COMPARATIVE EVALUATION OF 15-5, 15 METHYL PG F 2 ALPHA TROMETHAMINE SALT (CARBOPROST) BY INTRAMUSCULAR ROUTE AND DESAMINOOXYTOCIN AS BUCCAL TABLETS (BUCTOCIN) FOR INDUCTION AND AUGMENTATION OF LABOUR

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SUMMARY

Carboprost by intramuscular route used in 100 patients near term for induction and augmentation of labour, while Desaminooxytocin buccal tablets were used in 65 patients for the same Regular satisfactory uterine contractions were recorded in 31 mts in induction series and 25 mts in augmentation series in group I while in 45 mts and 32 mts in Group II respectively. Average amount of carboprost used for induction is 0.855 ml while it is 0.225 ml for augmentation. In buctocin series average No. of tablets required for induction is 8.28 while for augmentation 7.7 tablets were required. Mean induction delivery internal in carboprost series is 17 hr 31 mts while it is 14 hr 29 mts in buctocin series. Mean augmentation delivery interval is 6 hrs with carboprost while 10 hrs 11 mts with buctocin tablets. Success rate is 100% with carboprost for induction as well as for augmentation while with buctocin it is 61.6% in induction group and 100% in augmentation group. In carboprost series 92% had vaginal deliveries while 8% had Caeserean Section. In buctocin series 97.5 had vaginal delivery while 2.5% had Caesarean Section (taking only successful cases in account). Both drugs are absolutely safe for the mother as well as for foetus if used by trained staff Patients acceptability is very high with buctocin as compared to carboprost (multiple injections are avoided). Carboprost is inexpensive as compared to buctocin due to very small doses to be used.

Introduction

Various methods of induction have been tried with a variable success from time to time. Medical induction with intravenous oxytocin was the method of choice till recent times but, there has been a shift towards use of prostaglandins by different routes and Oxytocin group of

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drugs by other routes than intravenous. Oxytocin group of drugs does not help in ripening of the cervix. A drug which simultaneously decreases cervical resistance and initiates uterine contractions should be an ideal substance for induction of labour in patients, with unfavourable cervix. Studies have revealed that prostaglandins reduce cervical stiffness and increase uterine activity. There are many studies comparing intravenous oxytocin with prostaglandin E as intravenous infusion, vaginal pessaries, oral tablets. In the present series the compounds used are 15S, 15 methyl PG F_2 alpha tromethamine saltmarketed as Carboprost by Upjohn for intramuscular use and desamino oxytocin (as Buctocin by Wanders) as buccal tablets. This prostaglandin compound is made into non-irritating solution for intramuscular and intra-amniotic route produced by modification at C-15 which protects it from inactivation. Desamino oxytocin is a synthetic derivative of oxytocin and differ from it only in the lack of an amino group in position one this compound is not inactivated by Serum oxytocinase specific in pregnancy and by tissue peptidases. That is why activity of D A O is 1.5-2 oxytocin and is readily absorbed from buccal mucosa.

In the present trial we studied and compared the effect of Buccal tablets for induction and augmentation in 65 patients with results of carboprost in 100 patients.

Material and Methods

In all 165 patients were selected for induction and augmentation of labour divided into two categories.

Group I—consisted of 100 patients including 50 for induction and 50 for augmentation by intramuscular 15 S, 15 methyl PGF_2 alpha tromethamine salt.

Group II—includes 65 patients-36 for induction and 29 for augmentation where Desamino oxytocin buccal tablets were used.

Besides indications certain other criteria like age, parity, period of gestation, presentation, position, pelvic findings and absence of contraindications were observed.

All patients were prepared and examined as per performa especially noting the modified bishop inducibility score.

Dosage

Group I—to start with an initial test dose of .05 ml (12.5 ugm) of carboprost was given by intramuscular route and then 0.1-0.3 ml (25-75 ugm) by tuberculin syringe and was repeated at 2-3 hourly intervals depending upon the response of uterine contractions till the time of delivery. Whole nursing staff was trained and educated in this regard so as to avoid any chance of overdosage causing hyperstimulation and problems. If need be one dose was also given after delivery to prevent postpartum haemorrhage.

Group II—Each tablet containing 50 IU of DAO were put transbucally in alternate cheeks every 30 minutes till rhythmic and satisfactory uterine contractions ensued. After that either dose was reduced to half tablets $\frac{1}{2}$ hourly or spacing of tablets increased as need be. The tablet was discontinued if the labour continued to progress favourably. Account was kept on the total tablets used. Maximum of 12 were used.

If patient does not deliver within 36 hours of starting induction it was taken as failure and secondary induction with intravenous oxytocin or carboprost (if buctocin cases) was done after 36 hrs. All the patients were watched very care-

fully. FHS were monitered by Doppler foetal heart detector with special emphasis for any decelerations during or after contractions.

Observations

Observations in the present clinical trial are as follows:

1. *Age*: age pattern is shown in Table I nothing significant.

