THE VALUE OF SPARTEINE SULPHATE* AS AN OXYTOCIC

A PRELIMINARY REPORT†

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Since Dale's discovery in 1906[1] of the effect of posterior pituitary extract on the uterus, followed by the use of pituitrin as an oxytocic by Blair Bell[2] in 1909, very little progress was made in this field until the posterior pituitary extract was separated into two factors by Kamm *et al.*[3] in 1928, resulting in the isolation of pitocin. This major break-through in obstetric therapy was further assisted by the isolation of a pure oxytocin from animal pituitary glands by Livermore and Du Vigneaud[4] in 1949. Oxytocin was subsequently synthesized by Du Vigneaud *et al.*[5]

The satisfactory role of oxytocin in obstetrics has been extensively investigated and reported, and needs no repetition. However, the use of intravenous oxytocin has the disadvantage of confining the patient to bed, requiring constant supervision and regulation of the drip speed, and has the potential risk of producing uterine tetany, with the danger of foetal asphyxia, accidental haemorrhage, and possible rupture of the uterus. Furthermore, oxytocin is not universally successful in its action, and unpleasant side-effects are known. In an attempt to ease the patient's discomfort, different methods of oxytocin administration (sublingual, transbuccal and intranasal)[6-10] have been used. The dangers of oxytocin are not decreased by changing the method of administration,[11] and the control of the drug is considerably more difficult when given intranasally than by the intravenous route.[9]

In view of the recent favourable reports on the use of sparteine sulphate as an oxytocic[12-14] it was decided to undertake a double-blind trial of this drug in order to assess: (1) its clinical value in the induction of labour, (2) its effect in hypotonic inertia, (3) its safety, both for mother and foetus, and (4) a satisfactory dosage scheme. Although it was not primarily intended to make a comparison between sparteine sulphate and other methods of induction, viz. medical induction (castor oil, bath and enema), artificial rupture of the membranes, or intravenous oxytocin, it eventually became evident that if sparteine sulphate (or placebo) did not achieve its purpose another form of oxytocic would be necessary and a comparative assessment would thus become possible in some cases.

PHARMACOLOGY OF SPARTEINE

Sparteine (Fig. 1) was discovered in 1852 by Stenhouse,[15] in the flowering tops of broom, *Sarothamnus scoparius*. It has also been found in the seeds of various species of lupin, whose alkaloids are identical with sparteine. Laborde[16] (1885) was the first to announce that, in the frog, sparteine caused an increase in the strength of the heartbeat with a decrease in its rate. Attention was subsequently focused primarily on the effect of sparteine on the heart. In 1895 Cushny and Matthews[17] suggested that the principal action of sparteine was similar to that of curare in frogs and mammals, producing paralysis of the motor nerve ends. The slowing of the heart rate was

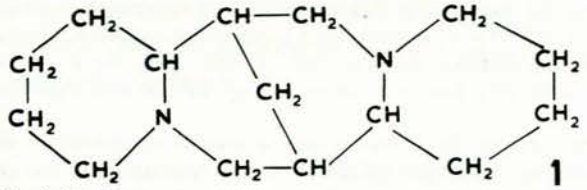

Fig. 1. Sparteine.

