



Does the Use of Oral Contraception Depress DZ Twinning Rates?

D. Campbell¹, B. Thompson², C. Pritchard³, M. Samphier³

¹Department of Obstetrics and Gynaecology, and ²MRC Medical Sociology Unit, University of Aberdeen; ³MRC Medical Sociology Unit, University of Glasgow, Scotland

Abstract. Data based on total births from a geographically defined population with zygosity determined from blood samples and placentation and with data on the use of oral contraceptives routinely collected in early pregnancy showed no association between oral contraceptive use prior to pregnancy in either MZ or DZ twinning. Three mutually exclusive control groups of singletons were used to take account of age, parity and secular trends.

Key words: Twinning rate, Oral contraception, Secular trend

INTRODUCTION

Twinning rates have declined over the past 20 years throughout the world [7,10,11]. The decline is attributed to a fall in DZ twinning. Indeed, a slight increase has been reported in recent MZ twinning rates [4,9], but the data are difficult to interpret [3]. The reason for the variable decline in DZ twinning rates between countries but starting at about the same time, is not fully understood. Suggested causes have included hormonal or pesticidal substances widely used in agriculture [7] and decline in sperm quality [12].

MacGillivray [13] examined the data for Scotland and concluded that the main explanation for the decrease in DZ twinning was the fall in maternal age and parity. However, he considered that there was a possibility that oral contraception, introduced about 1964 and which became very popular and widely used, might be implicated by adversely affecting the hypothalamic pituitary function and thereby twinning. In contrast, James [9] and Emery [4] have suggested that a slight increase in MZ twinning rates could be rela-

ted to prior oral contraceptive use leading to delayed implantation of the fertilised ovum with early division into two embryos.

Two main studies have related the use of oral contraception to twinning rates. In France, Hemon et al [6] studied 673 mothers of twins delivered in several different hospitals compared with the mothers of the preceding singleton birth at each place. Thus, the twin and singleton (control) births were matched for time and place. They concluded that there was a decrease in DZ twinning rate after oral contraception use but were guarded in accepting a causal relationship without better documentation.

In Australia, Macourt et al [14] sent questionnaires to 2,000 mothers who were members of the Australian Multiple Birth Association, about half of whom replied. The ages of the twins are not stated. They reported that the ratio of MZ to DZ twins was altered in pill users and concluded that use of oral contraception increased MZ twinning.

There are several problems associated with both these studies. Data on use of oral contraception was collected retrospectively. In the French study, the mothers of twins and their controls were interviewed in hospital soon after the birth, whereas the mothers of twins in Australia were filling in a questionnaire at home an unspecified time after the birth. Zygosity was not accurately determined in either study. The French study relied on the Hardy-Weinberg formula which may give inaccurate results [1,8], whereas the Australian study based zygosity on whether the mothers thought that like-sexed twins looked alike. It is well known that maternal age and parity affect twinning and the French study considered these (and weight) as possible confounding variables, but they were ignored in the Australian study as was any secular change in the use of oral contraception. Neither study was based on a total population of twin pregnancies.

A preliminary study in Aberdeen, which showed DZ twinning was reduced after use of oral contraception in multiparae only, highlighted some of the problems of considering twins and adjacent singleton (control) births in the same hospital [16]. All the births took place in the Aberdeen Maternity Hospital where virtually all the twins from the North-east of Scotland are delivered, whereas the singleton controls were to mothers resident in the Aberdeen City District. For many years there was a differential use of oral contraception by age and parity and between the "city" and "country" women which eventually disappeared once the general practitioners became fully integrated in providing contraceptive services within the National Health Service.

The present analysis aims to overcome the deficiencies of these earlier studies, in so far as it is based on the total population of a geographical area, zygosity was properly determined and details of oral contraceptive use were obtained routinely in early pregnancy.

METHOD

Population

Total births to women resident in the Aberdeen City District (approximate area 18,500 hectares, total population 200,000) were used for the years 1969-1983 inclusive. All births took place in the Aberdeen Maternity Hospital and were included in the computerised Aberdeen Maternity and Neonatal Data Bank [15]. Over the years 25 twin and 157

singleton births have followed ovulation induction, but it may be noted that one pair of twins was MZ with a monochorionic, monoamniotic placenta.

Three matched singleton control mothers were identified for each mother who delivered twins. Every control was matched for year of birth and then three separate control groups were matched 1) for age only, 2) for parity only, and finally 3) for age and parity.

