Oral iodine supplementation does not reduce neutralizing antibody responses to oral poliovirus vaccine

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Iodine deficiency is a major cause of impaired mental development, goitre, and cretinism in many parts of the world. Because existing immunization programmes can be used to deliver oral iodized oil (OIO) to infants at risk, it was important to know whether OIO could adversely affect the antibody response to vaccines, such as trivalent oral poliovirus vaccine (OPV).

A randomized, double-blind, placebo-controlled clinical trial was conducted in Subang, West Java, Indonesia, in which 617 eight-week-old infants received either OIO or a placebo (poppy-seed oil) during a routine visit for their first dose of OPV as part of the Expanded Programme on Immunization (EPI). The infants received two boosters of OPV at 4-week intervals after the first dose, and were followed up when 6 months old. Neutralizing antibody titres to poliovirus serotypes 1, 2, and 3 were compared in serum samples that were taken from 478 of these infants just before the first dose of OPV and at 6 months. It was found that oral iodized oil did not reduce the antibody responses to any of the three serotypes of OPV. These results indicate that oral iodine may safely be delivered to infants at the same time as oral poliovirus vaccine according to current EPI immunization schedules.

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Introduction

Although the use of iodized salt is regarded as the long-term solution to iodine deficiency disorders (IDD) (*1*), interim measures for iodine supplements are needed in areas where iodized salt is not yet available or widely used (*2*). One suggestion for areas with a high risk of IDD and child mortality is to provide oral iodized oil (OIO) supplements to infants through the existing immunization services (*3*). The extensive coverage provided by these services would reduce the overhead costs of OIO supplementation (*4*). However, the administration of OIO at the same time as trivalent oral poliovirus vaccine (OPV) has not been recommended because of the absence of clinical studies on the effect of iodized oil on the immune response of vaccinees to OPV (*5*).

The effect of iodized oil on the infectivity of poliovirus vaccine has been studied *in vitro* (*6*); the oil contained 480 mg iodine per ml and, when mixed with an equal volume of vaccine, was found to reduce poliovirus infectivity in the rapid stability test (RST). This test consisted in incubating monovalent Sabin strains (poliovirus types 1, 2, or 3) or trivalent OPV (from different sources of manufacture) with poppy-seed oil (alone and with addition of iodine), followed by determining virus infectivity in cell culture. Reduction in titres ranged from about 1 to 5 log units, depending markedly on the time of incubation, the vaccine source, and poliovirus type (type 3 being the most susceptible to iodine treatment). However, when iodized oil and poliovirus were mixed and assayed immediately, no reduction in infectivity was observed. The authors of the study concluded that, although oral administration of iodized oil at the same time as OPV was unlikely to impair seroconversion in the recipient, clinical confirmation was required before the procedure could be recommended by the WHO Expanded Programme on Immunization (EPI) (*6*).

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Reprint No. **0006**

Oral iodized oil supplementation has recently been shown to improve infant survival in a clinical trial in Indonesia in which infants received OIO or placebo immediately after their first dose of OPV (*7*). While this trial suggested that OIO improved infant survival, it was still not known whether OIO interfered with OPV. The aim of the present study was to examine the effect of OIO on the antibody response to OPV in the same clinical trial.

Materials and methods

The study design — a randomized, double-masked, placebo-controlled clinical trial — has been described in detail elsewhere (*7*). The study population was drawn from an area of mild-to-severe IDD in Subang, West Java, Indonesia. The study was approved by the Institutional Review Board of the Johns Hopkins School of Medicine and by the ethical committees of WHO, Hasan Sadikin Hospital, University Pajajaran, and the Indonesian Ministry of Health. Written informed consent was obtained from a parent or guardian for all participants in the study. Iodine supplementation was given to infants aged 8 weeks during their first EPI contact, at which time they also received oral poliovirus and diphtheria–pertussis–tetanus vaccines. Placebo (poppy-seed oil) or OIO (100 mg Lipiodol, Laboratoire Guerbet, Aulnay-sous-Bois, France) was administered by mouth immediately after the first dose of OPV. The infants completed the EPI immunization schedule with two additional visits at four-week intervals and a final follow-up evaluation at 6 months of age.