thought to be due to a direct action on the heart muscle and a weak paralysing action on the vagus. Heathcote[18] reviewed the pharmacological action on different organs of various experimental animals. Of interest was the effect on the uterus of the rabbit and guinea-pig, in which it produced a rise of tone and an initiation of rhythmical contractions, which were unchanged by atropine. Adrenaline given after sparteine caused relaxation in the guinea-pig uterus. In the dog, a dose of 30 mg. per kg. body weight produced a cessation of respiratory movement. It was concluded that, in addition to its curare-like action on the motor nerve ends, sparteine also paralysed the central nervous system and parasympathetic ganglion cells. It had no direct action on striated muscle, but initially depressed and then stimulated plain muscle of the intestine. Cardiac muscle fibres were considerably depressed at first but recovered soon afterwards. In this respect it resembled the action of quinidine. Lu[19] showed that it caused a slowing of the heart rate and reduction in contractility, prevented and arrested auricular fibrillation, and abolished ventricular extrasystoles. In the treatment of arrhythmias it is less toxic as well as less effective than quinidine, by which it has been superseded for this purpose. The effect of sparteine on the blood pressure of the dog is fleeting, even after large doses. In general, it appears to have a parasympathetic inhibitory action on the smooth muscle of the gastro-intestinal tract. Further effects of sparteine on the motility of the isolated rabbit uterus were reported by Ligon,[20] who demonstrated that in the presence of contractions there was an increase in amplitude, rate, or tone. In higher concentrations this was followed by depression of amplitude or rate, with or without a decrease in the tone towards the original level. There was no qualitative difference in the effect on the uterus of the virgin, rutting or pregnant rabbit, but the magnitude was greatest in the pregnant doe and least in the virgin. The pregnant uterus responded selectively to smaller doses than those used in the treatment of cardiac disease. Uterine tetany was not produced even after a tenfold increase in the concentration of sparteine.[21]

*'Synastrin' (Petersen Limited).

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The *toxic dosage* of sparteine in experimental animals serves as a means of assessing the minimum lethal dose applicable in the human. 3 - 6 G. is quoted as the MLD for an average 130 lb. person.[12] The average clinical dose varies between 150 and 300 mg., and the MLD is 20 - 40 times as great. A dosage of 300 mg. given intravenously produces dizziness, palpitations, and tingling of the hands and fingers. The skin becomes moist, and perspiration profuse. These effects appear within a few minutes after the injection and disappear gradually over the next few hours. Repeated small doses are apparently harmless; 2·5 G. has been given within 24 hours to a patient in labour.[22] No toxic effects have been noticed on the foetus.

MATERIAL, METHOD AND RESULTS

A double-blind study was carried out on a group of pregnant patients admitted to the New Somerset Hospital, Cape Town. A preliminary trial with sparteine sulphate only (not included in the present statistical evaluation) was conducted on 30 patients. The satisfactory results obtained led to the present study based on 125 patients, 75 of whom received sparteine sulphate, while 35 received placebo with or without another form of oxytocic; 15 patients were excluded because their records were inadequate. The difference between the numbers in the two groups is explained by the fact that patients who did not respond were given further courses of treatment that subsequently were shown to be sparteine-sulphate courses. The indications for the use of the drug were divided broadly into two, viz. *induction of labour* and *hypotonic inertia.*

Before the drug was given, a vaginal examination was made to determine effacement and dilatation of the cervix. For the purpose of this study, a cervix was regarded as uneffaced if judged to be more than 1 cm. in thickness. The membranes were neither stripped nor ruptured, nor was the cervix stretched. All medical inductions were recorded.

Initially a course of 4 intramuscular injections of either placebo or sparteine sulphate, chosen at random, was given at hourly intervals. Each sparteine ampoule contained 1 ml. of fluid with 150 mg. of sparteine sulphate dissolved in sodium chloride to make the solution isotonic. The placebo ampoule contained 0·9% sodium chloride solution. Later in the trial the dosage was changed to 2 injections of 300 mg. of sparteine sulphate given at an interval of 2 hours. The course was discontinued once labour was established. A full course was often given unnecessarily and the total dosage frequently exceeded the requirements. The numbered ampoules (the contents being unknown) were recorded. No special attention was given to the patients. A detailed recording of the frequency and duration of the uterine contractions was made and all sedation given was recorded. Patients in whom an urgent indication for induction of labour existed could not be included in this series, since one had no means of knowing whether sparteine sulphate or placebo was being used.

