Advances in Contraception 7 (1991) 379–387

A study of bleeding patterns with two injectable contraceptives given postpartum and the effect of two non-hormonal treatments

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Abstract

349 women were given Depo-Provera and 304 were given Nur-Isterate immediately after delivery.

No significant difference in duration or amount of bleeding was found between the two injectables over 6 months. Although the incidence and duration of bleeding were greater when injectables were used postpartum than when used electively, they were not excessive. This option should therefore not be withheld. Treatment with anti-inflammatory and anti-fibrinolytic agents were not effective in controlling bleeding.

Introduction

Bleeding problems associated with injectable contraceptives are the major cause of dissatisfaction with this method. The pathogenesis of the bleeding is not clearly understood, and the management of prolonged and/or heavy bleeding is often difficult and unsatisfactory. No large controlled study demonstrates the efficacy or rationale of the recommended approaches: oral or intramuscular estrogens, combined oral contraceptives or repeat Depo Provera injections, and anti-inflammatory or anti-fibrinolytic agents [1].

In the past, only 20% of our patients attended postnatal clinics. We hoped that by initiating effective contraceptive practice when women are available and optimally motivated – as they are at delivery – this would enhance acceptance and increase continuation rates. Over the past decade, acceptance has steadily increased, and now about 90% of our patients accept injectable contraceptives before discharge from maternity centers in the hospital services. All contraceptive methods are discussed by family planning advisors during antenatal visits and the woman's choice is recorded. This is discussed again after delivery by the midwife or doctor before the injection is given.

Murphy [2] reported an increase in bleeding when injectables were used in the puerperium. We undertook this study to determine whether bleeding problems are or are not a significant problem, and whether one type of injection is associated with more problems than the other. As we are reluctant to use estrogens during lactation, we undertook to determine the effect of two non-hormonal treatments, one anti-inflammatory and one anti-fibrinolytic agent.

Objectives

The objectives of this study were to examine:

1. The extent of bleeding among women using Depo Provera (DP) (medroxy-progesterone acetate) and Nur Isterate (NI) (norethisterone enanthate) in the puerperium (given within 6–12 hours after delivery);

2. Whether one injectable is associated with more bleeding than the other; and

3. Whether non-hormonal methods of treating bleeding problems are effective.

Methods

Three hundred and forty nine women were given DP, and 304 were given NI within 6–12 hours after delivery. Patients kept a chart on which they recorded the days on which they bled and indicated the number of pads used when bleeding. The study period was 6 months (3 injection intervals for NI; 2 for DP).

Women who bled for more than 10 days consecutively (after the first two weeks of lochia) were treated with either Naproxen (nafasol, a non-steroidal anti-inflammatory agent) 250 mg 3 times a day for 5 days, or Cyklokapron, an anti-fibrinolytic agent (tranexamic acid) 1.5 g/day for 5 days.

The effect of treatment on bleeding was measured by the number of days of bleeding and the number of pads used daily after the treatment was completed.

Results

The duration of bleeding over a 10-day interval (Tables 1 and 2)

There was a fairly equal distribution of women in each category at the first return visit. During the second injection interval with DP, 78.5% of women bled for 0–10 days; 8.7% for 11–20 days; 4.0% for 21–30 days; and 8.7% bled for 31 days or more. With NI there was also an even distribution of women in each category during the first injection interval. At the end of 6 months, 86% of women bled for 10 or fewer days in the third injection interval.

Comparison of number of bleeding days with the two injectables (Figure 1)

The points on the graph are the mean days of bleeding plotted against the mean days after each injection for each of the visits. Each point has a bar showing a 95% confidence interval for the mean days of bleeding. The line joining DP1 and 2 intersects the confidence bands at NI 1, 2 and 3.

We conclude that there is no difference between the two injectables with respect to duration of bleeding.

Table 1. Duration of bleeding: Depo Provera

No. bleeding days per injection interval	*1st visit 224 women mean days 86.87 (SD 11.9)*	%	*2nd visit 149 women total mean days 83.72 (SD 12.68)*	%
0 – 10	63	28.1	117	78.5
11 – 20	53	23.6	13	8.7
21 – 30	51	22.7	6	4.0
31 +	57	25.4	13	8.7

Table 2. Duration of bleeding: Nur Isterate

No. bleeding days per injection interval	*1st visit, 211 women mean days 53.5 (SD 9.38)*	%	*2nd visit, 170 women mean days 56.5 (SD 11.12)*	%	*3rd visit, 129 women mean days 55.6 (SD 12.18)*	%
0 – 10	44	20.8	135	79.4	111	86.0
11 – 20	70	33.2	24	14.1	9	7.0
21 – 30	49	23.2	3	1.8	4	3.1
31 +	48	22.7	8	4.7	5	3.9

There was no significant difference over the total 6-month period of study in the duration of bleeding between DP and NI (mean 35.9 (SD 31.55) and 33.2 (SD 20.58) respectively) (Table 3).

