Acta Paediatrica Academiae Scientiarum Hungaricae, Vol. 22 (3), pp. 237—241 (1981)

Efficiency of tetanus toxoid booster in leukaemic children

By

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Received January 5, 1981

Tetanus toxoid booster was given to 18 leukaemic children in remission who had received at least a basal DPT vaccination. No side effect was observed. All children, regardless of intensity of the cytostatic treatment responded with a sufficient antitoxin production. Recommendations are given as to the method of tetanus prevention in leukaemic children.

In a previous study we found decreased immunoglobulin levels in the sera of leukaemic children, but their specific antibody titres induced by earlier vaccinations did not differ from those of healthy controls with the same vaccination history. It was also found that the pertussis agglutinin titres of leukaemic children whose DPT vaccination series had been interrupted because of their illness, were not lower than those of healthy matched controls with complete DPT vaccination series. The latter finding was considered to be an indication of a latent pertussis infection followed by an appropriate secondary immune response in leukaemic children.

The aim of the present study was to examine the immune response to tetanus toxoid booster in leukaemic children.

Materials and Methods

Patients. Altogether 18, 3 to 17 year old leukaemic children in remission were included in the study. Seventeen children had acute lymphoid leukaemia, among them one had a Wilms tumour as well. One patient had acute myeloid leukaemia. At the time of the study, 5 children received intensiv cytostatic (reinduction) therapy, 6 were on maintenance therapy and 7 had already been without treatment in complete remission for $^1/_2$ to 5 years.

Vaccination history of the patients. When still healthy, children were immunized against diphtheria, pertussis and tetanus according to the vaccination calender in Hungary. The vaccination schedule consists of a basal immunization with three DPT injection at 3, 4 and 5 months of age (DPT I) followed by a DPT booster at 3 and 6 years of age (DPT II and III). The vaccination schedule was suspended at the onset of leukaemia. All the children under study had been given a basal immunization with DPT at least.

Tetanus toxoid booster. Alum precipitated tetanus toxoid (12.5 BU per dose) was used.

Serological investigations. Blood was taken before and 9 to 11 and 30 to 64 days after the tetanus booster. Serum samples were tested for tetanus and diphtheria antitoxin, pertussis agglutinin and total IgG content. Tetanus antitoxin was measured by both passive haemagglutination and seroneutralization test in mice at a level of L + /400. Diphtheria antitoxin was titrated by passive haemagglutination. Pertussis antibody was tested by tube agglutination method. For measuring the total IgG content, Mancini's method was used.

Results

The tetanus toxoid injection caused neither local nor systemic reaction and had no impact on the leukaemic process.

Results of the serological tests are given in Tables I, II and III. It can be seen that all children developed specific antibody against tetanus toxoid, no matter how intensive the cytostatic therapy was. Except one patient on reinduction treatment, there was a significant rise in titre within 9 to 11 days after vaccination in all cases. While the children left without treatment generally produced higher antibody titres than those under treatment, even the latter had at last a four-fold titre rise in response to the vaccination. The antibody response was similar in children on

Table I

Antibody response to tetanus toxoid booster in leukaemic children in remission under intensive cytostatic treatment

Name	Age, years	Diagnosis	Previous DPT vaccinations	Serum sample*	Antibody titres				Total Ig G mg/dl
					Tetanus AT IU/ml		Diphtheria AT IU/ml	Pertussis antibody reciprocal titres	
					HA.	Neutr.	HA.		
M. A.	8	ALL	I, II	1.	4.0	2.5—12.5	0.25	512	573
				2.	32.0	12.5—62.5	0.25	512	573
				3.	64.0	312.5	0.25	512	573
L. F.	7	ALL	I, II	1.	4.0	2.5—12.5	2.0	1024	764
				2.	4.0	2.5—12.5	2.0	1024	836
				3.	16.0	12.5—62.5	2.0	1024	836
N. R.	4	AML	I	1.	1.0	0.5—2.5	0.12	4	573
				2.	8.0	2.5—12.5	0.12	4	573
				3.	8.0		0.12	4	645
K. M.	3	ALL	I	1.	2.0	0.5	0.5	16	454
				2.	256.0	12.5—62.5	0.5	16	406
				3.	256.0	312.5	0.5	16	406
F. Cs.	7	ALL	I, II	1.	1.0	0.1—0.5	0.12	512	573
				2.	256.0	62.5—312.5	0.12	512	573
				3.	2048.0	312.5	0.12	512	573

Symbols: * *1.;* before toxoid booster; *2.:* 9 to 11 days after toxoid booster; *3.:* 30 to 64 days after toxoid booster. *HA.:* passive haemagglutination. *Neutr.:* seroneutralization test in mice. *AT.:* antitoxin

TABLE II

Antibody response to tetanus toxoid booster in leukaemic children in remission under maintenance cytostatic therapy