Serum samples were collected from each infant at enrolment (8 weeks) and at follow-up (6 months) and kept frozen at –80 °C. Upon thawing, the sera were heat-inactivated at 56 °C for 30 min, diluted 1:4 in assay medium, and refrozen in aliquots until assayed for antibody activity in poliovirus microneutralization tests, as previously described (*8, 9*), using duplicate serial twofold serum dilutions and attenuated poliovirus strains TA-4, TB-3a, and TC-3a (poliovirus types 1, 2, and 3, respectively). The International Reference Serum 96/202 (National Institute for Biological Standards and Control, Potters Bar, Hertfordshire, England (*10*)), containing 25, 50 and 5 IU of antibody activity against poliovirus types 1, 2, and 3, respectively, was used to calibrate in-house reference sera against each poliovirus serotype according to directions provided by the supplier. The baseline (pre-immune) and follow-up (postimmune) sera from each subject in the study were assayed at the same time. Virus neutralization was scored by microscopic examination of replicate cultures at each dilution of serum after 10 days of incubation. The 50% endpoint dilutions were calculated (*11*) and the results expressed both as reciprocal $\log_2$ dilutions and in IU. The lowest detectable level of neutralizing antibody activity was 2 $\log_2$ units; sera with no detectable neutralizing antibody activity were therefore assigned a $\log_2$ dilution value of 1.5. Sera with high levels of neutralizing antibody activity, exceeding the dilution range of the test, were assigned a $\log_2$ dilution value of 12.5. The log-fold increase (LFI) in neutralizing-antibody activity was calculated for each subject with and without an adjustment for estimated decline in maternally derived antibody over the study period. The mean time from enrolment to follow-up was 120 days (95% confidence interval (CI): $\pm$ 0.72 days), and an adjustment of four antibody half-lives was applied uniformly to the pre-immune titres for all samples.

All poliovirus neutralizing antibody assays were conducted under masked conditions. After preliminary analysis of the neutralizing antibody results to confirm the applicability of the statistical approaches to be used, the identity, treatment allocation, and other characteristics of the subjects were disclosed. Maximum likelihood fitting in contingency table tests and analysis of variance were used to determine whether the treatment allocation groups differed according to sex, age at enrolment, or other factors that might confound the analysis of the main treatment effect. Geometric mean titres of pre-immune and postimmune sera and the mean LFI were calculated for the iodine and placebo groups. Analysis of variance was used to evaluate the effect of supplementation with iodized oil on the neutralizing antibody responses for each of the three poliovirus serotypes (*12*).

Results

Of the 617 infants enrolled in the study, 307 (49.8%) received OIO and 310 (50.2%) the placebo; 88 infants dropped out of the study before the age of 6 months and 22 died prior to follow-up. Thus, only 507 infants were reviewed at 6 months of age, but serum samples were not available for 29 of them, leaving a total of 478 (238 and 240 in the placebo and iodine groups, respectively) pairs of pre-immune and postimmune sera for evaluation. Maternal and infant characteristics in both groups are presented in Table 1 as frequencies (and percentages), or means ($\pm$ 95% CI). The treatment groups did not differ significantly with regard to any of the characteristics examined.

Geometric mean titres and confidence intervals for the placebo and iodine treatment groups are given in Table 2. Mean titres were higher after vaccination, but in many cases the individual post-vaccination titres were lower than the corresponding pre-vaccination titres. There were 42, 9, and 43 such instances for poliovirus types 1, 2, and 3, respectively; these occurred with similar frequencies in the placebo and iodine treatment groups (data not shown). High levels of neutralizing antibodies in the pre-vaccination sera make it difficult to interpret the seroconversion rates or LFI following immunization with OPV. Therefore adjustment was made for the presumed decline of maternal antibodies during the 4 months between the baseline and follow-up blood collec-

Table 1. **Selected baseline characteristics of study subjects, by allocation group**