Incidence of prolonged bleeding (Table 4)

The number of women who bled in excess of 21 days per injection interval on DP and more than 14 days per injection interval on NI (after excluding 14 days for lochia in the first injection interval) was 21% on DP and 25.5% on NI in the first injection interval; 12.7% on DP and 12.9% on NI in the second injection interval; and 8.5% of women in the third injection interval on NI.

Table 3. Duration of bleeding

Visit	*n*	*Days after injection Mean (SD)*	*Days of bleeding Mean (SD)*
Depo Provera			
1	221	86.87 (11.90)	25.72 (21.45)
2	143	170.59 (12.68)	35.54 (31.55)
Nur Isterate			
1	211	53.55 (9.38)	21.68 (12.53)
2	170	110.05 (11.12)	28.62 (17.90)
3	129	165.65 (12.18)	33.23 (20.58)

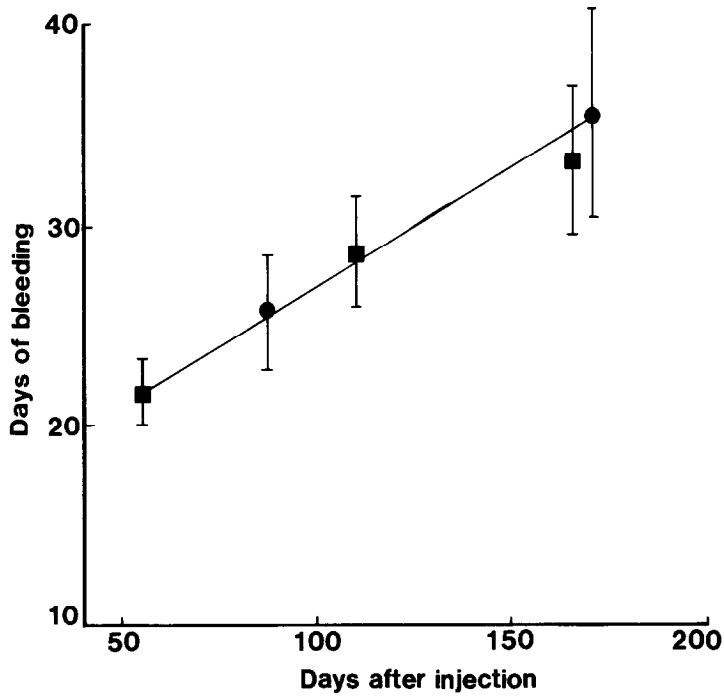

Figure 1. Comparison of bleeding days on 2 injectable contraceptives given immediately after delivery. ● = Depo Provera; ■ = Nur Isterate

Comparison with other studies of bleeding over 6 months (Table 5)

In the World Health Organization (WHO) study [3], 10.5% of women on DP and 4.1% on NI experienced prolonged or heavy bleeding over 6 months. Murphy [2] showed that 63.0% of women given DP during the puerperium experienced heavy or prolonged bleeding, compared with 3.8% of controls. In our study, 16.8% of women

on DP and 15.6% on NI experienced heavy or prolonged bleeding during the first 6 months after delivery. Only the percentage column (and not the mean number of days) has been adjusted to exclude the days of bleeding during lochia so that this can be compared with the WHO study where the injections were given electively.

Table 4. Incidence of prolonged bleeding

	Duration of use (months)	*No. of women*	*No. of women with prolonged bleeding*	*Bleeding days*
1st interval				
DP	3	224	47 (21%)	>35
NI	2	211	54 (25.5%)	>28
2nd interval				
DP	3	149	19 (12.7%)	>21
NI	2	170	22 (12.9%)	>14
3rd interval				
NI	2	129	11 (8.5%)	>14

Table 5. Studies of bleeding over 6 months

Author		*Duration of bleeding (mean no. of days)*	*% of women with prolonged bleeding*	
WHO, 1983	DP	10.2	10.5	
	NI	6.9	4.1	$p<0.001$
Murphy, 1979	DP	58.5	63.0	
Postpartum	Controls	20.8	3.8	$p<0.001$
Sapire, 1990	DP	35.9	16.8	
Postpartum	NI	33.2	15.6	NS

Table 6. Average number of pads used daily – Depo Provera

No. of pads	*1st visit, 224 women*	%	*2nd visit, 149 women*	%
0	0	0	97	65.1
1 – 4	162	71.9	47	31.5
5 or 6	51	22.7	4	2.7
7+	11	4.9	1	0.7

Table 7. Average number of pads used daily – Nur Isterate

No. of pads	*1st visit, 211 women*	*%*	*2nd visit, 170 women*	*%*	*3rd visit, 129 women*	*%*
0	0	0	73	42.9	79	61.2
1 – 4	176	83.4	92	54.2	47	36.5
5 or 6	27	12.8	4	2.3	3	2.3
7+	8	3.8	1	0.6	0	0

Amount of bleeding (Tables 6 and 7)

The average number of pads used daily was 1–4 in 71.9% of women during the first injection interval on DP; 96.4% of women used 0–4 pads between 3 and 6 months. On NI, 83.4% of women used only 1–4 pads at the first injection interval and 97.6% used 0–4 between 4 and 6 months. This shows that bleeding was not heavy.