A. Induction of Labour

In this group the following interpretations were made:
1. If labour was induced and established *within 6 hours* after the first injection it was considered a *success.*
2. If labour was induced and established *between 6 and 12 hours* after the first injection it was considered a successful result but a *poor response.*
3. If labour followed *more than 12 hours* after the first injection, or not at all, it was considered a *failure.*

In cases in which intravenous oxytocin or artificial rupture of the membranes was employed in addition to the trial substance, similar interpretations were made relative to the method employed.

The various indications for induction of labour in which sparteine sulphate was used are listed in Table I (there were 52 patients who received 63 courses of sparteine sulphate).

TABLE I. INDICATIONS FOR INDUCTION OF LABOUR WITH SPARTEINE SULPHATE

Primary indication	*Courses of sparteine*	*Associated with another indication (courses of sparteine)*
1. Pre-eclamptic toxaemia / Essential hypertension	15	17
2. Spontaneous rupture of the membranes	13	3
3. Non-response to artificial rupture of the membranes	13	2
4. Elective inductions (mainly in cases of 'false labour')	7	—
5. Postmaturity	5	5
6. Non-response to a previous course of sparteine sulphate	4	8
7. Accidental haemorrhage	2	2
8. Intra-uterine death	2	1
9. Non-response to intravenous oxytocin	2	1
10. Rh.-negative iso-immunization	—	1
	63	40

1. Pre-eclamptic toxaemia and essential hypertension. In this group of 15 cases 10 (two-thirds) were successful. The average sparteine-labour time was 10·7 hours, and if the failures are excluded this time drops to 2·5 hours. None of the successful cases had any associated form of uterine stimulant other than that of medical induction (5 cases), and this was given at least 18 hours before the sparteine sulphate with no resultant effect. In the 5 failures the cervices were uneffaced and the ostia either tightly closed or merely multiparous. Conversely, in the successful cases the cervices were effaced and about 2-fingers dilated. There did not appear to be any correlation between the severity of the condition and the response to sparteine, nor did the period of gestation seem to make any difference. All 3 primiparae in this group ended as failures, a fact that seems to be related to their cervical status.

2. Spontaneous rupture of the membranes. The conservative management of these cases presents a controversial problem. Ascending intra-uterine infection is dangerous to mother and child, and often these patients cannot be kept in hospital for any length of time. As part of our policy it was decided that if the foetus appeared to be reasonable in size there was no point in procrastinating, and immediate steps were taken to induce labour in these patients. The effect of sparteine sulphate was extremely gratifying; it was a success in every one of the 13 cases treated. The average sparteine-labour time was 2·7 hours. In every case except one, the membranes had been ruptured for over 12 hours with no labour ensuing. The

TABLE II. DURATION-OF-LABOUR AND INDUCTION-TIME RELATIONS BETWEEN SPARTEINE SULPHATE AND PLACEBO IN CASES OF SPONTANEOUS RUPTURE OF THE MEMBRANES

	Duration of labour (hr)		*S-labour time (hr)*	*P-labour time (hr)*
	S	*P*		
Average	10·9	13	2·7	28·9
Range	½ - 37½	2 - 34	½ - 5½	1 - 125½

S=sparteine sulphate, and P=placebo (also in Tables III and IV).

average duration of labour was 10·9 hours. It may be argued that had these cases been left alone long enough they might have gone into labour spontaneously; but in the placebo group only 2 cases were delivered without the assistance of an oxytocin drip, the membranes in both these cases having been ruptured for over 4 days before the placebo was administered. The average placebo-labour

TABLE III. DILATATION OF THE CERVIX IN CASES OF SPONTANEOUS RUPTURE OF THE MEMBRANES, TREATED WITH SPARTEINE SULPHATE OR PLACEBO

Dilatation of cervix	*No. of cases*	
	S	*P*
1 finger	5	0
2 fingers	5	6
Over 2 fingers	3	0

time was 28·9 hours in spite of the assistance of oxytocin drips, and the average duration of labour was 13 hours (Table II). In spite of the small numbers concerned, the distribution of age, parity and gestation period was fairly similar in the sparteine and the placebo groups, and forms a satisfactory means of comparison. The satisfactory outcome in these spontaneous-rupture cases may be attributable to the favourable cervical status (Table III), a factor that does not necessarily result in an early onset of labour but definitely appears to improve the chance of obtaining a satisfactory response with sparteine sulphate.

