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Thyrotropin releasing hormone and corticosteroids prior to preterm labour: a survey of current practice in nine European countries

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Abstract

There is considerable variation in the use of corticosteroids within Europe before possible preterm delivery. Thyrotropin releasing hormone is rarely used as synergistic treatment in most, but not all, European countries—presumably reflecting uncertainty about the effectiveness and safety of this agent.

Keywords: Corticosteroids; Thyrotropin releasing hormone; Preterm delivery

1. Background

Strategies to prevent, rather than treat, the problems of neonatal immaturity have obvious attractions. Corticosteroid administration to the mother prior to preterm delivery is one such strategy [1]. It is clearly effective but appears to be under-utilized. Extensive laboratory research has shown that the administration of protirelin, better known as thyrotropin releasing hormone (TRH), together with corticosteroids, further accelerates the production and release of surfactant, speeds lung water resorption, and matures the fetus in other respects. By early 1993, data available from controlled trials in human pregnancy had suggested that

these effects may also be translated into clinical benefits [2], but considerable uncertainty still remains.

We have, therefore, conducted a survey of antenatal corticosteroids and TRH use in nine European countries, to assess the extent to which practice is consistent with current evidence from controlled trials.

2. Materials and methods

The survey was mounted under the auspices of the European Union Antenatal TRH Network. Two National Co-ordinators (usually an obstetrician and a neonatologist/paediatrician) from each of the nine countries in the Network (Belgium, Denmark, France, Greece, Netherlands, Portugal, Republic of Ireland, Spain and the UK), were asked to identify an obstetrician/neonatologist in hospitals in which women likely to deliver preterm might be cared for. Questionnaires (translated if necessary) were then sent to the named person in each of these hospitals in September 1994. The questionnaire asked about details of the size of the hospital, the drugs administered to pregnant women when preterm birth was anticipated, and policies for the administration of antenatal corticosteroids and TRH specifically.

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Table 1
Number of responding hospitals, total number of births, number of births < 32 weeks gestation and policies for the use of corticosteroids and thyrotropin releasing hormone (TRH) prior to expected preterm delivery in nine European countries

Country	Hospitals responding	Total births in responding hospitals (1000's)	Births <32 weeks	Policy for use prior to expected preterm delivery											
				Corticosteroids					TRH + corticosteroids						
				Never used	<10%	10–49%	50–89%	≥90%	Not known ^a	Never used	<10%	10–49%	50–89%	>90%	Not known ^a
UK	160	476	8211	1%	9%	11%	39%	37%	3%	86%	9%	1%	2%	1%	1%
Spain	16	39	740	0	6%	25%	19%	50%	0	81%	6%	0	0	0	13%
Greece	12	38	1289	0	17%	8%	33%	42%	0	84%	0	8%	0	0	8%
Belgium	43	41	768	4%	49%	12%	19%	12%	4%	46%	33%	5%	14%	2%	0
Portugal	27	62	706	15%	22%	33%	22%	0	8%	96%	0	0	0	0	4%
France	39	85	2031	0	51%	28%	10%	5%	6%	77%	15%	0	0	3%	5%
Holland	21	32	2154	0	24%	29%	10%	38%	0	86%	14%	0	0	0	0
Ireland	16	40	436	0	0	19%	31%	50%	0	94%	0	0	0	0	6%
Denmark	31	55	692	6%	29%	16%	23%	23%	3%	100%	0	0	0	0	0
Total	365	868	17027	3%	21%	17%	28%	28%	3%	82%	11%	2%	2%	1%	2%

^aIncludes not answered.

3. Results

Questionnaires were mailed to the 546 identified hospitals. Replies were received from respondents in 365 hospitals (67%). The total number of births in 1993 in the responding hospitals was approximately 870 000, which represents 34% of the total births in the nine countries in that year (median 36.6%, interquartile range 11.4–78.6%). Two percent of these births were below 32 weeks gestation in the responding hospitals (Table 1). There was considerable variation in the number of deliveries per year between responding hospitals (median 2100, interquartile range 1350–3131), probably reflecting differences in the organisation of maternity care between the nine countries.

Ninety-four percent of the responding hospitals reported an intention to prescribe corticosteroids when preterm birth was anticipated, and 56% used it for $\geq 50\%$ of women in these circumstances. In contrast, 15% of the hospitals reported using a combination of corticosteroids and TRH (Table 1). Of those hospitals who used TRH, 50% used TRH at a dose of $400 \mu\text{g} \times 4$, but others used $200 \mu\text{g} \times 2$ (10%), $200 \mu\text{g} \times 4$ (16%), $400 \mu\text{g} \times 2$ (8%) or $>1600 \mu\text{g}$ total dose (12%). Four percent did not reply to this question.

4. Discussion

This survey appears to demonstrate a more extensive use of corticosteroids to pregnant women when preterm birth is anticipated than found in the early 1990s [3]. This may represent an increasing acceptance by obstetricians and neonatologists of the evidence supporting the use of corticosteroids; it may also reflect policy rather than practice.

The survey has also shown caution in many European hospitals about whether TRH is a valuable and safe synergistic agent to be used in conjunction with corticosteroids. If those who returned questionnaires are more likely to be those who use TRH, the survey may have over-estimated the use of TRH. Nevertheless, despite the fact that it is licensed only as a one-dose diagnostic agent, from this survey TRH appears to be used prior to preterm labour in a substantial number of hospitals.

The use of TRH may be further encouraged by the publication of results of a randomized trial of antenatal TRH ($400 \mu\text{g} \times 4$) and corticosteroid administration conducted in New Zealand suggesting beneficial effects

[4]. The publication of the results of an Australian multicentre trial, ACTOBAT ($200 \mu\text{g} \times 4$) suggest that enthusiasm for using TRH in routine practice may, however, have been premature [5]. This makes it even more imperative to conduct a large randomized trial rapidly to clarify the role of TRH in combination with corticosteroids in practice. Consensus about undertaking such a trial was agreed within the European Union Antenatal TRH Network. Respondents from 244 hospitals of the 365 surveyed, with a total of 605 264 births per year (13 411 below 32 weeks) expressed their willingness to participate in an international multicentre trial. The trial will evaluate a course of four $400 \mu\text{g}$ doses compared with placebo in women receiving corticosteroids before 32 weeks gestation, and recruitment started in late 1995.

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