold increase over pre-immunization anti-Vi antibody level).

[e] Significantly different from pre-immunization level (P <0.05) by Student's *t*-test.

at 2 weeks and 6 weeks after immunization with Vi vaccine were 75.5% and 67.0%, respectively (Table 2). Subjects who received the WCK vaccine showed only a limited increase in antibody levels, with seroconversion rates of 25% and 31.3% at 2 and 6 weeks, respectively, after vaccination (Table 2). Further analysis of the data showed that 21/110 (19%) of the subjects who received the Vi vaccine, and 6/33 (18%) who received the WCK vaccine had protective levels of anti-Vi antibody (⩾1 μg/ml) even before vaccination, with a GMT value of 2.29 and 2.06 μg/ml, respectively (P <0.0005 and P <0.05, respectively) (Table 3). The GMT values for Vi antibodies induced after vaccination in this group (5.78 and 7.30 μg/ml at 2 weeks and 6 weeks, respectively) were significantly higher than those observed in subjects with lower, non-protective, antibody levels prior to immunization (1.12 and 1.51 μg/ml at 2 weeks and 6 weeks, respectively) (P <0.005) (Table 3). Of the 21 subjects in the high titre group, 10 (47%) were from the state of Kelantan, three (14%) each from Pahang and Negeri Sembilan, two (10%) from Johore, and one (5%) each from Kedah, Perak and Trengganu. Among subjects who received the WCK vaccine, a similar proportion (6/33, 18%) had protective, pre-immunization levels of anti-Vi antibody, which were boosted slightly following vaccine administration (P >0.05 at 2 weeks and P <0.05 at 6 weeks) (Table 3). The seroconversion rate in subjects with non-protective levels of anti-Vi antibodies (<1.0 μg/ml) prior to immunization was notably higher (76–84% at 6 and 2 weeks, respectively) than the rate (48–57% at 6 and 2 weeks, respectively) in those with protective pre-immunization anti-Vi levels (⩾1 μg/ml) (Table 3). In the WCK group, the seroconversion rates were higher in those with protective levels of anti-Vi antibodies (⩾1 μg/ml) prior to vaccination (33–67% at 2 and 6 weeks, respectively), compared to those with non-protective pre-immunization anti-Vi levels (<1.0 μg/ml) (26–37% at 2 and 6 weeks, respectively) (Table 3).

Discussion

The results from our study show that the reactogenicity of the WCK vaccine, in terms of both systemic and local reactions, was significantly higher than that of the purified Vi vaccine. This observation agrees well with previous reports of substantially lower rates of local and systemic reactions after Vi vaccination compared with WCK vaccine (*12*). The seroconversion rate following Vi vaccination obtained in the present study was approximately 67–75%, but was 76–84% in subjects with pre-immunization titres below 1.0 μg/ml (naïve or unprotected subjects); this is also consistent with the 75–80% rate noted in other studies in endemic areas. With regard to other studies carried out in Asian populations of the same age range as the present study, a seroconversion rate of 79% was obtained in Nepal (*5*), 68% in Indonesia (C. Simanjuntak, unpublished data), 71% in China (*13*), and 93% in the Republic of Korea (*14*). The present study also showed that seroconversion occurred in the majority of subjects after only 2 weeks from vaccination, thus illustrating the immunologically sensitized nature of the subjects living in endemic areas. Previous studies have not addressed this issue in detail because the blood samples were usually taken one month after immunization. The poor ability of the WCK vaccine to induce anti-Vi antibodies was noted previously (*15*) and believed to be due to heat

Table 3. **Geometric mean titres (GMT) of anti-Vi antibodies (μg/ml) following vaccination with Vi polysaccharide and whole-cell killed (WCK) typhoid vaccine in young male adults with high and low pre-immunization antibody levels, Malaysia**

Vaccine	Pre-immunization titres	*n*	% with ⩾1 μg/ml anti-Vi	GMT pre-immunization (μg/ml)	GMT post-vaccination (μg/ml) (2w,6w)	% seroconversion (2w,6w)[a]	Maximum magnitude of rise from pre-immunization levels
Vi	<1 μg/ml	89	—	0.35	1.12 1.51	84 76	4-fold
	⩾1μg/ml	21	19	2.29[b]	5.78[c] 7.30[c]	57 48	3-fold
WCK	<1 μg/ml	27	—	0.28	0.36 0.41	26 37	1.6-fold
	⩾1 μg/ml	6	18	2.06[d]	2.52[e] 3.12[d]	33 67	1.4-fold

[a] % seroconversion refers to ⩾4-fold increase over pre-immunization anti-Vi antibody level: 2w (upper) and 6w (lower) refers to values obtained at 2 weeks and 6 weeks after vaccination.

[b] Significantly higher than group with anti-Vi level of <1.0 μg/ml (P <0.0005).