The control groups were generated using the Data Bank index which identifies chronological sequences of pregnancy events to individual women ordered by a Hospital Unit Number. A randomised selection procedure was adopted to produce matches of equiprobability from over 41,000 possible singletons for the 384 twin births. All the required controls were achieved except for two which could not be matched for age and parity – these unmatched mothers of twins were both primiparae, one aged 37 and the other 38.

Zygoty

Zygoty was determined from blood samples and placentation [2]. Inevitably, over the years, some samples were not provided by the Labour Ward or they were unsuitable for testing when they reached the laboratory. In reporting the results below, twins for whom zygoty is unknown have been included in “all twins” with a separate analysis for those confirmed as MZ or DZ.

Oral Contraception

Throughout the years, use of oral contraception has been recorded routinely at a woman’s first visit to the Antenatal Clinic and before any clinical examination, ie, when twins were undiagnosed. The interval between discontinuation of oral contraception and the last menstrual period was calculated in months, particular attention being given to identifying “pill withdrawal bleeds” (Table 1). For some women information on the use of oral contraception was not available because the medical notes were incomplete or could not be traced. In such circumstances, irrespective of for whom the item was missing, both

Table 1 - Oral contraceptive use relative to last menstrual period (No. of women)

Oral contraceptive use	Twins	Control matched for		
		Age	Parity	Age and parity
Not used	137	123	133	119
Used LMP				
In early pregnancy	3	7	7	9
Withdrawal bleed	25	10	11	8
Months: 2	39	53	45	54
3	28	18	15	17
4	18	9	11	8
5	8	10	5	8
6	4	11	12	11
7 - 12	32	26	26	31
13 and over	59	52	50	48
Not stated	23	39	41	53
No information	8	26	28	16
Total women	384	384	384	382

the mother of twins and her control have been excluded in the analysis. This accounts for some slight variation in the numbers in the tables for the different control groups.

RESULTS

Table 2 illustrates the secular changes in use of oral contraception by mothers of twins. Since the mid 1970s over three-quarters of mothers giving birth to twins had used the pill prior to that conception. In the 15 years overall, the proportion of users of oral contraception in the three singleton control groups had been similar to that for mothers of twins (Table 3).

Table 2 - Use of oral contraception. Aberdeen City District twin births, 1969 - 1983

	Not used (%)	Used (%)	Not known (%)	Total (N =100 %)
1969-71	55.9	41.2	2.9	102
1972-74	44.6	54.0	1.4	74
1975-77	23.2	76.8	/	69
1978-80	25.0	73.6	1.4	72
1981-83	19.4	76.1	4.5	67
1969-83	35.7	62.2	2.1	384

Table 3 - Use of oral contraception before pregnancy. Singleton control groups matched with twin births (384), 1969 - 1983

	Oral contraception (% values)		
	Not used	Used	Not known
Control Group 1			
Age matched	32.0	61.2	6.8
Control Group 2			
Parity matched	34.6	58.1	7.3
Control Group 3			
Age and parity matched	31.2	64.6	4.2
Twin births	35.7	62.2	2.1

A series of statistical analyses of matched pairs was carried out using the non-parametric McNemar test [5].

1) Women who had used oral contraception were compared with those who were known to have been non-users. Mothers of twins were considered all together as well as separately for those having MZ and DZ twins. Comparisons were made with the three control groups of mothers separately (Tables 4, 5, 6) and no significant differences were found in the use of oral contraception.

Table 4 - Analysis of matched pairs: comparison of oral contraception used/not used by mothers of twins with singleton controls matched for maternal age

	Control group 1		P
	Used	Not used	
All twins (350)			
Used	161	65	NS
Not used	67	57	
MZ twins (133)			
Used	71	21	NS
Not used	19	22	
DZ twins (184)			
Used	72	38	NS
Not used	43	31	

Table 5 - Analysis of matched pairs: comparison of oral contraception used/not used by mothers of twins with singleton controls matched for parity

	Control group 2		P
	Used	Not used	
All twins (348)			
Used	151	70	NS
Not used	68	59	
MZ twins (131)			
Used	64	23	NS
Not used	21	23	
DZ twins (184)			
Used	73	38	NS
Not used	42	31	

2) Some authors [eg,4,14] have suggested that the interval between cessation of oral contraception and pregnancy is critical in the effect on twinning. Although the French and preliminary Aberdeen studies failed to reveal any such significant association, the hypothesis was considered in the present analysis. Matched pair analyses were carried out as above for different intervals, namely pregnancy within two months of oral contraception, within three months, within six months and within one year. None of the results were significant and only that for conception within two months of cessa-