Treatment of prolonged bleeding

Women who presented for treatment bled significantly more than those who did not present for treatment (mean 49.4 and 26.7 days respectively).

The mean number of days before bleeding stopped after both treatments was not statistically significantly different (means 4.69 and 4.96 days respectively). After treatment was discontinued, the amount of bleeding was not different between the two groups.

As there was no significant difference in the effect of treatment with Cyklokapron and Naproxen, we extended this aspect of the study to determine whether treatment was in fact effective or not by doing a 'double-blind' study. In view of the greater cost of Cyklokapron, we decided to concentrate on Naproxen.

Placebo-controlled study

This study used an open, randomized, double-blind design. Patients who bled in excess of 10 consecutive days or used 8 or more pads per day after the initial period of 14 days of lochia had finished, were treated with either group A or group B tablets which were identical in appearance. Which was Naproxen and the placebo was known only to the manufacturing company.

Duration of bleeding after treatment

This was not significantly different between the two groups (Table 8) (11.80 and 14.40 days respectively for group A and group B).

Table 8. Bleeding days after Rx: nafasol/placebo (NS)

Group	*n*	*Mean*	*SD*
1	26	11.80	2.64
2	22	14.40	3.72

Table 9. Average number of pads after Rx: nafasol/placebo (NS)

Group	*n*	*Mean*	*SD*
1	26	4.53	1.26
2	22	4.50	1.18

Table 10. Placebo-controlled study

	n	*Continued bleeding*	*Stopped bleeding*
Group A	26	6	20
Group B	22	7	15

Amount of bleeding

There was no significant difference in the average daily number of pads used after treatment (group A mean 4.53 and group B mean 4.50 pads) (Table 9).

The proportion of women that stopped bleeding after treatment in the two groups were not significantly different (Table 10). In group A, 6 continued bleeding and 20 stopped; in group B, 7 continued bleeding and 15 stopped. A two-way analysis of variance confirmed that there was no treatment difference.

Conclusions

1. Although the incidence and duration of bleeding are greater when injectable contraceptives are used postpartum, they are not excessive when compared with the elective use of injectables.

2. There is no significant difference in the incidence, duration and amount of bleeding between Depo Provera and Nur Isterate.

3. The anti-inflammatory and anti-fibrinolytic agents cannot be considered effective for treatment of bleeding in women using injectable contraceptives.

Although the incidence and duration of bleeding are greater when injectable contraceptives are used immediately after delivery, they are not excessive. This option should therefore not be withheld. The importance of pre-treatment counselling and support during follow-up regarding bleeding disturbances cannot be over-emphasized.

Acknowledgements

I wish to express my appreciation to Sisters D. Fransman and F. Harnekar. They recruited, counselled and treated the patients on this study. This work would not have been possible without their conscientious efforts. My thanks also to Mr S. Isaacs, Department of Medical Information, Groote Schuur Hospital, and Professor J.S. Maritz, Medical Research Council, Tygerberg, for the statistical analysis.

I wish to thank Lennon Ltd. for their support and assistance in preparing the placebo-controlled study and for supplying the Naproxen and placebo for this purpose, and also Adcock–Ingram Laboratories Ltd for supplying Cyklokapron, and to thank Berlimed and Upjohn companies for their support.

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MS received 6 Dec. 90.
Accepted for publication 5 Apr. 91.

Resumé

Immédiatement après l'accouchement, on a administré par injection du Depro-Provera à 349 patientes et du Nur-Isterate à 304 autres.

Aucune différence significative n'a été observée ni dans la durée ni dans le volume des pertes sanguines entre ces deux groupes au cours des 6 mois suivants. Bien que les écoulements aient été plus fréquents et aient duré plus longtemps lorsque ces préparations étaient injectées après l'accouchement que si elles étaient administrées sur demande, ils n'étaient pas excessifs. Cette solution ne devrait donc pas être refusée. Le traitement aux anti-inflammatoires et anti-fibrinolytiques n'a pas permis de régler efficacement les saignements.

Resumen

Inmediatamente después del parto, se administró por inyección Depo-Provera a 349 pacientes y Nur-Isterate a otras 304.

No se observó ninguna diferencia significativa en la duración ni el volumen de las pérdidas de sangre entre estos dos grupos en el curso de los 6 meses siguientes. Si bien las pérdidas eran más frecuentes y de mayor duración cuando dichas preparaciones se inyectaban después del parto que cuando eran administradas a solicitud, no eran excesivas. Esta solución no debería denegarse, por lo tanto. El tratamiento con antiinflamatorios y antifibrinolíticos no resultó eficaz para controlar las pérdidas.