[c] Significantly higher than group with anti-Vi level of <1.0 μg/ml (P <0.005).

[d] Significantly higher than group with anti-Vi level of <1.0 μg/ml (P <0.05).

[e] Not significantly higher than group with anti-Vi level of <1.0 μg/ml (P >0.05).

denaturation of the Vi antigen during vaccine production. This observation was confirmed in the present study where only 25–31% seroconversion was noted among the recipients of this vaccine (26–37% in naïve or unprotected individuals with pre-immunization titres below 1.0 μg/ml).

An important advance in typhoid serology was made recently by Klugman et al. (*9*), who were able to define a serological correlate of protective immunity mediated by anti-Vi antibodies against typhoid fever. Based on this correlate, studies in endemic areas have shown that between 6% (in Kenya) (*16*) and 40% (in South Africa) (*9*) of children already had protective levels of anti-Vi antibody before vaccination. This important observation has recently been extended to adolescents (16–20 years of age) in South Africa and has been attributed to ongoing antigenic exposure (*10*). However, the data are limited for adults living in endemic areas. In agreement with the study of Keddy et al. (*10*), we noted in the present study that a significant proportion (19%) of the adult subjects (aged 18–25 years) who received the Vi vaccine had seroprotective levels of anti-Vi antibody ($\geqslant$1.0 μg/ml) even before vaccination. Following the administration of Vi vaccine to this group, subjects showed a significantly stronger response in the induction of anti-Vi antibody levels in serum (approximately 5-fold higher), compared to subjects who had lower, non-protective, pre-immunization antibody levels, although the magnitude of the rise was similar in the two groups (3–4-fold rise compared to pre-immunization levels). This is surprising since it would be expected that high levels of pre-existing anti-Vi antibodies in recipients would reduce the immunogenicity of the vaccine through neutralization. An explanation for this observation may be that individuals with high pre-immunization titres had experienced a previous infection with *S. typhi* and thus generated a strong anamnestic response when given the vaccine. Although the magnitude of the response was significantly higher in those with protective levels of anti-Vi before immunization, the proportion of subjects who seroconverted was actually higher (76–84% at 6 and 2 weeks, respectively) in the group possessing non-protective anti-Vi levels than among subjects already protected before immunization (48–57% at 6 and 2 weeks, respectively).

The present results suggest that up to 20% of young adults in Malaysia may be seroprotected against typhoid fever. The reasons for this are not clear but may be related to immunological sensitization as a result of geographical factors, i.e. originating from areas of higher endemicity. In this respect, it is interesting to note that almost half (10/21, 47%) of the recruits in this group came from the east coast state of Kelantan, which is known to have the highest incidence of typhoid fever in the country. In 1994, for example, 45% of all the typhoid cases in peninsular Malaysia were reported from Kelantan (Ministry of Health, Malaysia, unpublished data, 1999). It is also possible that the high pre-immunization anti-Vi levels could be due to the subjects being asymptomatic carriers. However, since typhoid carriers are three times more likely to be women (*17*), and the likelihood of becoming a carrier increases with age, it seems unlikely that the young male recruits in our study were typhoid carriers. Taking into consideration the limitations associated with the relatively small numbers in the study and other potential biases (e.g. only healthy males, single ethnic group, 18–25 years of age), this finding nevertheless suggests that in typhoid-endemic areas it is likely that significant protective immunity as a result of natural exposure exists among the population, especially since the seroprotective level that was defined (*9*) may actually be an overestimate of the true antibody level required for protection (*9*).

The key issue in the use of immunization for the prevention and control of typhoid fever is the absence of widespread use of currently available vaccines (*1, 2, 4*). Further uncertainty on the choice of vaccine was generated by a recent report from Engels et al. (*18*), which concluded that the WCK vaccine offered the greatest protection for the longest time when compared to the Ty21a or Vi vaccines. Vi polysaccharide vaccines have several clear advantages over the WCK vaccine, but before a policy decision on whether to incorporate the use of this vaccine in national immunization programmes can be made, it is clear that cost–benefit and local epidemiological studies on the immune status of the target population in endemic regions, and how these subjects might respond to immunization, must first be carried out. The present study has further confirmed the good safety and immunogenicity profile of the Vi vaccine. Most importantly, it has also reinforced the recent suggestion (*10*) that Vi antibodies are commonly elevated amongst individuals living in typhoid-endemic regions and are not only associated with a recent infection or chronic carriage. Furthermore, by demonstrating the strong immunogenicity of the Vi vaccine in endemic areas that included a significant proportion of immunologically sensitized adults with elevated, seroprotective, pre-immunization Vi-antibody levels, this study has indicated the possible use of this vaccine as a "booster" immunogen among such individuals, in addition to its main application as a primary immunoprophylactic agent in susceptible populations. Also, since subjects are not usually screened before immunization and 20% are already naturally protected, the vaccination of these persons to enhance their anti-Vi antibody levels poses no significant safety problems. ■

Conflicts of interest: none declared.