Maternal characteristics[a]	Placebo (*n* = 240)	Iodine (*n* = 238)	*P*-value[b]	LR χ^2 test
Goitre grade				
0	209 (89.3)	205 (87.2)	0.688	2.26
1A	15 (6.4)	20 (8.5)		
1B	6 (2.6)	6 (2.6)		
2	3 (1.3)	4 (1.7)		
3	1 (0.4)	0 (0.0)		
No. with prior maternal iodine supplementation				
No	199 (83.3)	197 (83.1)	0.983	0.000
Yes	40 (16.7)	40 (16.9)		
No. with vitamin and mineral supplements during pregnancy				
No	33 (16.5)	36 (18.2)	0.488	0.481
Yes	167 (83.5)	162 (81.8)		
Occupation				
Housewife	225 (94.1)	213 (89.9)	0.084	2.98
Other	14 (5.9)	24 (10.1)		
Mean age (years)	25.3 ± 0.71	25.6 ± 0.72	0.577	
No. of pregnancies	2.3 ± 0.21	2.3 ± 0.18	0.783	
No. of deliveries	2.2 ± 0.20	2.2 ± 0.18	0.840	
No. of live births	2.2 ± 0.20	2.2 ± 0.17	0.887	
No. of <5-year-olds in household	1.3 ± 0.07	1.3 ± 0.09	0.849	
Educational level (years)	6.6 ± 0.28	6.9 ± 0.32	0.224	
Infants' characteristics[a]				
Sex				
Males	116 (48.3)	116 (48.7)	0.929	0.008
Females	124 (51.7)	122 (51.3)		
Breastfeeding				
No	9 (3.8)	5 (2.1)	0.278	1.176
Yes	230 (96.2)	233 (97.9)		
Fluid supplement to breastfeeding				
No	213 (92.6)	208 (89.3)	0.210	0.343
Yes	17 (7.4)	25 (10.7)		
Solid supplement to breastfeeding				
No	118 (51.3)	102 (43.8)	0.105	1.777
Yes	112 (48.7)	131 (56.2)		
Month of enrolment				
June	50 (20.8)	45 (18.9)	0.918	0.011
July	53 (22.1)	62 (26.1)		
August	81 (33.8)	76 (31.9)		
September	47 (19.6)	47 (19.7)		
October	9 (3.8)	8 (3.4)		
Weight at birth (kg)	3.2 ± 0.20	3.2 ± 0.20	0.758	
Weight at enrolment (kg)	4.8 ± 0.09	4.8 ± 0.09	0.535	
Age at enrolment (days)	55.4 ± 1.24	55.2 ± 1.11	0.812	
Time to follow-up (days)	120.8 ± 1.17	119.8 ± 0.82	0.196	
No. with acute diarrhoeal illness concurrent with immunization				
No	228 (95.0)	221 (92.9)	0.325	0.967
Yes	12 (5.0)	17 (7.1)		

[a] Figures are the numbers identified (percentages in parentheses), or means ± 95% confidence intervals.

[b] *P*-values were calculated for hypothesis tests comparing placebo and iodine groups by likelihood-ratio (LR) χ^2 tests (numbers) or analysis of variance (means).

tions, assuming a half-life of 1 month for the neutralizing antibody activity (*13*). The LFI values are shown in Table 2. Analysis of variance indicated that the differences in mean titre or LFI between the placebo and iodine groups were not significant for any of the poliovirus serotypes.

Table 2. **Neutralizing antibody titres to poliovirus types 1, 2 and 3 in infants in the placebo and iodine groups**

Poliovirus	Sample	Treatment group[a]					
		Placebo (n = 240)		Iodine (n = 238)			Difference
		Mean $\log_2$ titre	IU	Mean $\log_2$ titre	IU	P-value	(iod-plac)[b]
Type 1	Pre-vaccination	6.25 ± 0.24	0.26	6.25 ± 0.26	0.26	0.999	0.000
	Post-vaccination	10.91 ± 0.29	6.49	10.78 ± 0.33	5.95	0.579	–0.125
	Log-fold increase (LFI)	4.66 ± 0.41	–	4.54 ± 0.45	–	0.687	–0.125
	Adjusted LFI	8.54 ± 0.39	–	8.39 ± 0.42	–	0.608	–0.151
Type 2	Pre-vaccination	5.74 ± 0.26	0.63	6.05 ± 0.28	0.79	0.104	0.319
	Post-vaccination	11.14 ± 0.17	26.8	11.24 ± 0.21	28.7	0.469	0.100
	Log-fold increase (LFI)	5.40 ± 0.31	–	5.18 ± 0.34	–	0.352	–0.219
	Adjusted LFI	9.18 ± 0.28	–	8.97 ± 0.31	–	0.335	–0.204
Type 3	Pre-vaccination	5.05 ± 0.26	0.09	5.03 ± 0.25	0.09	0.901	–0.023
	Post-vaccination	9.61 ± 0.35	2.05	9.99 ± 0.34	2.66	0.131	0.377
	Log-fold increase (LFI)	4.56 ± 0.42	–	4.96 ± 0.43	–	0.194	0.400
	Adjusted LFI	8.15 ± 0.38	–	8.60 ± 0.39	–	0.109	0.451

