Immunization status of internationally adopted children in Italy

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Received 13 February 2006; accepted 13 February 2006

Available online 28 February 2006

Abstract

An increasing number of internationally adopted children is coming to Italy, and their immunization status is unknown. We evaluated the immunization status of such children in Palermo, Italy.

We searched for the presence of a BCG scar in 88 children, 49 boys and 39 girls (mean age 76 ± 32 months), most of whom (98%) came from Eastern Europe. Presence of BCG scar was observed in 59 (67.1%) of them, included five children without any pre-adoptive medical records. Twenty-three out of 29 children without any evidence of BCG scar were tested by Mantoux. Seven (30.4%) of 23 were tuberculin positive and diagnosed as having latent tuberculosis infection. We also examined immunization status against poliovirus 1–3, tetanus, diphtheria, pertussis, measles, mumps, rubella and hepatitis B of 70 internationally adopted children and we compared it with the pre-adoptive immunization records of their birth country. Protective titers (≥1:8) against poliovirus 1–3, were found respectively in 67.1%, 91.4%, 42.8% of 70 immunized children, and only 38.5% of them had at the same time full protection against all three types of poliovirus. Protective titers against tetanus and diphtheria were found in 91.4% and 95.7% of 70 vaccinated children. Presence of antibodies against pertussis, measles, mumps and rubella was observed respectively in 16 (32.6%) of 49, 40 (62.5%) of 64, 28 (56%) of 50 and 24 (85.7%) of 28 children who had received the vaccine. As regards hepatitis B, only 20 of 29 vaccinated children had detectable hepatitis B surface antibodies, while four of 29 vaccinated and two of 41 not vaccinated children were positive for both hepatitis B surface antibodies and hepatitis B core antibodies. Finally three of 41 not vaccinated children were both hepatitis B surface antigen and hepatitis B core antibodies positive.

No relation was found between health status and immunization and between age and antibody positiveness of vaccinated children except for hepatitis B, therefore the youngest immunized children were more likely to be hepatitis B surface antibodies positive.

Our data suggest that internationally adopted children should be tested for their immunization status on arrival in the adopting country, because they are not protected in a sufficient way against vaccine-preventable diseases and their pre-adoptive immunization records sometimes are lacking and frequently are scarcely reliable.

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Keywords: Internationally adopted children; Immunization; Vaccine-preventable disease

1. Introduction

During last decade international adoption of children has increased in Italy, in close connection with the reduction of births and the number of adoptable Italian children. The number of international adoptions have more than doubled from 1600 to 3398 between 1993 and 2004 [1]. In addition, the distribution of birth countries of these children has changed markedly over time: before 1990 the main birth countries of the internationally adopted children were Brazil, Chile and India, the Eastern European countries are now the main source, accounting for more than 60% of children placed in 2000–2004 [1].

Internationally adopted children are a particularly vulnerable population [2–4], as they come from underdeveloped countries with inadequate health care resources, and have numerous health problems, including retarded growth, iron...
females (mean age 76 ± 32 months, range 17–153 months).

The majority of them came from Eastern Europe: Ukraine (64), Russia (11), Poland (4), Rumania (3), Bulgaria (2), Hungary (2); the remaining two came from India. All of them resided in orphanages before adoptions and were referred to our center by their adoption agencies, the Juvenile Law Court of Palermo or adoptive parents’ groups. They represented 92.6% of the children who had been internationally adopted in the district of Palermo during the studied years. Most of them (81/88) were seen in our center within 4–6 weeks of their arrival in Italy. Only 7/88 children came to our center after a longer time (six subjects after 8–10 months, and one after 2 years).

The majority of the internationally adopted children (83/88, 94.3%) had medical records from their birth countries that had been translated from the original into the Italian language by official bilingual translators of the Italian Embassy. The remaining five children lacked medical records from their birth countries. The medical records included the child’s medical history and vaccinations received in the native country. Informed consent to participate in the study was requested to adoptive parents and the study protocol was approved by the Ethical Committee of Pediatric Department of Palermo University. The presence of the scar for Bacillus Calmette-Guerin (BCG) vaccination was searched in each child and compared with the pre-adoptive immunization records. When the BCG scar was present, chest-X-ray and erythrocyte sedimentation rate (ESR) were performed. When the BCG scar was lacking, a tuberculin skin test (TST) was performed by the Mantoux technique with purified protein derivative (PPD, five tuberculin units). Chest radiograph and ESR were also performed when the TST was weakly or strongly positive (≥ 5 and 10 mm, respectively, after 48–72 h). Seventy-five/eighty-eight of the internationally adopted children (40 males, 35 females) provided a blood sample to determine antibody titers against tetanus, diphtheria, pertussis, poliovirus 1–3 and measles–mumps–rubella (MMR). Serologic markers for hepatitis B infection, surface antigen (HBsAg), surface antibody (HBsAb), core antibody (HBcAb), were also assayed. Seven children could not be tested because their new Italian parents refused to give informed consent for serological assays, and six others had been vaccinated during the 8–10 months between their arrival in Italy and their evaluation at our center.

