POSSIBLE DRUG TERATOLOGY IN 'CLEFT LIP AND PALATE ANOMALY'

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The Clefts of lip and palate are of heterogenous type. On the basis of aetiology 4 groups can be distinguished—cases due to (i) single mutant genes, (ii) chromosomal abnormality, (iii) teratogenic agents and (iv) multifactorial origin.

The last group forms a majority of the cases. However, quite a few clefts can be attributed to the effects of drugs and other teratogenic agents and these are the findings presented in this paper.

Material

The cases for this study were taken from the Cleft Lip and Cleft Palate cum-Genetic Counselling Clinic of the department of Dental Surgery at AIIMS. 168 cases with this anomaly were used for this study. Majority of these cases came from Delhi and its neighbourhood. The patients and their family members were studied for genetic, dental and iaterogenic details.

Findings

Over 7% had a positive family history of this anomaly and one or more of the patient's close relatives was also affected (Table 1).

We found that nearly 18% of the clefts in these patients could be attributed to the effects of teratological agents. The significant among them are as follows:

TABLE I

Shows Distribution of Clefts on the basis of Aetiology

Causes	No.	%
Positive history of Cleft	12	7.14
Drugs history	30	17.85
Others	126	75.01
Total	168	100.00

(a) 5.4% of cases were those where there was a positive history of attempted abortion in the first trimester of pregnancy, which had failed and the resulting child of this pregnancy had a cleft of lip and or palate.

(b) Over 4.0% of clefts could be attributed to the possible teratological effects if drugs taken by the mother to prevent abortion as she was threatened by abortion in early period of pregnancy.

(c) 5.4% of the cases were due to the effects of anti-nausea and sleeping drugs taken by the expectant mother during her early pregnancy to prevent pregnancy sickness, nausea, vomiting etc.

(d) Another 3% of the cases studied could be attributed to the teratological effects of contraceptive pills, drugs used for confirmation of pregnancy and anti-convulsant drugs by the mother taken near or at the time of her pregnancy.

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Discussion

The teratological effects of various drugs taken in early pregnancy are well documented in several reports (Smithells, 1966; Sutherland and Light, 1965; Wilson 1973 a and b). It is well known that anti-nauseats, like the famous thalidomide, produced a lot of malformations including clefts in the babies born in Western Europe, especially in West Germany in 1960 (Mellins 1963; Lenz, 1962). We found, over 50% of the cases could be attributed to the teratological effects of anti-nauseating and sleeping drugs taken in the early pregnancy. The other drugs used as abortifacients such as aminopterin, an antimetabolite and antagonist of folic acid often used for therapeutic abortion of women suffering from tuberculosis are known to cause cleft lip and palate anomalies in those children where abortion did not take place (Lenz 1962; Milunsky *et al* 1968; Cohen 1966). Similarly, synthetic progesterone used in cases of threatened abortion are also known to produce teratological effects in the babies of those mothers (Voorhess 1967; Wilkins 1960; Bongiovanni and Mc Padden 1960). Corticosteroids are well known to cause cleft lip and palate anomalies in experimental animals if given in early stages of pregnancy (Fraser and Fainstat 1951; Speidel and Meadow 1972). In the present study there is a positive relationship in nearly 10% of the cleft cases where a mother either tried to abort with the help of an abortifacient drug or took some drugs to prevent a threatened abortion in the early period of her pregnancy.

In some cases where a conception took place immediately after a therapeutic abortion, the cleft could be due to the latent persistent effect of the abortifacient drugs taken a few weeks earlier. Reports from other workers suggest that anticonvulsant drugs as well as contraceptive pills taken by the mother before and during pregnancy can lead to several malformations including cleft palate anomaly in the developing foetus (Lowe 1973; Thierrch 1956). In this study 2% of cases were found to be related to such drugs.

Another significant finding of this study is that there is a difference of side involvement in cases with positive family history as compared to those of teratological origin. In unilateral cleft lip with or without palate, 71.4% were of the right side involvement among the cases where there was a positive family history of cleft while only 39.2% were involved in those affected by a teratological agents. Similarly, when it involved the left side only 28.6% and 60.8% were involved from familial and teratological causes respectively (Tables II and III).

TABLE II

Shows Positive History of Cleft

	CBCLP	CUCLP		CL & AL		ISOCP	TOTAL
		RT	LT	RT	LT		
Male	3	3	2	2	—	—	10
Female	2	—	—	—	—	—	2
Total	5	3	2	2	—	—	12

Right Side: 5-71.4%.
Left Side: 2-28.6%.

TABLE III

Shows Cleft and Side Distribution in Subjects Due to Effects of Teratological Agents

	CBCLP	CUCLP		CL & AL		ISOLATED	TOTAL
	—	RT	LT	RT	LT	—	—
Male	2	4	7	2	—	2	17
Female	3	3	4	—	3	—	13
Total	5	7	11	2	3	2	30

Left Side Involvement: 14-60.8%.
Right Side Involvement: 9-39.2%.

It shows that when the cleft is hereditary it involves the right side more predominantly than the left side (two and a half times more). However, when the cleft has teratological origin, the effects are opposite to those of the hereditary cleft i.e. the left side involvement is nearly one and a half times more than that of the right side.

Another important finding is that more males are affected where the cleft is due tohereditary factors, but there is no significant sex difference when the cleft has a teratological agent.

Summary

This report deals with 168 cases of cleft lip ± palate examined. Nearly 18% of these could be attributed to the teratological effects of drugs taken by the mother during her early pregnancy. The involvement of the left side was significantly higher than that of the right side among these cases. However, there was no sex difference in the involvement.

Having concluded that drugs can cause anomalies like cleft of the lip and palate, it is advisable that whenever possible the use of such drugs should be avoided during early stages of pregnancy.

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