TABLE I

Age Yrs	Carborpost Total No.	%	Buctocin No.	%
20	4	4	2	3
21-30	86	86	62	95.5
30	10	10	1	1.5

86% in carboprost series and 95.5% in buctocin series are between 20-30 years of age.

2. *Parity*: Distribution of cases according to parity in 2 groups is shown in Table II.

Table II Parity Distribution.

3. Gestational age pattern in both groups is shown in Table III.

Table III—Gestational Age in Both Groups.

TABLE III
Gestational Age in Both Groups

Gest wks	Carboprost Total No.	%	Buctocrin Total No.	%
Upto 37 wks	8	8	2	3.07
37-40	83	83	53	82.8
>8	9	9	10	15.4

It is evident from the above table that there are more patients with gestational age upto 37 weeks in carboprost series while more overdue patients are there in buctocin series.

4. Indications of inductions are shown in Table IV.

TABLE II
Parity Distribution

Parity	Carboprost Induction No.	%	Carboprost Augmentation No.	%	Buctocin Induction No.	%	Buctocin Augmentation No.	%
Primi	36	72	31	62	24	66.6	20	68.9
Multi	14	28	19	38	12	33.3	9	31.02
Total	50	100	50	100	36	100	29	100.1

TABLE IV
Indications for Inductions

Indication	Carboprost No.	%	Buctocin No.	%
Pre-eclamptic toxaemia	29	58	20	55.5
Post dated pregnancy	8	16	7	19.4
H/O bleeding in ANC	2	4	2	5.5
Less foetal movements	7	14	3	8.3
Premature rupture of membranes	2	4	4	11.1
Congenital anomaly	1	2	—	—
Unstable lie	1	2	1	2.7

A number of patients had multiple indications for induction like patients of P E T also had.

Associated factors like decreased foetal movements in 2 patients intrauterine growth retardation in 3 patients in carboprost series.

5. *Modified Bishop Score*: in both groups in relation to parity is shown in Table V.

delivered within 36 hours of buctocin induction while in carboprost series they had long IDI but delivered within 36 hours without needing secondary induction. In carboprost series the 56 hours was taken by a primigravida induced at 34 weeks for anencephaly and at Bishop score of 2. In multigravida the results are comparable in both series.

7. Augmentation delivery interval: in

TABLE V

Bishop score	Carboprost								Buctocin							
	Induction				Augmentation				Induction				Augmentation			
	Prim		Multi		Primi		Multi		Primi		Multi		Primi		Multi	
	No	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
0- 3	9	25	2	14	1	3	—	—	10	42	2	17	2	10	—	—
4- 6	17	47	10	72	9	29	8	42	11	46	7	58	4	20	3	3
7-13	10	28	2	14	21	68	11	58	3	12	3	25	14	70	6	6
Total	36		14		31		19		24		12		20		9	

There were more primigravidas with 0-3 score in buctocin series:

6. *Induction Delivery in Interval*: IDI in relation to parity and Bishop Score have been shown in Table VI.

IDI in primigravida ranges from 14 hours 40 minutes to 35 hours in group 1 and 10 hours 55 minutes to 18 hours in group II.

The figures in carboprost series may appear high but the fact remains that primigravida with low bisop score never

relation to parity and B. score has been shown in Table VII.

The augmentation delivery interval in primigravida ranges between 5 hours 39 minutes to 7 hours 40 minutes in carboprost series and 8 hours 10 minutes to 17 hours 30 minutes in buctocin cases. While in multigravida it is 5 hours 50 minutes to 6 hours 26 minutes and 4 hours 22 minutes to 11 hours 1 minute respectively. Both drugs seem very effective for augmentation of labour.

TABLE VI

Bishop score	Parity	Carboprost			Buctocin		
		No.	Range in Hr. & Mts.	Mean in hr. & mts.	No.	Range in Hrs. & Mts.	Mean in Hrs. & Mts.
0- 3	Primi	9	29-56	35	1	18	18
	Multi	2	8-30	19	2	19.10-23.30	21.20
4- 6	Primi	17	10-30	21	2	9.40-12.10	10.55
	Multi	10	4-11	7.50	3	10.5-21.15	15
7-13	Primi	10	6-22	14.40	—	—	—
	Multi	2	5-9	7	3	3.15-11.14	7.06

TABLE VII

Bishop score Induction	Parity Group	Carboprost No.	Carboprost Range in Hr. & Mrs.	Carboprost Multi in Hr. & Mts.	Buctocin No.	Buctocin Range in Hr. & Mts.	Buctocin Mean in Hr. & Mrs.
0- 3	Primi	0	—	—	1	17.30	17.30
	Multi	0	—	—	0	—	—
4- 6	Primi	9	5-10	7.40	4	3.35-16.20	9.43
	Mean	8	2-10	6.26	4	9.52-12.10	11.01
7-13	Parity	21	1-22	5.39	15	1.16-11.30	8.10
	Multi	11	3-9	5.50	5	2.05-7-30	4.22

8. Interval between administration of drug and onset of regular uterine contractions is shown in Table VIII.

It is evident that labour set in within 1 hour in all cases with group I, while in 75% of the cases in group II. (in 66% in induction group and 86.2% in augmentation group). The average time taken in 31 minutes and 25 minutes for induction and augmentation in carboprost series 45 minutes and 32 minutes respectively in buctocin series.