Table 6 - Analysis of matched pairs: comparison of oral contraception used/not used by mothers of twins with singleton controls matched for age and parity

	Control group 3			P
	Used	Not used		
All twins (359)				
Used	180	49		NS
Not used	62	68		
MZ twins (140)				
Used	78	16		NS
Not used	21	25		
DZ twins (184)				
Used	84	28		NS
Not used	32	40		

tion of oral contraception for mothers of twins and controls matched for age and parity are given here (Table 7). Women were included as having a pregnancy within two months of discontinuing oral contraception if they had taken the pill up to and into early pregnancy or their last menstrual period was recorded as a pill withdrawal

Table 7 - Analysis of matched pairs: interval two months or less between oral contraceptive use and conception. Comparison of mothers of twins with singleton controls matched for age and parity

	Controls		P
	Pill within 2 months of conception	The remainder	
All twins (359)			
Pill within 2 months of conception	14	47	NS
The remainder	57	241	
MZ twins (140)			
Pill within 2 months of conception	5	20	NS
The remainder	19	96	
DZ twins (184)			
Pill within 2 months of conception	6	22	NS
The remainder	29	127	

bleed, or the interval between use of oral contraception and their last menstrual period was within two months.

CONCLUSION

The present study shows no association between oral contraceptive use prior to pregnancy and either MZ or DZ twinning. However, details were not available on the type of oral contraceptive used.

In contrast to other studies, these findings are based on total births from a geographically defined population, with zygosity determined from blood samples and placentation and with data on the use of oral contraception routinely collected prospectively. Three mutually exclusive control groups of singleton were used to take account of age, parity and secular trends.

Acknowledgment. Dr. D.M. Campbell gratefully acknowledges a grant for clerical assistance received from The Eugenic Society.

REFERENCES

1. Allen G (1981): Errors of Weinberg's difference method. In L Gedda, P Parisi, WE Nance (eds): *Twin Research 3: Twin Biology and Multiple Pregnancy*. New York: Alan R Liss, pp 71-74.
2. Corney G, Robson EB, Strong SJ (1972): The effect of zygosity on the birthweight of twins. *Ann Hum Genet* 36:45-59.
3. Elwood JM (1985): Temporal trends in twinning. In H Kalter (ed): *Issues and Reviews in Teratology, 3*. New York and London: Plenum Press, pp 65-93.
4. Emery AEH (1986): Identical twinning and oral contraception. *Biology Soc* 3:23-27.
5. Fleiss JL (1981): *Statistical Methods for Rates and Proportions*. Chichester, England: John Wiley, pp 112-119.
6. Hémon D, Berger C, Lazar P (1981): Twinning following oral contraceptive discontinuation. *Int J Epidemiol* 10:319-328.
7. James WH (1972) Secular changes in dizygotic twinning rates. *J Biosoc Sci* 4:427-434.
8. James WH (1976): The possibility of a flaw underlying Weinberg's differential rate. *Ann Hum Genet* 40: 197-199.
9. James WH (1980): Secular changes in twinning rates in England and Wales. *Ann Hum Biol* 7: 485-487.
10. James WH (1982): Second survey of secular trends in twinning rates. *J Biosoc Sci* 14:481-497.
11. James WH (1983): Twinning rates. *Lancet* i:934-935.
12. James WH (1986): Recent secular trends in dizygotic twinning rates in Europe. *J Biosoc Sci* 18: 497-504.
13. MacGillivray I (1981): The probable explanation for the falling twinning rate in Scotland. In L Gedda, P Parisi, WE Nance (eds): *Twin Research 3: Twin Biology and Multiple Pregnancy*. New York: Alan R Liss, pp 15-19.
14. Maccourt DC, Stewart P, Zaki M (1982): Multiple pregnancy and fetal abnormalities in association with oral contraceptive usage. *Aust NZ J Obstet Gynaecol*, 22:25-28.
15. Samphier M, and Thompson B (1981): The Aberdeen maternity and neonatal and data bank. In: *Prospective longitudinal research*. SA Mednick, AE Baert (eds): Oxford: Oxford University Press.
16. Thompson B, Campbell DM, MacGillivray I (1982): Twinning and oral contraception in North East Scotland. Paper presented at the International Workshop on Multiple Pregnancies, Malmö, Sweden. Unpublished.

Correspondence: Dr. D.M. Campbell, Department of Obstetrics and Gynecology, University of Aberdeen, Foresterhill, AB9 2ZD, Scotland.