3. Non-response to surgical induction of labour. In this group the response to treatment with sparteine sulphate was not very encouraging. There were 12 patients, who were given 13 courses, with only 7 successes (± one-half). Four of the 6 failures required prolonged oxytocin drips to complete labour. Considering that these patients had had medical as well as surgical attempts at induction in addition to sparteine sulphate, the poor response to intravenous oxytocin labels them as extremely refractory to induction therapy. They were all less than 36-weeks pregnant, with undilated and uneffaced cervices. Judging from the cases that responded, it would appear that, providing the os is more than 1-finger dilated, there is a reasonable chance of sparteine sulphate being effective. In the successful cases the average sparteine-labour time was 2·7 hours, with a preceding average surgical induction-sparteine time of 10·5 hours. It is difficult to assess to what extent the preceding surgical induction assisted in producing a favourable response in the successful cases. However, this does not alter the management of these cases for, should there be no response within a limited time, sparteine sulphate can be given with a reasonable chance of success, provided the cervical status is satisfactory. If there is no response to sparteine sulphate a poor response can be anticipated with intravenous oxytocin as well.

4. Elective induction of labour (mainly associated with 'false labour'). A fair number of patients are admitted to the labour ward with a history of having had prolonged, vague or intermittent contractions before admission. If observation fails to establish the presence of contractions after 24 hours, these patients, not being in labour, are discharged. Some of them are subsequently readmitted with a similar story. The inconvenience to the mother as well as to the labour-ward staff is but one aspect of this problem, which sometimes has a demoralizing effect on the patient eventually. In these cases we used sparteine sulphate as a 'trial of induction', provided the foetus appeared to be of satisfactory size. No preceding medical inductions were given. In our 7 cases, 4 responded initially (i.e. success in ± one-half), while 2 more responded within 2 hours when given a second course about 24 hours later. The average sparteine-labour time in these cases was 2·7 hours. The remaining case was left alone and came into labour spontaneously 62 hours after the course of sparteine sulphate. As in the groups mentioned above, the failures occurred in patients whose cervices were not favourable for induction.

5. Postmaturity. Three of the 4 cases induced primarily for postmaturity responded within 2 - 7 hours (average 4·3 hours). The fourth case was given a second course of sparteine 12 hours later and went into labour within 2 hours. If in addition the cases not primarily induced for postmaturity are taken into account, then there was a successful result in 9 out of 10 cases. In the single unresponsive case a refractory hypotonic inertia required intravenous oxytocin for 57 hours before delivery. These good results can possibly be associated with the fact that 70% of cervices were effaced. The presence of intact membranes in 7 of the cases did not affect the outcome adversely.

6. Accidental haemorrhage (no. 7 in Table I). Only 2 cases were treated, and both responded favourably.

7. Intra-uterine death (no. 8 in Table I). No valid conclusions can be drawn from this small series of 3 cases, in which one case responded promptly, another after 8 hours, and the third not at all. Only 2 of them were induced primarily because of intra-uterine death.

8. Non-response to intravenous oxytocin (no. 9 in Table I). It seemed highly unlikely that sparteine sulphate would be successful after a failure of induction with intravenous oxytocin. In the 3 cases included in this series (all primigravidae) there was a poor response to oxytocin in spite of prolonged administration, the contractions disappearing when the drips were turned off. All three cases responded to sparteine sulphate, one after a single injection of 150 mg. It is debatable whether these cases would have responded to sparteine sulphate *per se,* and it would seem reasonable to postulate a complementary effect on the part of sparteine sulphate on a uterus previously primed by oxytocin.

