

COMMERCIAL GAMMAGLOBULIN (CGG) AS A POSSIBLE VEHICLE OF TRANSMISSION OF HB_sAg IN FAMILIAL CLUSTERING

Luiz Caetano da SILVA, Hoel SETTE Jr., Francisco ANTONÁCIO and José Daniel LOPES

S U M M A R Y

An epidemiological study, carried out from 1973 through 1975, of 151 familial members of 51 patients with viral hepatitis positive for HB_sAg showed a high incidence of that antigen (14.6%), which is much higher than the incidence found by others. This fact lead us to investigate the possible means of transmission and it became apparent the common use of CGG with prophylactic purposes. Dividing the familial members into two groups, with (group A, 97 subjects) and without (group B, 54 subjects) previous administration of CGG, a significant difference ($p < 0.05$) was observed in regard to positivity for HB_sAg, which was higher in group A (19.6% and 5.6% respectively). Furthermore, the search for HB_sAg in 31 batches of CGG disclosed the presence of this antigen in 7 (22.6%). In conclusion, CGG was probably an important vehicle of HB_sAg in our country during that period.

I N T R O D U C T I O N

Several papers have been published on the incidence of HB_sAg among familial members of patients with type-B hepatitis^{2,3,4,5,6}. As there are geographical differences of incidence of HB_sAg throughout the world, it seemed to us that an epidemiological study should be carried out in São Paulo, Brazil.

During our investigation, however, the role of commercial gammaglobulin (CGG), used for the prophylaxis of that disease became apparent as a possible source of contamination with HB_sAg. For this reason, no epidemiological conclusion of familial clustering could be drawn. On the other hand our results disclosed the importance of CGG on the transmission of Type-B hepatitis.

M A T E R I A L S A N D M E T H O D S

From 1973 through 1975 we studied 151 familial members of 51 patients positive for HB_sAg, 47 of which in the acute stage and 4

with chronic Type-B hepatitis (Table I). They were all thoroughly interrogated about the possible means of transmission of HB_sAg, including the previous use of CGG.

All collected sera were stored at -20°C for variable periods of time up to one year.

Testing for HB_sAg was performed by the method of counter immunoelectrophoresis¹. Radioimmunoassay (RIA, AUSRIA II, Abbott Lab.) was also performed in 36 of these sera.

Thirty one different batches of CGG from different Laboratories were tested for the presence of HB_sAg by RIA. For this purpose they were used pure (16% solution) and diluted 1:2 in 0.15 M sodium chloride.

R E S U L T S

HB_sAg was detected in the sera of 22 out of 151 familial members of patients with Type-B hepatitis (14.6%). The familial members were divided in two groups: 97 who referred previous injection of CGG (Group A)

This work was supported by a grant from «Financiadora Nacional de Estudos e Projetos (FINEP)» Instituto de Medicina Tropical de São Paulo, Hospital das Clínicas da FMUSP, São Paulo, Brasil.

which revealed 19 HB_sAg positive sera (19.6%), and 54 without previous CGG administration (Group B), where only 3 (5.6%) were positive. The difference between those two groups was statistically significant ($p < 0.05$, $X^2_{calc} = 5.75$).

Seven out of 31 batches of CGG were positive for HB_sAg (22.6%). Some samples showed positive results only after 1:2 dilution (Table II).

Transaminase and bilirubin levels were studied in all 19 positive sera from Group A. Abnormal findings were detected in 15, 11 of which showed SGPT levels higher than 300 U Karmen.

Two HB_sAg positive patients from Group B showed abnormal transaminase levels. None had taken CGG previously and both referred sexual intercourses.

