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INTRANASAL USE OF SYNTHETIC OXYTOCIN IN MANAGEMENT OF BREAST-FEEDING

BY

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The role of oxytocin in the initiation and maintenance of lactation is now well established (Petersen, 1944; Cross, 1955; Berde, 1959). It has been used clinically as a means of inducing milk ejection for some time (Newton and Newton, 1948, 1951). Soon after oxytocin had been synthesized by du Vigneaud *et al.* (1953) it was shown that synthetic oxytocin exerted the same effect on the myoepithelial cells of the mammary gland as the naturally occurring hormone (Nickerson *et al.*, 1954; Berde and Cerletti, 1957; Beller *et al.*, 1958). Oral and nasal applications of the posterior pituitary hormones have been used for many years (Donaldson, 1921; Hofbauer *et al.*, 1927).

Recently several papers have appeared concerning the intranasal use of synthetic oxytocin. Berde and Cerletti (1960) have compared the effects of administering oxytocin by the intravenous, intramuscular, and intranasal routes on the lactating mammary gland of the rabbit. Newton and Egli (1958) studied the effect of intranasal oxytocin in lactating women. Baumgarten and Hofhansl (1959) and Baumgarten and Watzek (1959) showed that the intranasal administration of oxytocin induced ejection of milk within 70 seconds of inhaling five international units, and also that it was effective in relieving engorgement of the breasts. Hollenbach (1959), Stewart and Nelson (1959), and Wenner (1959) have all used the spray with good effect in the management of breast-feeding. Hendricks and Gabel (1960) have used intranasal oxytocin for the induction of labour.

This report of a double-blind trial is the first to appear in this country concerning the intranasal use of synthetic oxytocin in the management of breast-feeding.

Plan of the Trial

Primigravidae with normally protractile nipples, who had been delivered spontaneously of normal healthy infants, were selected for the trial. No twin pregnancies were included. The selection of patients was designed to exclude variables which might otherwise have occurred as the result of difficulty in establishing breast-feeding because of poor nipples or because the mother or the baby was ill. Fifty patients were issued with a nasal spray, which contained either synthetic oxytocin ("syntocinon") or an inert placebo solution with the same physical characteristics. The solutions were contained in small bottles at a pressure of one atmosphere and they were stored at 4° C. After inserting the nozzle of the spray into one nostril and occluding the other, it was operated by depressing the wings of the nozzle so that a fine spray of the contained solution could be inhaled. The active sprays contained approximately 5 ml. of a solution of oxytocin at a concentration of 40 I.U./ml. By depressing the nozzle while counting "one" and inhaling once the patient inhaled 4–5 I.U. of synthetic oxytocin.

Twenty-five sprays containing synthetic oxytocin and 25 containing the placebo were randomly issued to the selected patients, so that the contents of each bottle were unknown both to the patients and to the observer. The patients were instructed to inhale once from the spray about two to five minutes before starting each feed; treatment began with the first feed on the second day after delivery and continued until the contents of the bottle were exhausted.

Infants were put to the breast at three-hourly intervals for the first 48 hours after delivery; thereafter, in most cases, the time between feeds was extended to four-hourly intervals. Routine expression of the breasts, either before or after feeding, was not practised. Oestrogens were not given routinely, but only to patients who developed early engorgement of the breasts; in these cases 5 mg. of stilboestrol was given by mouth, and this dose was repeated if necessary.

Results

The results of treatment were evaluated by assessing the incidence of breast engorgement in the two groups, as judged by clinical observation and the necessity for the use of either oestrogens and/or analgesics. Two types of breast engorgement were distinguished, early (vascular) and late (milk) (Douglas *et al.*, 1957). These are distinct entities, the discomfort experienced by the patient is much the same, but the time of onset, cause, and treatment are vastly different. Engorgement was assessed arbitrarily. I examined the breasts each day and awarded a score for the degree of engorgement observed—that is, 0, +, ++, +++, ++++. In addition, the maximum loss of weight, the amount of weight gained since birth and the day of discharge or the tenth day after delivery (whichever was earlier), and the average size of feeds measured by test-weighing on the seventh day were recorded for each baby in the series.

One patient was rejected from the group using oxytocin because the baby was ill and could not be put to the breast; one patient issued with placebo spray was excluded from the trial because she failed to use it. Thus there were 24 patients in each group, and analysis of these groups showed that they were almost exactly comparable with regard to sex and weight distribution of the babies and also with regard to maternal age and the duration of pregnancy (Table I). The average length of use of the oxytocin spray was 70 hours (before 14 feeds) and of the placebo spray 78 hours (before 16 feeds).