Résumé

Comparaison de l'innocuité et de l'immunogénicité d'un vaccin antityphoïdique polyosidique Vi et d'un vaccin tué à germes entiers chez des recrues de l'armée de l'air malaisienne

Objectif Réaliser une étude comparative de l'innocuité et de l'immunogénicité d'un vaccin antityphoïdique polyosidique Vi et d'un vaccin antityphoïdique tué à germes entiers.

Méthodes L'étude a été réalisée chez de jeunes recrues (18-25 ans) de l'armée de l'air malaisienne, dont 125 ont reçu le vaccin polyosidique Vi et 114 le vaccin tué.

Résultats Le vaccin Vi était nettement moins réactogène que le vaccin tué du point de vue des réactions locales et générales. Après administration du vaccin Vi, des taux de séroconversion (pourcentage de sujets présentant un quadruplement du taux d'anticorps prévaccinal) de 75,5 % au bout de 2 semaines et de 67 % au bout de 6 semaines ont été observés, contre 25 % et 31,3 % respectivement chez les sujets ayant reçu le vaccin tué. Sur les 110 sujets vaccinés par le vaccin Vi pour lesquels on disposait de données sérologiques, 21 (19 %) avaient déjà des taux séroprotecteurs d'anticorps anti-Vi ($\geqslant$1 μg/ml) avant la vaccination. La plupart d'entre eux provenaient d'une région de Malaisie où la fièvre typhoïde est fortement endémique. Il est intéressant de noter que la vaccination induisait une élévation considérable de ces taux d'anticorps (multiplication par 5), davantage que chez les sujets qui avaient un faible taux d'anticorps au départ. En revanche, les taux de séroconversion après administration du vaccin Vi étaient plus élevés chez les sujets ayant un faible taux d'anticorps anti-Vi avant la vaccination (76-84 %) que chez ceux qui avaient déjà des taux protecteurs (48-57 %).

Conclusion L'étude a permis de réaffirmer l'innocuité et l'efficacité du vaccin antipolyosidique Vi et a mis en évidence un avantage méconnu jusqu'alors, à savoir une forte immunogénicité qui renforce considérablement les taux d'anticorps protecteurs chez une proportion significative de sujets déjà sensibilisés vivant dans des régions où la fièvre typhoïde est endémique.

Resumen

Comparación de la inocuidad e inmunogenicidad de dos vacunas antitifoídicas — una basada en el polisacárido Vi, y otra muerta de células enteras — en reclutas de la Fuerza Aérea de Malasia

Objetivo Realizar un estudio comparativo de la inocuidad e inmunogenicidad de una vacuna antitifoídica de polisacárido Vi y una vacuna antitifoídica muerta de células enteras (WCK).

Métodos El estudio se llevó a cabo con reclutas jóvenes (18–25 años) de la Fuerza Aérea de Malasia. Un total de 125 individuos recibieron la vacuna de polisacárido Vi, y 114 la vacuna WCK.

Resultados La vacuna Vi fue significativamente menos reactogénica que la WCK a nivel tanto sistémico como local. Tras la administración de la vacuna Vi se observaron tasas de seroconversión (porcentaje de individuos en los que el nivel basal de anticuerpos se multiplicó por 4 como mínimo) del 75,5% y el 67% a las dos y seis semanas, respectivamente, de la inmunización, frente al 25% y el 31,3% observados entre los que recibieron la vacuna WCK. De los 110 vacunados con Vi para los que se disponía de datos serológicos, 21 (19%) presentaban niveles preinmunización seroprotectores de anticuerpos anti-Vi ($\geqslant$ 1 μg/ml). La mayoría de los individuos de este grupo procedía de una región de Malasia de alta endemicidad de fiebre tifoidea. Un dato interesante es que esos niveles de anticuerpos se vieron estimulados considerablemente por la administración de la vacuna (multiplicación por 5) en comparación con los individuos con bajos niveles preinmunización. Por el contrario, las tasas de seroconversión de quienes recibieron la vacuna WCK fueron mayores en los individuos con niveles bajos de anticuerpos anti-Vi antes de la inmunización (76%–84%), en comparación con quienes presentaban niveles protectores $\geqslant$ 1 μg/ml antes de la inmunización (48%–57%).

Conclusión El estudio confirma la inocuidad y la eficacia de la vacuna de polisacárido Vi y muestra una ventaja hasta ahora desconocida de su uso, a saber, que se trata de un potente inmunógeno que estimula considerablemente los niveles protectores de anticuerpos en una importante proporción de los individuos ya inmunosensibilizados que viven en regiones de fiebre tifoidea endémica.

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