T A B L E I

Incidence of HB_sAg in 151 familial members according to previous administration of commercial gammaglobulin (CGG)

Groups	Presence of HB _s Ag		Total
	YES	NO	
A	19 (*) (19.6%)	78 (80.4%)	97
B	3 (*) (5.6%)	51 (94.4%)	54
Total	22 (14.6%)	129 (85.4%)	151

(*) $p < 0.05$

T A B L E I I

Presence of HB_sAg in batches of commercial gammaglobulin (CGG)

Commercial laboratory	Number of batches	Number of positive batches
A	20	5
B	5	2
C	6	0

DISCUSSION

Our results show a high incidence of HB_sAg (14.6%) in familial members of pa-

tients with Type-B hepatitis. This incidence is higher than that found by SZMUNESS et al.⁶ (6.7%). On the other hand, HB_sAg was found in 0.85% of 17,748 normal blood donors in São Paulo, Brazil¹, and this incidence is probably very close to the expected for the normal population.

The possible means of transmission among familial members are not well established⁶. Many causes, as sexual intercourses, different types of contact, contamination with saline and insects are frequently mentioned⁵.

As far as we know, CGG has not yet been incriminated as a vehicle of HB_sAg. Our results demonstrate this possibility at least with CGG prepared in our country where, interesting enough, it is often used with prophylactic purposes.

There are no available information on the method of fractionation, purity and origin of CGG in our country. Preliminary studies on DEAE cellulose fractionation and immunoelectrophoresis in order to check purity of CGG are on their way by our group.

More extensive studies on gammaglobulin and other blood products should be carried out to demonstrate other sources of HB_sAg contamination. Needless to say that better checking for the presence of HB_sAg of pools of human plasma used for CGG preparation is certainly necessary. However, after 1975, we were no longer able to detect any other batches of contaminated CGG or human cases of type B hepatitis in which CGG could be incriminated.

R E S U M O

Gamaglobulina comercial como possível veículo de transmissão de HB_sAg em grupos familiares

Estudo epidemiológico, feito de 1973 a 1975 em 151 familiares de 51 pacientes com hepatite por vírus e positivos para HB_sAg, mostrou incidência desse antígeno (14,6%) mais alta que a encontrada por outros Autores. Este fato levou-nos a investigar os possíveis meios de transmissão e tornou-se aparente o uso de CGG com propósitos profiláticos. Dividindo os fa-

miliares em dois grupos, com (Grupo A, 97 indivíduos) e sem (Grupo B, 54 indivíduos) prévia administração de GGC, uma diferença significativa ($p < 0,05$) foi observada com relação à positividade para HB_sAg, mais alta no Grupo A (19,6% e 5,6%, respectivamente). Além disso, a pesquisa de HB_sAg em 31 lotes de GGC demonstrou a presença desse antígeno em sete (22,6%). Em conclusão, a GGC foi provavelmente importante veículo de HB_sAg em nosso país, durante aquele período.

ACKNOWLEDGEMENTS

We are indebted to Maria do Carmo Berthe Rosa for collaboration.

REFERENCES

1. ANTONÁCIO, F. — Antígeno Austrália em doadores de sangue. [Tese]. São Paulo, Faculdade de Medicina da USP, 1971.
2. BERRI, B.; WROBEL, D. M.; SINCLAIR, J. C. & FEINMAN, S. J. — Hepatitis B antigen in families of blood donors. *Ann. Intern. Med.* 79: 690-693, 1973.
3. HEATHCOTE, J.; TSIANIDES, A. & SHERLOCK, S. — A urinary substance in patients with acute type-B hepatitis and their household contacts. *Lancet* 2: 593-595, 1973.
4. IRWIN, G. R.; ALLEN, A. M.; BANCROFT, W. H.; KARWACI, J. J.; PINKERTON, R. H. & RUSSEL, P. K. — Hepatitis B antigen and antibody. Occurrence in Families of asymptomatic HB Ag carriers. *J. Amer. Med. Ass.* 227: 1042-1043, 1974.
5. MITCH, W. E.; WANDS, J. R. & MADDREY, W. C. — Hepatitis B transmission in a family. *J. Amer. Med. Ass.* 227: 1043-1044, 1974.
6. SZMUNESS, W.; PRINCE, A. M.; HIRSCH, R. L. & BROTMAN, B. — Familial clustering of hepatitis B injection. *New Engl. J. Med.* 289: 1162-1166, 1973.

Recebido para publicação em 20/12/1976.