No significant difference was found between the incidence of early breast engorgement in the treated and control groups. Two patients receiving oxytocin required stilboestrol for early engorgement and one other patient needed an analgesic (tab. codein. co.) for the same reason. Only one patient using the placebo spray was treated for early engorgement. There was no case of late breast engorgement in either group (Table II).

TABLE I.—*Distribution of Mothers and Babies Within the Treated and Control Groups*

Spray	No. of Patients in Each Group	Average Age of Patients (Range)	Duration of Pregnancy in Weeks	Ratio of Male to Female Infants	Average Weight of Babies (Range)	
					lb. oz.	g.
Oxytocin ..	24	23 (18–33)	37–42	11 : 13	7 1½ (5·7–8·6)	3,218 (2,585–3,900)
Placebo ..	24	24 (16–37)	38–42	13 : 11	7 2 (5·3–9·1)	3,232 (2,394–4,128)

TABLE II.—*Incidence of Breast Complications in the Treated and Control Groups* (24 *Patients in Each Group*)

Spray	No. of Patients with Breast Engorgement			No. Supervised with Feeding	Lactation Suppressed	Breast Abscess
	Early	Late	Requiring Treatment			
Oxytocin ..	7	—	3	—	2	—
Placebo ..	5	—	1	6	8	1
Significance* (P<0·05)	0·5	—	0·25	0·02	0·05–0·02	0·5

* Statistical significance was calculated by comparing the samples using the χ^2 distribution.

TABLE III.—*Average Loss and Gain in Weight and the Size of Feeds Taken by Babies of Mothers in the Treated and Control Groups* (*There were* 24 *Patients in Each Group*)

Spray	Average Weight Loss on 4th day		Average Size of Feed on 7th day		Total Weight Gain from Birth until Discharge or 10th day	
	oz.	g.	oz.	g.	oz.	g.
Oxytocin	5·0	142	3·4	97	1·2	34
Placebo	7·3	207	2·3	65	0·8	23
Significance* (P<0·05)	0·02–0·01		<0·001		0·2–0·1	

* Statistical significance was calculated by estimating the standard deviation of the difference of the means and applying the t-test.

The amount of supervision given by the midwives to patients during breast-feeding on the fifth day was noted. None of the patients using oxytocin required supervision, whereas six of those using the placebo needed some help. This difference is statistically significant (P=0.02). Two patients using the synthetic oxytocin spray had lactation suppressed—one because of insufficient lactation and the other because of persistently cracked nipples; whereas eight of the patients using the placebo spray had lactation suppressed—six because it was insufficient, one because of sore nipples, and the other on the fourth day at the mother's own request. This difference is also within the range of statistical significance (P=0.05–0.02). Only one of the patients in the trial developed a breast abscess; she had used the placebo spray, and it occurred six weeks after delivery.

The babies of mothers who had used the oxytocin spray lost less weight on the fourth day (5 oz.; 142 g.) than the controls (7.3 oz.; 207 g.). Mothers who had been given synthetic oxytocin gave bigger average feeds on the seventh day than those who had used the placebo. The average feed, as measured by test-weighing, was 3.4 oz. (97 g.) in the treated group compared with 2.3 oz. (65 g.) in the control group. The differences between these two sets of observations, and especially the latter, are statistically significant (Table III). Although it is not of statistical significance, there was also a bigger average weight gain, 1.2 oz. (34 g.) in the treated group compared with 0.8 oz. (23 g.) in the control group.

The only side-effect observed was slight bleeding from the nose in one patient after using an oxytocin spray.

Discussion

This small series provides no evidence that the regular intranasal use of synthetic oxytocin from the second day of the puerperium had any effect in reducing the incidence of breast engorgement. The galactokinetic effect of oxytocin could only be expected to affect the incidence of late engorgement, which is due to the breasts being full of milk that will not flow freely. The majority of patients had finished their sprays by the fifth day, before the expected time of onset of milk-engorgement in primiparae; and, as in theory oxytocin should have no effect in early or vascular engorgement, the negative evidence of the trial in this respect is therefore not surprising and no conclusions can be drawn from it. To observe the effects of oxytocin in the treatment of late breast engorgement the spray would have to be used either later in the puerperium or for a much longer period of time.

The significant reduction in the number of patients in whom lactation was suppressed and who required supervision with breast-feeding in the treated group suggests that the regular intranasal use of synthetic oxytocin did have some effect in rendering the establishment of breast-feeding easier and more successful. This was also reflected in the behaviour of the babies whose mothers had received oxytocin—namely, the smaller average loss in weight and the bigger average test feeds.