[a] The number of subjects (n) is shown for each group (placebo and iodine treatment). Group mean $\log_2$ titres are the reciprocal 50% endpoint dilutions calculated from duplicate serial twofold dilutions in poliovirus microneutralization assays. Mean titres are shown with their 95% confidence intervals and are also expressed in International Units (IU). The log-fold increase (LFI) in titre is the difference between post-vaccination titre and pre-vaccination titre. The adjusted LFI is the difference between post-vaccination titre and pre-vaccination titre adjusted for decline in maternal antibody over the follow-up period.

[b] iod-plac, iodine-placebo groups.

The range of measured neutralizing antibody activity was 0.01–14 IU for type 1, 0.05–49 IU for type 2, and 0.01–11 IU for type 3 poliovirus. After immunization, 2 (0.4%), 1 (0.2%), and 16 (3.3%), respectively, of the infants had no detectable neutralizing antibodies to poliovirus types 1, 2, and 3. After adjusting for loss of maternal antibody, 16 (3.3%), 2 (0.4%), and 12 (2.5%) of the infants showed no increase in titre over pre-vaccination levels. The incidence of these non-responders did not differ between the placebo and iodine treatment groups (P = 0.299, 0.094, and 0.988 for poliovirus types 1, 2, and 3, respectively). For poliovirus type 1, rates for seroconversion, defined as an adjusted LFI of $\geqslant 2$, were 97.5% and 95.8% in the placebo and iodine treatment groups, respectively. The corresponding rates for the placebo and iodine treatment groups were, respectively, 100% and 99.2% for poliovirus type 2, and 97.5% in both groups for poliovirus type 3. After immunization, the numbers of samples testing above the upper limit of the measurement range were 188 (39.3%), 140 (29.3%), and 70 (14.6%) for poliovirus types 1, 2, and 3, respectively, with similar frequencies in the placebo and iodine treatment groups. When analysis was restricted to those subjects who had post-vaccination titres within the measurable range of the assay, the placebo and iodine treatment groups did not differ in terms of mean titre or LFI for any of the poliovirus types.

Anthropometric and morbidity data were also evaluated. No anthropometric factor exerted a significant effect on neutralizing antibody titres to all three poliovirus serotypes, except for a highly significant effect of the infant's age at enrolment on pre-vaccination titres. As age increased from 6 to 10 weeks, the neutralizing activity to all three poliovirus types in pre-vaccination sera declined, as would be expected for antibody of maternal origin. The effect of fluid supplements (in addition to breastfeeding) on the antibody response to type-3 vaccine was significant (P = 0.023). Age at enrolment affected responses to type-1 and type-2 vaccines (P = 0.035 and 0.0013, respectively). Infants with diarrhoeal illness concurrent with the first, second, or third vaccination dose had lower mean increases in neutralizing antibody activity to all three poliovirus types, but the difference was significant only for type-1 poliovirus (P = 0.020). There was no effect on increase in titre due to the presence of cough concurrent with vaccination. However, smaller increases in titres against type-1 poliovirus were associated with fever (P = 0.042) or difficult breathing (P = 0.044) at the time of the first visit.

Discussion

In this study the levels of neutralizing antibodies to all three poliovirus serotypes were similar to those reported recently by other investigators for infants vaccinated with OPV (*14,15*). We found no evidence that oral iodine supplementation reduced the immune response to OPV. A difference of <0.6 $\log_2$ units in mean titre between the groups that received placebo or iodine would have been significant for any of the serotypes.

