Debendox does not cause the Poland anomaly

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SUMMARY The suggestion that Debendox may cause the Poland anomaly is refuted by a study of the antenatal drug exposure in 46 cases of the Poland anomaly and 32 cases of isolated absence of the pectoralis major. Debendox had been prescribed in one case of the Poland anomaly and in one case of isolated pectoralis absence, but in neither was the compound given during organogenesis. In none of the 78 cases could Debendox be causally implicated.

The Poland anomaly is a rare congenital malformation comprising unilateral absence of the pectoralis major muscle with an ipsilateral hand defect. Isolated absence of the pectoralis major may be a related malformation, and the two conditions possibly represent a spectrum of defects.

Debendox is an antiemetic drug used in pregnancy. It is a combination of dicyclomine hydrochloride 10 mg, doxylamine succinate 10 mg, and pyridoxine 10 mg. It has been marketed in the UK since 1958. It has been specifically suggested that Debendox may cause the Poland anomaly. In a recent study of Debendox and limb reduction deformities, out of 40,932 births there were 15 cases of limb reduction deformities. In only 3 was there a history of first trimester Debendox exposure, but in 2 of them the limb reduction deformity was the Poland anomaly. In the remaining 12 cases of limb reduction defects without first trimester exposure to Debendox there were no cases of the Poland anomaly.

In view of the specificity of teratogens, notably thalidomide, it was decided to pursue a specific causal relationship between the Poland anomaly, the related defect of isolated pectoralis absence, and the use of Debendox in pregnancy.

Materials and methods

Since 1970, a study of the aetiology of the Poland anomaly has been in progress. Cases were referred to me by paediatricians and plastic surgeons who know of my interest in it, but were not selected in any way. All cases were seen before it had been suggested that Debendox might cause the Poland anomaly. A special examination of the mother’s antenatal drug exposure was made in each case. The patients comprise two groups (1) 32 cases with isolated pectoralis major absence, and (2) 46 cases with the Poland anomaly. All cases were examined...
by me. Details of each mother's antenatal drug exposure were verified by examining the mother’s hospital antenatal records and by obtaining details of drug prescription from the family doctor. This report is solely concerned with Debendox and not with any other drugs or possible teratogens. The year of conception was estimated in each case. All but 2 patients were born in England and Wales, and most were living in the south or south west (Table).

Results

Drug ingestion in pregnancy. Details of drug ingestion during pregnancy could not be obtained in 6 cases born before 1924. Debendox had been prescribed in 2 of the remaining 72 cases, and details of these two cases are given below.

Case 1

Age 10 years; born 28.11.70; isolated pectoralis absence

First pregnancy of 18-year-old mother. Father a 21-year-old heroin addict. Mother had an adenotonsillectomy a few days after the estimated date of conception. Debendox, two tablets at bedtime, had been prescribed for vomiting at 12 and 14 weeks' post-conception, and taken for 4 weeks. Delivery at 39 weeks, birthweight 1·42 kg. Absence of the sternocostal and clavicular heads of the right pectoralis major was noted at birth. In addition, the child had a lumbar meningcele with an intramedullary teratoma, and hydrocephalus. The arms and hands were normal.

Case 2

Age 3 years; born 24.9.77; Poland anomaly

First pregnancy of 31-year-old mother. Debendox, two tablets at bedtime, had been prescribed for nausea 4 weeks after conception, but the mother when interviewed shortly after birth and 3 years later said the tablets had been taken only for a few days. Delivery at 40 weeks, birthweight 3·36 kg. The child had an absent sternocostal head of the right pectoralis major muscle, a hypoplastic right forearm, shortening of all 4 fingers on the right hand, with partial cutaneous syndactyly of the index and middle finger, and shortening of the flexor tendons to the middle finger.

Discussion

Twenty-six (14 Poland anomaly; 12 isolated pectoralis absence) cases were conceived before 1958, the year in which Debendox was introduced into the UK, and these cases could not have been caused by the drug. The critical period of embryogenesis for the Poland anomaly, which presumably also applies to isolated pectoralis absence, has been estimated to be 44–48\(^2\) or 43–46 days\(^3\) after conception. Therefore Debendox was taken well after the critical period in the first case, and well before the critical period in the second case. The larger number of cases conceived after 1963 is an ascertainment artefact, and is due to the fact that most cases were children referred by paediatricians.

A drawback to this study is that it is retrospective and there is no control group. It would be extremely difficult to obtain a control group in view of the fact that the cases span a 90-year period. The rarity of the defect makes a prospective study of a large number of cases impossible. Furthermore, it is not known how representative a sample of cases this is, either in terms of a geographical area or the general (as opposed to the hospital) population. Nevertheless, despite these theoretical disadvantages, in none of the 46 cases of the Poland anomaly or 32 cases of isolated pectoralis absence was there any evidence that Debendox could have caused the defect.

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References


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