B. Hypotonic Inertia

Patients with hypotonic inertia rarely require any interference in the first 12 - 18 hours of their labour, but as time goes by without any satisfactory increase in cervical dilatation a form of oxytocic stimulant becomes desirable. As an alternative to artificial rupture of the membranes or an oxytocin drip, it was decided to use sparteine sul-

phate. In general the drug was used in hypotonic inertia in the following two groups of circumstances:

1. More than 12 hours since the onset of labour, with the cervical os still less than 2-fingers dilated.
2. Poor but definite contractions present, with no appreciable increase in cervical dilatation over the preceding 6 hours, the cervix being more than 2-fingers dilated.

Gross disproportion was excluded before any patient was taken into the series. A precise definition of success relative to the sparteine-delivery interval was extremely difficult in view of the variation in cervical dilatation and preceding duration of labour in each case. The assessment of a successful response was thus based on the clinical observation of a definite improvement in contractions after injection of the trial substance, together with an assessed increase in cervical dilatation.

Of the 22 cases of hypotonic inertia treated with sparteine sulphate, 16 (about three-quarters) showed an appreciable improvement. The effect of sparteine sulphate in

TABLE IV. LABOUR RELATIONSHIPS BETWEEN SPARTEINE SULPHATE AND PLACEBO IN HYPOTONIC INERTIA

Labour-S time (hr)	*Labour-P time (hr)*	*S-delivery time (hr)*	*P-D time (hr)*	*Duration of L (hr.) S*	*P*
19·4	18·1	9·1	16 0	28·5	34·2

L=labour, and D=delivery.

shortening these labours is illustrated by comparing it with the placebo group (Table IV). In order to exclude the effect of other oxytocic methods, only those cases that had received nothing but sparteine sulphate or placebo are

TABLE V. DILATATION OF CERVIX IN CASES OF HYPOTONIC INERTIA TREATED WITH SPARTEINE SULPHATE AND PLACEBO

Dilatation of cervix	*Sparteine*	*Placebo*
2 fingers and under	8	5
Over 2 fingers	4	4

compared. In these 2 grossly similar groups the duration of labour was shortened by about 6 hours (Table V).

Failures

Of the 75 patients treated with sparteine sulphate, 22 were failures (29·3%). In terms of courses of sparteine sulphate, in the 87 courses given there were 25 failures (28·7%). The indications for treatment in the unsuccessful cases are listed in Table VI.

TABLE VI. SPARTEINE-SULPHATE FAILURES ACCORDING TO INDICATIONS FOR ITS USE

Indication	*Courses of sparteine*	*Failures*	*% Failures*
1. Pre-eclampsia and hypertension	15	5	33·3
2. Spontaneous rupture of membranes	13	0	0
3. Non-response to surgical induction	13	6	46·1
4. Elective inductions ...	7	3	42·8
5. Postmaturity	5	1	20·0
6. Non-response to sparteine	4	2	50 0
7. Accidental haemorrhage	2	0	0
8. Intra-uterine death	2	1	50·0
9. Non-response to intravenous oxytocin	2	0	0
10. Hypotonic inertia	23	6	26·1
11. Hypertonic inertia	1	1	100·0

A distinct relation exists between the duration of pregnancy and the incidence of failures. The earlier in pregnancy the drug was used, the smaller was its chance of being successful (Table VII). The failures are likewise re-

TABLE VII. RELATION OF SPARTEINE-SULPHATE FAILURES TO PERIOD OF GESTATION

Duration of pregnancy (wk)	*Cases*	*Failures*	*% Failures*
Under 36	11	6	54·5
36 - 41	54	14	25·9
42 and over	10	2	20·0

lated to the degree of cervical dilatation (Table VIII) and effacement (in the failures 19 cervices were uneffaced and 3 effaced). In the cases that did not respond to sparteine sulphate and were subsequently treated with intravenous oxytocin or by surgical rupture of the membranes, the various responses are indicated in Table IX. Intravenous oxytocin did not produce as good a response as one would