A number of host and environmental factors, such as breastfeeding, nutritional status and concurrent enteric infections, may influence the response to OPV (*16*). Infection with nonpolio

enteroviruses, season of vaccination, and level of maternal education had significant effects on the responses to OPV in one study (*17*), but it appears that nutrition had no such effect (*18–20*). Age, sex, and the presence of other enteroviruses in stools did not have a significant effect (*20*). Concurrent diarrhoeal illness impaired early seroconversion with type-2 and type-3 poliovirus (*21*). We examined several of these factors to determine whether they were significant or might bias our comparison between the placebo and iodine groups. Both groups were very similar with regard to distribution of these factors (Table 1), which did not exhibit a significant effect on the antibody responses to the three serotypes taken together (Table 3). We did observe significant effects on the response to individual serotypes associated with the following factors: fluid supplements to breastfeeding (type-3 vaccine, $P = 0.023$), diarrhoeal illness concurrent with immunization (type-1 vaccine, $P = 0.020$), and age at enrolment and first dose of OPV (type-1 and type-2 vaccines, $P = 0.035$ and 0.0013, respectively). However, it is important to note that our study was not specifically designed to evaluate the effects of these factors, and further investigations would have to determine whether their influences on neutralizing-antibody activity are real.

A high proportion of infants had measurable levels of poliovirus-neutralizing antibodies prior to immunization. Other workers have made similar observations (*14, 15*). Pre-vaccination titres to all three poliovirus serotypes were negatively correlated with age at enrolment. The effect was highly significant for all three poliovirus types, consistent with the interpretation that this neutralizing-antibody activity was derived from the mother and declined with increasing age of the infant. A half-life of 1 month has been suggested for maternal antibodies to poliovirus (*13*) and we used this value to adjust pre-vaccination titres in the calculation of the log-fold

Table 3. **Analysis of variance of adjusted log-fold increase in titres**

Factor		No.	Adjusted log-fold increase in titres[a]		
			Type 1	Type 2	Type 3
Month enrolled					
June		95	8.10 ± 0.73	9.07 ± 0.45	8.26 ± 0.65
July		115	8.81 ± 0.54	8.92 ± 0.49	8.50 ± 0.52
August		157	8.57 ± 0.50	9.18 ± 0.35	8.25 ± 0.51
September		94	8.50 ± 0.57	9.09 ± 0.39	8.52 ± 0.58
October		17	7.00 ± 1.97	9.15 ± 1.26	8.50 ± 1.57
	P		0.179	0.933	0.932
Sex					
Male		232	8.47 ± 0.43	9.15 ± 0.32	8.52 ± 0.39
Female		246	8.46 ± 0.39	9.00 ± 0.27	8.23 ± 0.39
	P		0.994	0.465	0.303
Breastfeeding					
No		14	10.00 ± 1.85	9.64 ± 1.02	8.50 ± 1.89
Yes		463	8.45 ± 0.29	9.05 ± 0.21	8.37 ± 0.28
	P		0.069	0.344	0.877
Fluid supplement to breastfeeding					
No		421	8.39 ± 0.30	9.01 ± 0.22	8.27 ± 0.29
Yes		42	9.06 ± 0.94	9.46 ± 0.64	9.39 ± 0.79
	P		0.185	0.225	0.023
Solid supplement to breastfeeding	No	220	8.56 ± 0.41	8.93 ± 0.31	8.31 ± 0.42
	Yes	243	8.35 ± 0.39	9.16 ± 0.29	8.43 ± 0.38
	P		0.478	0.286	0.671
Concurrent diarrhoeal illness	No	449	8.55 ± 0.29	9.12 ± 0.21	8.43 ± 0.27
	Yes	29	7.12 ± 1.55	8.38 ± 0.98	7.50 ± 1.66
	P		0.020	0.096	0.114
Weight at birth		313	–0.118 ± 0.710	–0.387 ± 0.547	–0.562 ± 0.718
	P		0.746	0.167	0.126
Weight at enrolment		478	0.252 ± 0.407	0.216 ± 0.294	0.018 ± 0.390
	P		0.226	0.150	0.928
Age at enrolment		478	0.033 ± 0.031	0.037 ± 0.022	0.000 ± 0.030
	P		0.035	0.0013	0.988
Maternal education		476	0.111 ± 0.123	0.062 ± 0.089	0.093 ± 0.117
	P		0.076	0.173	0.119

[a] Sample sizes (No.) and group means or linear estimates ± 95% confidence intervals are shown. Analysis of variance was used to test the relationship between factor levels and the observed change in titre. Probabilities (*P*) are shown below the comparative statistics.

increases in titre. To exclude any bias that might have arisen from making this adjustment, we also analysed the unadjusted log-fold increases in titre and the post-vaccination titres themselves (results not shown). The finding was the same as that obtained with the adjustment—i.e. administration of OIO had no effect on neutralizing-antibody responses to OPV.

