

## HEPATITIS B VACCINATION AND INFANTILE IDIOPATHIC THROMBOCYTOPENIC PURPURA

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*SUMMARY: Since 1993, Iranian infants have been routinely vaccinated against hepatitis B. In the period of 1993-2002, twenty five children with infantile thrombocytopenic purpura (ITP) were admitted to the Childrens Medical Center in Tabriz, Iran whereas between 1982 and 1992, only two cases were hospitalized with the same diagnosis. This suggests a cause and effect relationship between hepatitis B vaccination and ITP.*

*Key Words: ITP, vaccination, hepatitis B vaccine, autoimmune disorders.*

### INTRODUCTION

ITP is an autoimmune disorder leading to a reduction of the number of peripheral blood platelets (1). For reasons not well understood, autoantibodies are generated against glycoproteins GpIb/Ix and GpIIb/IIIa and are situated on the surface of the platelets. Attachment of autoantibodies to these surface antigens leads to phagocytosis or complement-induced lysis of the platelets involved. This process may also involve megakaryocytes, leading to a decrease in platelet production (2,4). Autoantibodies against platelet surface antigens have been detected in 75% of the patients (2,3).

ITP appears in two forms: acute or chronic. The acute form occurs predominantly in children. 85% of cases are preceded by a viral infection. The disorder may last for one or two months period and is self limited.

Mumps, measles, rubella vaccine (MMR) has been implicated in the etiology of ITP (5-10). In Finland, 23 cases of ITP were reported among 70.000 MMR vaccines.

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The authors speculated that the vaccine leads to generation of antiplatelet antibodies (1). In another study, one case of ITP was recorded among 24.000 MMR vaccines (10).

Occurrence of ITP following DPT vaccination is rare. In a British study, only two cases were reported (8), this data is not significant when the widespread administration of DPT vaccine is considered. Two cases of ITP have been reported in conjunction with small pox vaccination (12). Small numbers of cases following recombinant HBV have been reported (13). There is no report of ITP following plasma-derived hepatitis vaccine (11).

### MATERIALS AND METHODS

#### **ITP cases between 1992 and 2002**

The files of all 25 infants under six months of age, hospitalized at the Childrens Medical Center in Tabriz, Iran, between 1993 and 2002 and discharged with ITP as the final diagnosis were included in the present study. The diagnosis was established based on the clinical findings (purpura, ecchymosis), platelet count, bone marrow findings and exclusion of other causes.

Table 1: The age of under 6 months infants with ITP.

Age (month)	No.	%
1	1	4
1.5	2	8
2	7	28
2.5	4	16
3	5	20
4	2	8
6	4	16
Total	25	100

The gender distribution of the investigated infants were 14 (56%) males and 11 (44%) females. Table 1 is a breakdown of cases by age.

Vaccination history: All infants had received routine vaccinations as required, except one infant who had received polio and hepatitis B vaccines at birth and manifested ITP at age 1.5 months. All others received the hepatitis and polio vaccine at age 1.5 month.

Prior history of infection: In 8 cases (32%) an upper respiratory infection preceded ITP by one to four weeks. Amoxicillin had been prescribed in 3 cases (12%) and acetaminophen in 20 cases (80%).

Clinical manifestations: Generalized purpura was manifest in all infants. In one case (4%) gastro-intestinal bleeding was recorded.

Platelet count: The platelet count data ranged between 7000-33000/ $\mu$ l. It was under 10000/ $\mu$ l in 4 (16%), 10000-20000/ $\mu$ l in 18 (72%), and 20000-33000/ $\mu$ l in 3 (12%) infants.

Hemoglobin data ranged 7.4-10 gm/dl in 12 (48%) and 10.5-13 gm/dl in 13 (52%) cases.

Bone marrow aspiration was performed in all infants. It was reported as normal in 8 (32%) cases and an increase in the number of megakaryocytes was recorded in 17 (68%) infants.

Treatment: 23 (92%) infants were treated with intravenous immunoglobulin, 2 (8%) received corticosteroids. All infants were discharged in forty-eight hours.

#### ITP cases between 1982 and 1992

During the period between 1982 and 1992, when hepatitis B vaccine was not routinely administered to the Iranian infants, only two cases of ITP were found among infants at the age of six months or younger and hospitalized at the Childrens Medical Center. One of them was male at the age of 6 months and the other was female at the age of 5 months. Both had received their childhood vaccinations as scheduled.

#### DISCUSSION

Hepatitis B vaccine is given at birth and 1.5 and 9 months of age. Since 1993, all Iranian infants have routinely received the vaccine. The present study reveals a 12.5 fold increase ( $P=0.029$ ) in the number of cases of ITP in infants less than six months of age during the first decade of routine hepatitis B vaccination as compared with the previous decade. On the other hand, the published cases of ITP following DPT vaccination are very rare despite worldwide administration of this vaccine (8). There are few published reports of ITP following administration of hepatitis B recombinant vaccine. In a retrospective study, Neau reported seven infants who had received recombinant vaccine during the period of three months prior to the onset of ITP (15). Sherlock reported three cases of ITP following the recombinant vaccine (16). Both in 1994 and 1995 two cases for each year were reported (11,13). In view of the worldwide large-scale administration of this vaccine, these small numbers appear insignificant. Admittedly, inability to measure anti-platelet antibodies is a short coming of this study. Nevertheless, we hope this report will generate interest in further research on this issue.

#### CONCLUSION

Comparison of two groups reveals a 12.5 fold increase in incidence and this is a statistically significant difference ( $P=0.029$ ).

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