The 75 children serologically tested (70 with and five without pre-adoptive immunization records) were from Ukraine (55), Russia (10), Poland (4), Rumania (2), Bulgaria (2), Hungary (2) and India (1).

The results of serological assays of 70 adopted children were compared with the pre-adoptive immunization records. The assays for tetanus, pertussis and MMR antibody as well as for hepatitis B virus (HBV) markers were carried out by standard enzyme-linked immunosorbent assay (ELISA). Diphtheria and poliovirus 1–3 antibodies titers were carried out with neutralization tests. The micro-neutralization assay to measure immunity to poliovirus was performed according to the guidelines for WHO/EPIC collaborative studies on poliomyelitis [11], the titration of samples starting at 1:5. Statistical analysis were performed using χ²-test and a P-value of <0.05 was considered to indicate significance.

3. Results

A BCG scar was observed in 59/88 (67.1%) internationally adopted children (included the five children without pre-adoptive medical records), whereas it was absent in 29/88 (32.9%) of them, despite certification of a previous BCG vaccination in their pre-adoptive immunization records (Table 1). All of the children with a BCG scar did not per-

<table>
<thead>
<tr>
<th>BCG scar positive</th>
<th>59/88 (67.1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCG scar negative</td>
<td>29/88 (32.9)</td>
</tr>
<tr>
<td>TST positive &gt; 10 mm</td>
<td>2/23 (8.7)</td>
</tr>
<tr>
<td>TST positive &gt; 5 mm</td>
<td>9/23 (39.1)</td>
</tr>
</tbody>
</table>

| 
| --- |
| Fifty-four with pre-adoptive records and five without pre-adoptive records. |
| Only 23 were submitted to TST. |
form TST, only ESR and a chest radiography that gave normal results in each adopted child. TST was carried out on only 23/29 children without a BCG scar, because the parents of the remaining six children refused it. Sixteen/twenty-three (69.6%) of them had a negative TST. Five (21.7%) had a moderately positive TST (TST ≥ 5 mm) (Table 1), with a normal ESR, normal chest-X-ray, and no clinical signs of tuberculosis. They were diagnosed as having latent tuberculosis infection (LTBI), and received isoniazid prophylaxis, because we did not have documentation of their previous exposure history. Their native countries were Ukraine (four children) and Bulgaria (one child). The two remaining internationally adopted children without a BCG scar had a highly positive TST (TST ≥ 10 mm) (Table 1). They did not have tuberculous symptoms; their ESR and chest-X-rays were normal and they were diagnosed as having LTBI and treated with isoniazid. Their native country was Ukraine.

All adopted children with pre-adoptive records have reported a complete immunization (≥3 vaccine doses) against poliovirus types 1–3, whereas, neutralizing antibody were detected in 82.8%, 98.6% and 62.8% of samples respectively (Table 2). The positive rates were lower if, according to WHO, only titers higher than 1.8 were considered protective (Table 2). In addition, if antibodies against all three types of poliovirus were considered together, only 27/70 (38.5%) of the adopted children were contemporaneously fully protected (titers > 1:8) against the three poliovirus types.

Two children were simultaneously sero-negative to all three types of poliovirus: one, who is 5 years old, coming from Ukraine, was residing in Italy for 1 month. This child, in despite of documentation of complete vaccination in her pre-adoption record, also lacked antibodies against tetanus, diphtheria and hepatitis B, all of which are compulsory vaccinations in Italy (Table 3). The second one (4 years old), from Bulgaria, was living in Italy for 2 years and lacked a pre-adoption immunization record from the native country. The other four children without certificate were fully protected against poliovirus 1–3.

For tetanus and diphtheria (Table 4), 91.4% and 95.7%, respectively, of the tested children with pre-adoptive records had antibody titers higher than the cut-offs (0.1 and 0.01 IU/ml, respectively), which are considered to be protective [12,13]. However some authors define full protection against diphtheria and tetanus only with values higher than 0.1 IU/ml [14,15] and 0.5 IU/ml, respectively [16]. By these criteria, only 72.8% of the children would be fully protected against tetanus and 85.7% against diphtheria, on the contrary, all of the children have reported in their pre-adoption immunization records a full immunization (≥3 vaccine doses).

Among the five children without certificate only one, who is 3 years old, was negative for diphtheria.

