Change in immunisation schedule and sudden infant death syndrome in Hungary

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Abstract

Infant mortality in Hungary was higher than in other European countries; however, the reported incidence of sudden infant death syndrome (SIDS) has been lower than those for Western Europe and the United States. Childhood immunisation has been reported to be a protective factor for SIDS. In Britain, the change to an earlier immunisation schedule for diphtheria, pertussis, and tetanus appeared to be associated with a shift in the age distribution of SIDS. In 1999, immunisation for Haemophilus influenzae type b (Hib) was introduced for Hungarian infants at the age of 2 months. Data for total infant mortality and SIDS in Hungary were analysed between 1990 and 2002. Infection was the major cause of death among Hungarian infants followed by SIDS. Following introduction of Hib immunisation, there was a decrease in deaths due to meningitis from an average of 3.5% of all infant deaths between 1990 and 1998 to an average of 1% of all infant deaths between 1999 and 2002 (p = 0.00). There was also a significant decrease in the proportion of SIDS in the age range ≥2 months from 48% in the earlier period to 39% after introduction of the vaccine (p = 0.03). The decrease in SIDS might be due in part to decrease in unrecognised Hib infections or to induction of antibodies by the tetanus toxoid to which the Hib polysaccharide is conjugated that are cross reactive with bacterial toxins implicated in SIDS.

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1. Introduction

The infant mortality rate in Hungary has been higher than that reported for other European countries, but this decreased to 7.16 per 1000 live births in 2002 (Fig. 1). In contrast, data on sudden infant death syndrome (SIDS) obtained from the Hungarian Central Statistical Office indicated that the SIDS incidence has been at constant low level since 1980 ranging from 0.12 to 0.37 deaths per 1000 live births (Fig. 2). In most industrialised countries, the SIDS incidence dropped significantly following the introduction of programmes in

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2–4 month range with the largest decrease noted for infants at 4 months of age [4,5].

Immunisation of Hungarian infants and children started in 1938 with diphtheria toxoid; BCG and diphtheria–pertussis–tetanus (DPT) vaccinations were added in 1954. In the last decade, vaccination for polio and Haemophilus influenzae type b (Hib) were introduced. Immunisation of all infants has been compulsory since 1954 and 99.8% of infants are covered by these [6].

In the United States, it was reported that following introduction of the Hib vaccine during 1990 for infants at 2 months of age, there was a 13% decrease in SIDS in two areas of California. This was before press articles in August 1991 about the protective effect of supine sleeping. During the 8 months after the article, the incidence of SIDS in these two areas decreased a further 52%. The authors suggested that the immunisation reduced invasive Hib infections and that type b H. influenzae, like Bordetella pertussis, might be too fastidious to be detected by routine microbiological samples taken during autopsy [7].

The protective effect of DPT immunisation was also suggested to be due in part to the induction by the toxoids in the vaccine preparation of antibodies cross reactive with pyrogenic toxins of Staphylococcus aureus [5]. These toxins have been detected in more than half of SIDS infants from five different countries, including Hungary [8–10].

In April 1999, compulsory Hib immunisation at 2 months was introduced for infants born after 1 February 1999. The vaccine contains the Hib capsular polysaccharide conjugated to tetanus toxoid. The aim of this study was to assess the ages of infants who died of SIDS before the introduction of the tetanus toxoid-Hib vaccine with those who died after the change in immunisation schedule to determine if there was a pattern

Fig. 1. Infant mortality rate per 1000 live births (data of the WHO Regional Office for Europe).

Fig. 2. Incidence of SIDS in Hungary 1980–2002.
similar to that observed following the initiation of DPT immunisation in the United States and Britain.

2. Materials and methods

2.1. Investigation of sudden unexpected infant deaths in Hungary

In Hungary, all sudden deaths in infancy are investigated by the police and a forensic pathologist. National data on SIDS deaths have been collected since the 1980s. Until the end of 1989, it was compulsory to perform an autopsy for every infant death. The autopsy rate among infants has remained high, and autopsy is mandatory in every sudden, unexpected or suspicious death. These investigations are performed mainly at a university Department of Forensic Medicine. Post-mortem investigation consists of scene of death investigation, autopsy and histology examinations; however, there is no national standard autopsy protocol. Toxicology, microbiology and immunohistochemistry are not used by all investigators.

2.2. Sources of data

Infant mortality for Hungary was analysed between the period 1990 and 2001. Data on natural and violent causes of infant death were obtained from the National Children’s Health Institute and the Hungarian Central Statistical Office. Deaths due to infection included those caused by protozoa, parasites, meningitis, influenza, viral and bacterial pneumonia, respiratory tract infections, intrauterine infection, bacterial sepsis, and perinatal infections.

The inclusion criteria for SIDS cases were autopsy confirmed deaths occurring between 1 week and 12 months of age between January 1990 and December 2001. SIDS was defined according to the original definition by Beckwith, “…the sudden death of any infant or young child which is unexpected by history, and in which a thorough postmortem examination fails to demonstrate an adequate cause of death” [11]. SIDS was accepted as a cause of death in 1980; however, inflammation in the respiratory tract or in the inner ear sometimes excluded the diagnosis of SIDS in some early cases.

The $\chi^2$ test with Yates correction factor was used to compare the numbers of total infant deaths and SIDS for the two periods.