Two explanations are possible to account for the greater ease in the establishment of breast-feeding and the improved milk production. The first is that the regular intranasal use of oxytocin ensured more complete, more rapid, and easier emptying of the breast by the baby. From our clinical observations this certainly occurred, and was undoubtedly the result of oxytocin provoking and enhancing the ejection of milk; the more efficient emptying of the breast might then have led secondarily to a greater secretion of milk (Cross, 1957). The other explanation is that oxytocin exerts a galactopoietic as well as a galactokinetic effect (Benson and Folley, 1956a). Benson and Folley (1956b, 1957) and Benson *et al.* (1960) have shown that oxytocin retards mammary involution in rats; and other workers (Ôta and Yokoyama, 1958) have also postulated that oxytocin released in the puerperium in response to suckling exerts a central effect, as well as a local and peripheral action—that is, the initiation of milk-ejection—by stimulating the

release of prolactin from the anterior pituitary gland. Further clinical and experimental work is necessary to elucidate the role of oxytocin in this respect.

Summary

Oxytocin was regularly administered by means of a nasal spray to primiparae from the second day of the puerperium. No serious side-effects were noted. The use of the spray resulted in the easier establishment of breast-feeding and in an improvement of milk production. No significant reduction in the incidence of early breast engorgement was obtained. Nasal oxytocin has a place in the management of lactation and breast-feeding, but further work is necessary to define its usefulness more exactly and to elucidate the underlying physiological mechanisms.

I thank the midwives of Charing Cross Hospital for their invaluable co-operation, and Professor Norman Morris for his encouragement and for allowing me to carry out this trial on his patients. I am grateful to Dr. H. Holgate, of Sandoz Products Ltd., for providing me with the nasal sprays containing "syntocinon" and the placebo.

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A joint meeting of the two main committees of the 14th World Health Assembly has received a report which states that, out of 1,336m. people in currently or formerly malarious areas, 298m., or 22.3%, are now living in areas where malaria has been eradicated, while over 612m., 45.9%, are covered by malaria eradication programmes. Preliminary malaria eradication activities (pre-eradication surveys and pilot projects) are now under way in areas containing a population of 170m., 12.7%. A population of 255m., 19.1%, is still living in areas where no eradication scheme has been planned. The report points out that a number of malaria eradication programmes have not progressed according to schedule, for technical, operational or administrative reasons, and "experience has shown that, while it is relatively easy to find solutions to technical and operational shortcomings, it is much more difficult to correct administrative imperfections."

PREVALENCE AND NATURAL HISTORY OF ASTHMA IN SCHOOLCHILDREN

BY

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Information regarding the prevalence of asthma in children is not extensive. Logan and Cushion (1958) reported that in a number of general practices in England and Wales, 1.23% of boys and 0.64% of girls under 15 years were known to have asthma. These figures are likely to be below the true prevalence of the condition, since many children receive no treatment from the family doctor either because the condition is mild or because remedies are obtained elsewhere. In Bergen, Eilertsen (1954) found a prevalence of 1.77% in children of 7, and in Stockholm, Kraepelien (1954) found an overall prevalence in children of 7 to 14 of 1.37%, which fell from 1.61% in those aged 7 to 0.87% in those aged 14. Neither of the Scandinavian authors separated the sexes.

An asthma clinic for schoolchildren within the school health service was started in Birmingham in 1953, and in 1956 an attempt was begun to study the prevalence of asthma in schoolchildren in the city. The investigation was undertaken with the assistance of the school medical officers and was carried out during the 12 months from September, 1956, to October, 1957.

Method of Investigation

Schoolchildren in Birmingham are examined at three routine medical inspections. The first is normally during the first year at school when they are 5 or 6, the second is five years later when they are 10 or 11, and the final inspection is just before they leave school and they are then 13 to 15. The school medical officers were asked to identify and record all children with asthma, as defined in the protocol, found at these medical inspections and to make inquiries regarding asthma in all children who, because of sickness or for any other reason, were not at the medical inspection but were on the nominal roll of those due for examination at that time. Care was also taken to find out which children in special schools, residential and non-residential, suffered from asthma among those in the age-groups used for medical inspections. It was felt necessary to make specific inquiry in the case of each child regarding the presence of asthma. As already mentioned, the condition may give rise to no serious distress in children mildly affected and to no loss of school time.

For the purpose of the investigation "asthma" was defined simply as recurrent wheezing and dyspnoea not known to be of extrapulmonary origin. At first sight this definition might appear too simple, but from experience it was known that a mistake in a positive diagnosis of asthma in children of school age is extremely rare. In over 500 cases referred to the asthma clinic by a large number of practitioners none had been mistaken. Such confidence in the diagnosis would not be possible in younger children or in adults. The diagnosis was checked in the first 173 cases reported in