No relation was observed between immunity for polio–diphtheria–tetanus and age of the children. The previous immunization records of 70 internationally adopted children also diverged from the serological results obtained for not compulsory vaccination in Italy namely pertussis, measles, mumps and rubella. The antibodies against these infectious diseases in many of them were absent, even if their pre-adaptive records reported previous vaccinations, whereas presence of antibodies were observed among many of these children, though their pre-adaptive immunization records did not refer previous vaccinations (Table 5).

Vaccinated children were more likely to be antibodies positive than not immunized children only for rubella (Table 5). According to the immunization records, the vaccine doses

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**Table 3**

| Vaccine Schedule Italy | 2005–2006
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vaccine</strong></td>
<td><strong>Schedule</strong></td>
</tr>
<tr>
<td>Diphtheria–tetanus–pertussis</td>
<td>3, 5, 11–13 months, 5–6 years, 11–15 years</td>
</tr>
<tr>
<td>Inactivated polio</td>
<td>3, 5, 11–13 months, 5–6 years</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>birth (only if mother HBsAg−) – 3, 5, 11–13 months</td>
</tr>
<tr>
<td>Haemophilus influenzae type b</td>
<td>3, 5, 11–13 months</td>
</tr>
<tr>
<td>Measles, mumps, rubella</td>
<td>13–15 months, 5–15 years</td>
</tr>
<tr>
<td>Pneumococcal</td>
<td>3–36 months</td>
</tr>
<tr>
<td>MenC</td>
<td>3–36 months</td>
</tr>
<tr>
<td>Varicella</td>
<td>13–24 months, 11–15 years</td>
</tr>
</tbody>
</table>

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**Table 4**

<table>
<thead>
<tr>
<th>Antibody against</th>
<th>Vaccine positive/no.</th>
<th>Antibody positive/no.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>of children with reported vaccinations in their pre-adoption records</td>
<td>of children without reported vaccinations in their pre-adoption records</td>
</tr>
<tr>
<td>Pertussis</td>
<td>16/24 (66.7)</td>
<td>12/21 (57.1)</td>
</tr>
<tr>
<td>Measles</td>
<td>40/64 (62.5)</td>
<td>36/50 (72.0)</td>
</tr>
<tr>
<td>Mumps</td>
<td>28/50 (56.0)</td>
<td>20/40 (50.0)</td>
</tr>
<tr>
<td>Rubella*</td>
<td>24/28 (85.7)</td>
<td>22/24 (91.7)</td>
</tr>
</tbody>
</table>

* Values higher than 15 IU/ml.
children with reported vaccinations & no. of children
---
Hepatitis B markers | HBsAb+ | HBsAb+ | HBsAb+ |
|-------------------|--------|--------|--------|
Children with | 20 | 4 | 0 |
immunization | | | |
records | | | |
Children without | 3 | 2 | 3 |
immunization | | | |
| | | | |

* HBsAg+ children had positive serum HBsAb in their pre-adoptive records, whereas all children without hepatitis B reported previous vaccination.

4. Discussion

International adoptions have been increasing in our country during the last decade, pressuring health workers to deal with new and troublesome problems. In particular, infectious diseases need appropriate screening [17–21], however the care of adopted children also poses challenges to the acceptance of vaccinations reported in pre-adoption certificates, because these may be not written, wrongly reported or not correspond to the recommended Italian vaccination schedule [5–10].

In this respect, we evaluated 88 internationally adopted children for tuberculosis, nearly all (86/88) coming from Eastern Europe, and we examined immunization status against poliovirus, tetanus, diphtheria, measles, mumps, rubella and hepatitis B of 75 of them. 70 reported a pre-adoption immunization record and five lacked medical record from their birth countries. Internationally adopted children are at risk for having active or latent tuberculosis, because this infection is highly prevalent in places from which many of them come, namely Eastern Europe and South Asia [19,20]. For this reason tuberculosis screening is recommended as soon as they arrive in the adopting country. In our casuistry, 83/88 of the internationally adopted children had a pre-adoptive record that certified a BCG vaccination. However, 29/88 lacked a BCG scar, of whom seven had a positive TST and were diagnosed as having LTBI. Our results are in accordance with previous studies, mainly on internationally adopted children coming from East Europe [3,18–21], and emphasize the importance of maintaining a high index of suspicion for the sake of these children and also to prevent the transmission of tuberculosis to other household members, as reported previously [22].