TABLE VIII. RELATION OF SPARTEINE-SULPHATE FAILURES TO CERVICAL DILATATION

Dilatation of cervix	*Cases*	*Failures*	*% Failures*
Os closed	8	6	75·0
1 finger	26	9	34·6
1½ fingers	19	4	21·0
2 fingers	17	3	17·6
Over 2 fingers	5	0	0

have expected. Of 6 cases not treated by either oxytocin or rupture of the membranes, 4 cases responded to a second course of sparteine sulphate and the remaining 2 cases were delivered after 29 and 62 hours respectively, without any additional oxytocic procedure. By definition these cases must be considered as failures, but from the practical point of view the first 4 could really be con-

TABLE IX. RESPONSE TO INTRAVENOUS OXYTOCIN OR SURGICAL INDUCTION IN CASES THAT FAILED AFTER SPARTEINE SULPHATE

Response	*Intravenous oxytocin*	*Surgical induction*
Good	4	2
Poor	8	4
Failure	—	—

sidered as successes. In the last 2 cases sparteine sulphate should have been repeated to expedite delivery. As labour was induced in both these cases, it would be reasonable to accept the inductions as successful in spite of the delayed onset of labour that requires them to be classified as failures. If these 6 cases are not counted as failures the incidence of failures drops from 29·3% to 21·3%.

Maternal Complications

(*a*) *Pre-eclamptic toxaemia and essential hypertension.* This constituted the only significant antepartum complication among the patients treated with sparteine (32 out of 75 cases—42·7%). None of the patients showed any aggravation of the condition in response to sparteine sulphate. Fleeting minor elevations of blood pressure were recorded but no direct causal relationship could be established. There were 5 patients with blood pressures over 180/120 mm.Hg. Their condition remained satisfactory throughout. Although Kraus[23] and Reist[24] were against

using sparteine sulphate in this type of case, judging from the fairly large number of cases presented there does not appear to be any contraindication.

(*b*) *Blood loss*. Sparteine sulphate was not given in the third stage in this series. Other authors have reported on its use in the postpartum period. [12,14,23] It would appear to have an immediate but not sustained uterotonic effect.[12] Whether its use in the first stage affected subsequent postpartum bleeding it was not possible to determine, for it was a routine to use oxytocics either with the birth of the anterior shoulder or after the third stage. Postpartum haemorrhage occurred in 5 cases of this series, 3 being due to a relaxing uterus and one associated with a caesarean section and the fifth with an incomplete rupture of the uterus (details follow). The incidence of postpartum haemorrhage (6·6%) compares well with the general rate for the obstetrical wards of the hospital (6%).

(c) *Incomplete rupture of the uterus*. It is considered that this case should be reported in some detail. The patient was a 30-year-old gravida-7, para-4, and had had a caesarean section for placenta praevia 3 years before. She was admitted at 38 weeks, the membranes having ruptured spontaneously. Her blood pressure was 105/60 mm.Hg. She was given a course of injections (placebo) with no effect, and 13 hours later she was given a second course of injections (sparteine sulphate). Labour started within 1 hour. Only two injections were given, because she felt 'queer and dizzy' soon after the contractions commenced. No drop in blood pressure occurred but there was a slight elevation in the pulse rate. The contractions became weaker and then stopped; and 13 hours later a third course of injections (sparteine sulphate) was given. Contractions started soon afterwards and continued until the delivery 6½ hours later of a 6½ lb. live male infant (Apgar 9). After delivery the patient had a postpartum haemorrhage of 30 oz. The uterus was explored and an incomplete rupture found. Laparotomy and subtotal hysterectomy were performed. The possibility of sparteine sulphate having been instrumental in causing the rupture needs to be considered. At no stage did the patient get severe hypertonic contractions, and the absence of antepartum bleeding would suggest that the rupture occurred shortly before delivery rather than soon after the first injection of sparteine sulphate. There appears to be enough circumstantial evidence for postulating that her uterus might also have ruptured after a spontaneous onset of labour.