Name	Age years	Diagnosis	Previous DPT vaccinations	Serum sample	Antibody titres				Total Ig G mg/dl
					Tetanus AT IU/ml		Diphtheria AT IU/ml	Pertussis antibody reciprocal titres	
					HA	Neutr.	HA		
M. A.	7	ALL	I. II	1.	0.5	0.5–2.5	0.12	512	453
				2.	4.0	0.5–2.5	0.12	1024	573
				3.	8.0	2.5–12.5	0.12	1024	537
B. I.	9	ALL	I. II	1.	1.0	0.5–2.5	2.0	1024	645
				2.	8.0	2.5–12.5	2.0	1024	573
				3.	32.0	12.5–62.5	2.0	1024	573
S. I.	4	ALL	I	1.	1.0	0.1–05	0.03	512	453
				2.	16.0	12.5–62.5	0.03	512	537
				3.	32.0	62.5–312.5	0.03	512	537
C. C.	4	ALL + Wilms	I	1.	1.0	0.5–2.5	0.5	32	
				2.	32.0	12.5–62.5	0.5	32	
				3.	32.0	312.5	0.5	32	
Z. Z.	3	ALL	I	1.	1.0	0.5–2.5	0.12	8	454
				2.	1024.0	62.5–312.5	0.12	8	454
V. M.	3	ALL	I	1.	2.0	0.5–2.5	2.0	32	537
				2.	128.0	312.5	2.0	32	537
				3.	128.0	312.5	2.0	32	537

Symbols: see table I.

intensive and in those on maintenance therapy. The results of the seroneutralization tests show that the vaccination induced a protective *i.e.* biologically active, antitoxin production.

The antibody response was specific, i.e. the vaccination had no impact on either the diptheria or the pertussis titres.

While the total IgG content of sera was low in children on cytostatic therapy as compared to that in children without treatment, the vaccination caused no change in the IgG level in either of the two groups.

DISCUSSION

We found a good secondary antibody response to tetanus toxoid in leukaemic children in remission. The intensity of cytostatic treatment seamed to have no influence on the immune responsiveness of the patients. Our finding is in accordance with the experience of others using other antigens for immunization [1, 2, 3, 4].

From the observations, the following practical conclusions can be drawn.

If they suffer an injury, leukaemic children who had received a basal tetanus immunization previously, can

TABLE III

Antibody response to tetanus toxoid booster in leukaemic children in remission without therapy for $^1/_2$ to 5 years

Name	Age years	Diagnosis	Previous DPT vaccinations	Serum sample	Antibody titres				
					Tetanus AT IU/ml		Diphtheria AT IU/ml	Pertussis antibody reciprocal titres	Total Ig G mg/dl
					HA.	Neutr.	HA.		
P. M.	10	ALL	I, II	1.	1.0	0.5—2.5	0.12	512	931
				2.	256.0	62.5—312.5	0.12	512	931
				3.	256.0	62.5—312.5	0.12	512	931
P. I.	11	ALL	I. II	1.	2.0	0.1—0.5	2.0	512	764
				2.	256.0	312.5	2.0	1024	836
				3.	128.0	312.5	2.0	1024	836
R. S.	13	ALL	I, II	1.	2.0	12.5	2.0	2048	1552
			III	2.	256.0	12.5—62.5	2.0	2048	1552
				3.	512.0	62.5—312.5	2.0	2048	1373
G. G.	9	ALL	I, II	1.	0.5	0.1—0.5	0.12	256	931
				2.	256.0	62.5—312.5	0.12	256	931
				3.	512.0	62.5—312.5	0.12	256	836
H. A.	9	ALL	I, II,	1.	1.0	0,5—2,5	2.0	1024	836
			III	2.	32.0	312.5	2.0	1024	836
				3.	32.0	312.5	2.0	512	931
N. Z.	11	ALL	I, II,	1.	0.1	0.02—0.1	0.06	128	931
			III	2.	256.0	62.5—312.5	0.06	128	931
				3.	1024.0	312.5	0.06	128	1075
K. K.	17	ALL	I, II,	1.	8.0	0.5—2.5	0.5	1024	1075
			III	2.	256.0	312.5	0.5	1024	1194
				3.	256.0	312.5	0.5	1024	1194

Symbols: see table I.

be protected against tetanus by a single toxoid booster.

The greater the chance for leukaemic children to survive, the more often the question of their vaccination arises. The commonly accepted practice of omitting active immunization seems justified with live vaccines and inactivated vaccines causing serious reactions. Moreover it is reasonable to think that the healthy and properly vaccinated population will protect the susceptible leukaemic child against diphtheria, pertussis, poliomyelitis and measles. The same, however, is not true for tetanus, therefore we propose to revaccinate them with monovalent tetanus toxoid at the time when according to the vaccination calendar DPT booster is recommended. Our observations give no information about the antibody response of leukaemic children to the primary antigenic stimulus with tetanus toxoid. Therefore, the above suggestion refers only to booster injections. The

primary immune response of such patients to tetanus toxoid remains to be investigated.

Acknowledgements

We are indebted to Miss O. Funk, Mrs. G. Horváth and Mrs. M. Komáromi for skilful technical assistance.

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