Our data also underline that many internationally adopted children, in despite of their satisfactory vaccination records, do not have adequate protection against poliomyelitis. Indeed, only 67.1%, 91.4% and 42.8% of our 70 studied children had antibody titers ≥ 1:10 for poliovirus 1–3, respectively, and only 38.5% of them were fully protected against all three types of poliovirus. Of great concern, two of our studied children were sero-negative for all three types of poliovirus. Our findings are similar to previous studies on internationally adopted children [5,7,8] that showed complete poliovirus immunization of no more than 2/3 of them. These findings are high divergent when compared with those reported in the Italian population. A recent study [23] of Italian children (aged 0–15 years) showed that the rates of antibodies (titer > 1:8) against poliovirus 1–3 were respectively 97.3%, 96.6% and 92.2%. The reasons of these low rates in antibodies against poliovirus among internationally adopted children are uncertain and might be due to out-dated, poorly stored or biologically less powerful vaccines, and inaccurate immunization records from their birth countries. We also observed lower seroprevalence to types 3 and 1 than to type 2 poliovirus. The precise causes of this finding, already reported in some parts of developing world [7,24], are not clear. Available data suggest that type 2 poliovirus infection (or type 2 polio-vaccine virus) and infections of other enteric pathogens, very common in some developing countries, may interfere with the immune response to type 1 and 3 polio-vaccine virus [25]. Moreover, the intervals between oral doses of each type of vaccine might be important in view of the prolonged enteric excretion of vaccine virus and...
its potential interference with response to subsequent doses [26]. However, further investigations of these and other factors, that might influence the serological response to OPV, in children of developing countries, are needed. A very good immunological response was observed in all of the 70 adopted children who were reported to have received at least three doses of diphtheria and tetanus vaccines, with seropositivity of 95.7% and 91.4%, respectively, using cut-off values 0.01 IU/ml for diphtheria and 0.1 IU/ml for tetanus. Conflicting data concerning these vaccinations are reported in the literature, ranging from high to low antibody rates [5–10]. However, a full comparison of our data with those reported in literature would not be valid because these values may vary according to laboratory methods used and cut-off values chosen, which are not always reported [5–10]. The available data in Italy regards vaccines administered to the children between 12 and 24 months, that for diphtheria and tetanus indicates a percentage of 96.5% [27].

As regards the other vaccinations recommended by the Italian immunization schedule, the antibodies against Bordetella pertussis, measles virus, mumps virus and rubella virus were found in only a part of the children whose pre-adoption records reported vaccinations and no relation between immunization and age was found. Conversely, antibodies were present in several adopted children whose pre-adoption records did not report the vaccinations, perhaps as result of a past infection or not registered vaccination. Also these findings clearly indicate that the pre-adaptive immunization certificiates of the internationally adopted children are scarcely reliable. Any way if we analyze the vaccines administered to Italian children between 12 and 24 months Ministry of Health data indicates for pertussis a percentage of vaccinated children of 95.6% and for MMR of 83% [27].

Hepatitis B is a world wide problem in all adopted children coming from developing countries, with the highest rates of infection in those from eastern Europe [3,8,20], especially from Romania [21]. Many of our studied children, 41 of 70 (58.5%), according to their vaccine certificates, were not immunized against hepatitis B. This finding is consistent with the fact that hepatitis B vaccination is not usually performed in most countries from which they come and where instead the virus is highly spread, suggesting the need for hepatitis B serological screening as soon they come to the adopting country. In Italy, children between 12 and 24 months vaccinated against hepatitis B exceed the 95%, since it is a compulsory vaccination [27].

On the other hand, nine adopted children, three of who were reported to have received hepatitis B vaccination in their country of origin, had serological evidence of a past hepatitis B infection, specifically anti-HBc and including three with HBsAg. These data suggest that serological screening on immunization status for hepatitis B should be performed in all newly internationally adopted children to identify and, when found, to treat patients with hepatitis B infection not diagnosed in their native country.

Finally, with our work we found that a high proportion of children in the international adoption group was not protected in a sufficient way against those diseases which are targeted with vaccinations in Italy. At this regard, in agreement with the Italian laws, at present we can refer only to a Circular by the Ministry of Health [28] that suggests re-vaccinating subjects who have unknown, incomplete or undocumented vaccination status.

However, we and other groups [5–10] have observed sometimes lack of immunization schedules and frequently that there are divergences between the registered records of the original countries and the results of serological screenings. Therefore, as guidelines following this study, we suggest that all the internationally adopted children, with and without any official immunization records, should be always tested for their immunization status as soon as they come to the adopting country, in order to perform vaccinations whether antibodies titer are inadequate. Future research efforts are necessary to implement the proposed guidelines regarding immunization status of internationally adopted children, because at present only limited data are available to determine the most cost-effective approach to ensure their complete immunization while avoiding a possible extra-immunization effects.

Acknowledgments

We thank Professor Pietro Ammatuna, Professor Anna Giammanco and Professor Rosa Di Stefano for their assistance during the execution of the virological and bacteriological tests.

We gratefully acknowledge Dr James J. Goodert for the revision of this manuscript and Prof. Alessandra Casuccio for the statistical analysis.

This study was supported by grants from Ministero dell’Università e della Ricerca Scientifica e Tecnologica (MURST).

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