(d) *Side-effects*. Two patients complained of giddiness and slight nausea after receiving the injections. Subsequent analysis showed that one of these two had received placebo. The incidence of side-effects was absolutely minimal.

Foetal Complications

It is most important to exclude the possibility of the drug being responsible for foetal complications. Only four cases of foetal distress were recorded in this series. Two of these babies were delivered with forceps; their signs of distress were first noticed towards the end of the first stage of labour associated with a degree of cephalopelvic disproportion. The other cases were both associated with prolonged labours, ultimately terminated in one case by caesarean section. Besides these four, two more babies were born with Apgar ratings of less than 7, one badly distressed, being born with the cord tightly wound around its neck, and the other delivered by caesarean section because of an elbow presentation. The signs of foetal distress were in each case attributable to obvious obstetric complications and the sparteine sulphate could not be incriminated. Four dead babies were born in this series, three as the result of intra-uterine death and the fourth with a prolapse of the cord. Two neonatal deaths occurred, both in small premature babies some days after birth.

DISCUSSION

The action of sparteine sulphate as an oxytocic has been demonstrated recently *in vivo*[25] and *in vitro*.[26-28] These studies are to some extent confirmed clinically by the present trial. The apparent high rate of failures (29·3%) is by no means discouraging and can be attributed partly to the strict criteria for success adopted and partly to the wide variety of cases used. An analysis of the failures should make it possible to be more selective in the choice of cases in future, ensuring a higher rate of success. It would appear that the cervix that is uneffaced and tightly closed (generally considered as 'unripe') is the most unlikely to be affected by sparteine sulphate. On the other hand, if the cervical os is dilated to about two fingers and the cervix effaced, the response should be good in most cases. An adverse response is not confined to sparteine sulphate, but is often encountered with intravenous oxytocin and even more frequently after surgical induction. If it is urgently necessary to terminate labour when the cervix is unripe, it is best not to use sparteine sulphate in view of the rather small chance of its being successful. However, if there is no urgency, sparteine sulphate may be preferable to other methods in that it avoids the predicament of ruptured membranes in a patient not in labour. Likewise, an unsuccessful response to induction with intravenous oxytocin forces one into either resorting to caesarean section or else subjecting the patient to repeated oxytocin drips, a procedure which is by no means pleasant, is potentially hazardous, and often achieves little but an undermining of the patient's morale. Failure with sparteine sulphate still allows one the choice of any of the other available oxytocic methods, with nothing but a delay of a few hours as the price to pay.

The delay in the onset of labour reported in some cases raises this question: After what period of time can one consider sparteine sulphate as having failed, and thus the use indicated of either another course or a different oxytocic procedure? The average sparteine-labour time in the successful cases was 2·6 hours, with a distribution range of ½ - 7 hours (Table X). Based on these figures, our working rule is to wait up to 6 hours before considering the sparteine to have failed.

TABLE X. AVERAGE SPARTEINE-LABOUR TIMES ASSOCIATED WITH VARIOUS INDICATIONS FOR INDUCTION OF LABOUR

Indication	*Average sparteine-labour time (hr)*	*Distribution range (hr)*
Pre-eclampsia; hypertension	2·5	½ - 4½
Spontaneous rupture of membranes	2·7	½ - 5½
Non-response to surgical induction	2·7	1 - 5
Elective induction	2·7	½ - 4
Postmaturity	4·3	2 - 7
Accidental haemorrhage	1·0	1
All groups	2·6	½ - 7

Satisfactory evidence that sparteine sulphate can improve the progress of an inert *hypotonic labour* is given

by a comparison of the labour times associated with sparteine sulphate on the one hand and placebo on the other. The shortening of labour by about 6 hours is highly significant (Table IV). Clinically, what was previously a slow, desultory labour, with poor and irregular contractions, was changed into a labour that in all respects resembled the normal, having good and regular contractions and an adequate rest phase between contractions.