Iodine deficiency is a major cause of preventable mental deficiency and has increased overall infant mortality in many populations (*22*). While iodized salt is regarded as the preferred long-term solution to IDD (*1*), interim measures are still needed (*2*). Both replacement of iodine in irrigation water (*23*) and supplementation by administration of OIO (*7*) have been shown to decrease infant mortality, but the choice between alternative interim methods of iodine delivery depends on a careful review of local circumstances (*24*). Iodization with water is often less satisfactory than use of iodized oil (*25*). In at least some areas, the time of primary vaccination according to the EPI schedule could be the first opportunity to provide iodine supplements to the infant, and possibly to the mother. Our results show that OIO did not reduce the immune responses of infants to OPV, but did improve infant survival in the same cohort (*7*), suggesting that the timetables for immunization and OIO administration are compatible. We conclude that supplementation with OIO may be safely combined with delivery of the first dose of OPV in the EPI schedule. ■

Acknowledgements

This study was supported by the Thrasher Research Fund, WHO Expanded Programme on Immunization (from funds provided by the Netherlands Ministry of Foreign Affairs), and the United States Agency for International Development (Cooperative Agreement DAN-0045-A-5094-00). We thank Peter A. Patriarca and Judy A. Beeler for their helpful reviews of the manuscript.

Résumé

La supplémentation en iode par voie buccale ne réduit pas la réponse en anticorps neutralisants au vaccin antipoliomyélitique buccal

La supplémentation en huile iodée administrée par voie buccale constitue un moyen provisoire de réduire la prévalence des troubles dus à une carence en iode, à savoir notamment l'arriération mentale, le goitre ou le crétinisme. Les programmes de vaccination infantile pourraient se charger d'assurer cette supplémentation en iode aux enfants exposés au risque, si du moins cette intervention n'interfère pas avec la réponse immunitaire au vaccin antipoliomyélitique buccal trivalent. C'est pour s'en assurer qu'un essai clinique randomisé en double aveugle avec groupe placebo a été effectué à Subang, dans le Java occidental (Indonésie). A cette occasion, 617 nourrissons âgés de huit semaines ont reçu soit de l'huile iodée (100 mg) soit un placebo constitué d'huile d'oeillette, par voie buccale, immédiatement après administration de leur première dose de vaccin antipoliomyélitique buccal par le Programme élargi de vaccination (PEV). La deuxième et la troisième dose de vaccin ont été ensuite administrées à intervalles de 4 semaines et les enfants ont été suivis jusqu'à l'âge de 6 mois.

On a déterminé le titre des anticorps dirigés contre le virus poliomyélitique de type 1, 2 et 3 dans des prélèvements de sérum effectués au moment de l'entrée dans l'essai (à l'âge de 8 semaines) et pendant la période de suivi (à l'âge de 6 mois) sur 478 enfants (238 et 240 paires de sérums provenant respectivement du groupe traité et du groupe placebo). Pour déterminer le titre des anticorps sériques, nous avons procédé à des épreuves de microneutralisation du virus dans des conditions d'anonymat général. Les résultats étaient exprimés sous la forme de l'inverse du $\log_2$ de la dilution ainsi qu'en UI. Pour chaque sujet, nous avons calculé l'accroissement logarithmique de l'activité des anticorps neutralisants avec ou sans correction pour tenir compte de la baisse du titre des anticorps d'origine maternelle pendant la durée de l'étude. Pour déterminer si le groupe traité et le groupe placebo différaient eu égard au sexe, à l'âge, au recrutement ou à d'autres facteurs susceptibles de fausser l'analyse de l'effet du traitement, nous avons utilisé la méthode du maximum de vraisemblance avec tables de contingence et procédé également par analyse de la variance. Nous avons calculé les titres moyens géométriques des sérums avant et après vaccination ainsi que l'accroissement logarithmique moyen dans le groupe traité et le groupe placebo. Nous avons également appliqué l'analyse de la variance pour évaluer l'effet de la supplémentation en iode au moyen d'huile iodée sur la réponse en anticorps neutralisants vis-à-vis de chacun des trois sérotypes de virus poliomyélitique.