3. Results

3.1. Common causes of death in Hungarian infants

Table 1 summarises the proportion of deaths between 1990–2002 attributed to the following groups: infection; SIDS, violent death (accidents and abuse), and other natural death causes. The most common cause of death in all the years examined was infection; however, there were no deaths due to diseases covered by the infant immunisation programme, tetanus, diphtheria, pertussis or polio. There were two deaths due to Hib pneumonia before introduction of the vaccine in 1999, but there were no deaths due to epiglottitis in the period 1990–2002. There was a decrease in deaths due to meningitis after 1999. In the period 1990–1998, meningitis accounted for an average of 3.5% (range 2.8–4%) of all infant deaths. In the period 1999–2002, this decreased significantly to an average of 1% (range 0.4–1.5%) of all infant deaths ($\chi^2 = 26.41$, $p = 0.00$); but there were no data to confirm that this was due to reduction in meningitis due to Hib.

3.2. Total infant mortality in relation to age at death

For total infant mortality, there was little if any change in the pattern of age distribution for the two
periods examined: period 1, 1990–1998 (Fig. 3); period 2, 1999–2002 (Fig. 4).

The highest percentage of deaths during both periods occurred during the first month of life: period 1, 2217/5849 (37.9%); period 2, 581/1580 (36.8%). The proportion of deaths declined in the second month: period 1, 1622/5849 (27.7%); period 2, 476/1580 (30.1%). In both periods, these figures were below 10% for months 3–6 and 11.5% for months 7–12 (Figs. 3 and 4).

3.3. SIDS in relation to age at death

For SIDS, the pattern for distribution by age at time of death differed from that of total infant mortality. During both periods, the highest proportion of SIDS occurred among infants at 2 months of age (Figs. 3 and 4): period 1, 128/297 (43.2%); period 2, 46/105 (43.8%). The proportion of SIDS deaths declined at 3, 4, 5 and 7–11 months decreased in the period 1999–2001 (Fig. 5).

The proportion of SIDS deaths in relation to total infant mortality increased slightly in period 2 (105/1580, 6.7%) compared with period 1 (297/5849, 5.1%).

The pattern for total infant mortality did not alter significantly between the two periods (Fig. 3). In period 1 before introduction of the vaccine, the proportion of deaths among infants 2 months of age or older was 3632/5849 (62%) compared with period 2 995/1580 (63%).

The proportions of SIDS deaths among children 2 months or older were 143/297 (48%) in period 1 but fell 41/105 (39%) in period 2 ($\chi^2 = 4.77$, $p = 0.030$) (Fig. 4). The greatest decreases were observed at 4 (4.9%), 5 (2.6%) and 7–12 (3.2%) months.

4. Discussion

The objective of the study was to determine if following the introduction of the Hib immunisation of
Hungarian infants at 2 months of age there was a decrease in the proportion of infants 2 months of age or older who died of SIDS. The proportion of SIDS infants 2 months of age or older decreased from 48% in 1990–1998 to 39% in the period 1999–2002. The difference was significant; and, as in the previous studies in Britain, the greatest decrease in deaths was noted among the infants at 4 months of age [4,5].

Before the public health campaigns to reduce the risk factors for SIDS, especially the prone sleeping position, there was a 13% decrease in SIDS following initiation of the Hib vaccine in the United States for two geographically different populations in California [7]. In Britain there was a change in the immunisation schedule for all infants implemented in October 1990 before the major public health campaigns to reduce the SIDS risk factors in 1991. DPT and Hib immunisations were initiated at 2 months of age instead of 3 months of age. There were significant decreases in the SIDS incidence among infants 2 months of age or older; and the greatest effect was observed at 4 months of age after two doses of the vaccines had been administered [4,5]. Ages of the SIDS infants in the study in the California study were not assessed.

It was suggested that the reduction in SIDS might be attributed to a decrease in undetected Hib infection in infants as these are fastidious organisms which might not be isolated if autopsy was delayed. This is a possibility as the numbers of deaths due to Hib infection have decreased in the Hungarian population following the new immunisation programme. The proportion of deaths due to bacterial meningitis decreased significantly. The other possibility is that immunisation induced antibodies cross reactive with pyrogenic staphylococcal toxins in response to the tetanus toxoid to which the Hib polysaccharide is conjugated [5]. Although Hib has not been isolated from Hungarian SIDS infants, *S. aureus* strains producing enterotoxins, particularly enterotoxin A have been isolated from these infants [9,12] and the toxins identified in their tissues [10].

The Hungarian infant mortality rate was among the highest of the Eastern European countries in the mid-1980s (22–24/1000 live births), but it decreased below the average for the EU countries in 1998 (9.7/1000 live births), and in 2002 it was 7.16/1000 live births [13,14]. Historically, infections have been the major causes of childhood morbidity and mortality [15]. The decreasing trend in infant mortality was due to development of health policy and health care networks, prevention of childhood infections, and early detection of developmental abnormalities. Fatal infections, inflammations and their complications are still the most frequent cause of death under one year of age in Hungary.

The important epidemiological risk factors for SIDS include low socioeconomic status [16,17], sleeping position [18], exposure to cigarette smoke [19,20], bottle feeding [21]. Risk factors for SIDS were examined for Hungarian families [22]. Lower socioeconomic factors and short intervals between pregnancies were associated with SIDS; however, other classical risk factors such as sleeping position, low birth weight, maternal smoking and feeding were not significantly different for SIDS families compared to controls. If as large epidemiological studies indicate, infant immunisation is an important protective factor for SIDS, the compulsory immunisation programme initiated in 1954 for Hungarian infants might be one factor contributing to the low incidence of SIDS observed in this population.

References