Evidence of its *safety* as an oxytocic drug comes from the absence of harmful effects on both mother and child. No ill-effects could be attributed to the drug throughout the trial, and these are the findings recorded by other authors as well.[12-14,29,30] It did not cause perceptible tetanic contractions of the uterus in any of the cases in this series, and very few instances were found in the literature in which such an effect was observed in the dosages commonly used.[12,27,28] As regards the baby, there was no evidence of sparteine sulphate having been responsible for any adverse effects. In general, both the maternal and foetal complications recorded were in keeping with those found under usual circumstances in an obstetric service of the kind in which the trial was conducted.

As regards *dosage*, there is much scope for individual variation. Most of the cases had 4 injections of 150 mg. at hourly intervals. As stated above, this was often unnecessary, and 3 injections would have been sufficient in over 70% of the cases. It appeared necessary to continue with the injections until labour was established and, as the average time for this seemed to be between 2 and 3 hours, we eventually gave 2 injections of 300 mg. each, with an interval of 2 hours between injections; 14 cases treated in this way all responded successfully. In addition, 7 cases responded after a single injection of 150 mg. In successful cases an average course would appear to be 300 - 600 mg. As much as 1,800 mg. in the course of 24 hours was given to each of three patients, but no toxic effects were noticed.

The virtual absence of side-effects, the safety to both mother and child, and the ease of administration, make sparteine sulphate a most valuable addition in the field of oxytocics. In view of its safety no special nursing or medical supervision is required and in some respects sparteine sulphate can be expected to replace intravenous oxytocin from its hitherto unchallenged position as master oxytocic.

SUMMARY

1. Sparteine sulphate was used in a double-blind trial to assess (a) its clinical value in induction of labour, (b) its effect in hypotonic inertia, (c) its safety with regard to mother and infant and (d) a satisfactory dosage scheme. 75 patients received sparteine sulphate and 35 placebo, with or without another form of oxytocic.

2. In the *induction of labour* group, a response was considered successful if labour occurred within 6 hours, partially successful if within 6 - 12 hours, and unsuccessful if later or not at all. 52 patients requiring 63 courses were included in this group. The average sparteine-labour time was 2 6 hours in the successful cases.

3. The various indications for induction of labour, with the resultant individual responses, are discussed. Pre-eclamptic toxaemia and hypertension, which formed 42·7% of the whole series, was not considered a contraindication to the use of sparteine sulphate.

4. In the *hypotonic inertia* group, the effect of sparteine sulphate was compared with that of the placebo. The average duration of labour was shortened by about 6 hours by using sparteine sulphate.

5. An analysis was made of the various failures. The worst results were obtained in those cases in whom the cervix was 'unripe'. The earlier in pregnancy sparteine sulphate was used, the less likely was it to succeed. Conversely. if the cervix was 'ripe' or the os two fingers or more dilated, the results were invariably good. The total success rate was 70·7%. If those cases that responded to a second course of sparteine sulphate were considered as successes, this figure was increased to 78·7%.

6. Maternal and foetal complications were analysed. Only 5 postpartum haemorrhages occurred in the series (6·6%). This compares well with the general rate of 6% for the obstetrical wards of the hospital. A single case of incomplete rupture of the uterus was associated with the use of sparteine sulphate. No causal relationship was found. Side-effects were virtually absent. Foetal distress occurred in 4 cases, all accounted for by obstetrical reasons not related to the use of sparteine sulphate.

7. In view of its safety to mother and foetus, its virtual absence of side-effects, and ease of administration, together with the fact that no special medical or nursing attention is required after its use, sparteine sulphate is expected to replace intravenous oxytocin in many cases in the future.

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