Les valeurs obtenues pour le titre des anticorps neutralisants dirigés contres les trois sérotypes viraux étaient analogues à celles que d'autres chercheurs ont trouvées chez des nourrissons vaccinés contre la poliomyélite par voie buccale. Nous n'avons rien relevé qui puisse inciter à penser que la supplémentation par de l'huile iodée diminue la réponse immunitaire au vaccin buccal. Une différence entre les deux groupes de $< 0{,}6$ $\log_2$ dans le titre moyen aurait été significative pour chacun des trois sérotypes. Le fait d'avoir pu constater que la supplémentation par de l'huile iodée ne réduisait pas la réponse en anticorps à l'un ou l'autre des trois sérotypes vaccinaux, nous permet de dire qu'il est possible de donner sans risque de l'huile iodée avec la première dose de vaccin antipoliomyélitique buccal selon le calendrier actuel du PEV.

Resumen

Los suplementos orales de yodo no reducen la respuesta de producción de anticuerpos neutralizantes contra la vacuna antipoliomielítica oral

La administración de suplementos de aceite yodado oral (AYO) es un método provisional eficaz para reducir la prevalencia de los trastornos por carencia de yodo (TCY), que son causa de deterioro del desarrollo mental, bocio y cretinismo. Los programas de inmunización infantil podrían encargarse de administrar el AYO a los lactantes en riesgo, a condición de que ello no interfiera en la respuesta de producción de anticuerpos contra la vacuna antipoliomielítica oral (OPV) trivalente. En consecuencia, se llevó a cabo un ensayo clínico aleatorizado en doble ciego en Subang, en el oeste de Java (Indonesia), en el que 617 lactantes de ocho semanas recibieron ya fuera AYO (100 mg) o bien un placebo (aceite de semilla de adormidera) por vía oral inmediatamente después de la primera dosis de OPV administrada por el Programa Ampliado de Inmunización (PAI). Posteriormente se administraron la segunda y la tercera dosis de OPV a intervalos de cuatro semanas, y se hizo un seguimiento de los lactantes a la edad de 6 meses.

Se determinaron los títulos de anticuerpos neutralizantes contra los serotipos 1, 2 y 3 del poliovirus en los sueros obtenidos en el momento del reclutamiento (a las 8 semanas de edad) y con ocasión del examen de seguimiento (a los 6 meses) de 478 lactantes (238 y 240 pares de sueros de los grupos tratados con placebo y con yodo, respectivamente). Se analizó la actividad de anticuerpos de los sueros mediante pruebas de microneutralización de poliovirus realizadas en condiciones de enmascaramiento. Los resultados se expresaron como el logaritmo binario de la inversa de las diluciones y en forma de UI. Se calculó el incremento logarítmico (IL) de la actividad de anticuerpos neutralizantes para cada sujeto con y sin ajuste en función de la disminución estimada de los anticuerpos de origen materno durante el periodo de estudio. Se utilizó el ajuste de máxima verosimilitud en las pruebas de tablas de contingencia y los análisis de la varianza para determinar si los grupos tratados con yodo y con placebo diferían según el sexo, la edad de reclutamiento u otros factores que hubiesen podido confundir el análisis del efecto terapéutico principal. Se calcularon la media geométrica de los títulos séricos antes y después de la inmunización y el IL medio del grupo tratado y el grupo placebo. Se realizó un análisis de varianza para evaluar el efecto de los suplementos de aceite yodado en la respuesta de producción de anticuerpos neutralizantes para cada uno de los tres serotipos del poliovirus.

Los niveles de anticuerpos neutralizantes contra los tres serotipos virales fueron similares a los notificados recientemente por otros investigadores para los lactantes inmunizados con la OPV. No hallamos ninguna prueba de que la administración de suplementos orales de yodo redujera la respuesta inmunitaria a la OPV. Una diferencia $< 0{,}6$ $\log_2$ unidades entre los títulos medios del grupo placebo y el tratado con yodo habría sido significativa para cualquiera de los serotipos. La observación de que el AYO no reducía la respuesta de producción de anticuerpos frente a ninguno de los tres serotipos de OPV indica que es posible administrar ese aceite sin ningún riesgo al mismo tiempo que la primera dosis de OPV prevista en las pautas actuales del PAI.

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