9. *Total Dose*: Used in both the groups is shown in Table IX. For Indus-

TABLE VIII

Time in Mts.	Carboprost Induction	Carboprost Augmentation	Buctocin Induction	Buctocin Augmentation
Upto 30	30	41	6	5
31-60	23	9	18	18
61-90			8	4
91-120			4	0
Average	31 mts.	25 mts	45 mts	32 mts.

TABLE IX

Bishop score Induction	Primi Group	Carboprost No.	Carboprost Range in Ml.	Carboprost Mean in ml.	Buctocin No.	Buctocin Range in Tablets	Buctocin Mean in tablets
0- 3	Primi	9	1.0-6.3	2.9	1	10	10
	Multi	2	0.3-1.9	1.1	2	8.11	9.5
4- 6	Primi	17	0.5-2.1	1.2	2	10	10
	Multi	10	0.2-0.9	0.5	3	10-11	10.3
7-13	Primi	10	0.2-0.3	0.61	—	—	—
	Multi	2	0.2-0.05	0.35	3	5.8	6.6
Augmentation Group							
0- 3	Primi	1	—	—	1	7	7
4- 6	Multi	0	—	—	0	7	7
4- 6	Primi	9	0.2-0.5	0.3	4	6-10	8
	Multi	8	0.1-0.4	0.2	4	—	10
7-13	Primi	21	0.1-0.7	0.2	15	2-10	7.2
	Multi	11	0.1-0.3	0.2	5	4-8	6.3

tion average amount of drug used in group I is 0.5 ml to 2.9 ml while in group II 6.6 to 10.3 tablets. For augmentation it is 0.2-0.3 ml in Group I and 6.3 to 10 tablets in Group II.

10. *Mode of Delivery*: In two groups shown in Table X.

TABLE X

Type of Delivery	Carboprost No.	Carboprost %	Buctocin No.	Buctocin %
Normal Delivery	64	64	33	82.5
Ventouse Delivery	14	14	2	5
Forceps Delivery	12	12	3	7.5
Face to pubes Delivery	—	—	—	—
Assisted Breech Delivery	2	2		
Lower Segment Caesarean	8	8	11	2.5

Various indications for Ventouse and Forceps delivery were maternal exhaustion to cut short 2nd stage of labour, in high risk patients and unrotated head. Indication for caesarean section in both series is shown in Table XI. One patient in buctocin series had to undergo caesarean section because of unstable lie-turning to breech after 12 hours of induction.

TABLE XI

Indication	Carboprost	Buctocin
Acute Foetal distress	7	0
Prolonged rupture of membranes >24 hours	1	0

This may be apparent from the table that incidence of FD is higher in carboprost series (so is the caesarean section rate) as compared to buctocin. But the fact remains that not enough patients in buctocin series passed into proper labour so as to develop foetal distress. All these patients who did not respond primarily had to undergo caesarean sections after 36 hours for failed induction and prolonged labour.

11. *Success Rate*: In different groups is shown in Table XII.

It is evident that Desamino Oxytocin is not effective for induction in primigravida (S.R.—12.5%) although in multigravida it is 66.6%. For augmentation success rate is 100% in both the series.

12. *Side Effects*: No cases of hyperteos, tachy systole rupture uterus, secondary uterine inertia in both the series, 3 cases of mild primary postpartum haemorrhage was seen in buctocin series.

13. *Apgar of Newborn*: Infants born were unaffected by the drug in both the

TABLE XII

Induction Group

Parity	Total No.	Successful No.	Cases %	Total No.	Successful No.	Cases %
Primi	36	36	100	24	3	12.5
Multi	14	14	100	12	8	66.6
			Augmentation Group			
Primi	31	31	100	20	20	100
Multi	19	19	100	9	9	100

series. 93% of groups I and 95% of group II had an apgar of 8/10 at birth. 2.5% of carboprost series had an apgar score of 4/10 at birth, both were mid-cavity forcepts deliveries applied for acute foetal distress in 2nd stage. 5% of group II had an apgar of 4-6, one was Kielland's Forceps for unrotated head and another was ventouse delivery for foetal distress.

Neonatal period was unremarkable. No neonatal morbidity and mortality except mild jaundice in both series.

14. *Outcome in Failure Cases*: Table XIII shows that out of 24 cases—3 cases had spontaneous delivery without further induction within 72 hours. Reinduction with intravenous oxytocin was done in 17 cases while with carboprost in 4 cases.

TABLE III

1. Spontaneous Delivery without further induction	3 cases (IDI-36.30 to 72 hrs.)
2. Secondary induction with	
(i) Intravenous oxytocin	17
(ii) Carboprost	4

Tertiary and quarternary induction was done with intravenous oxitocin in 1 patient. Charge of pelvic score was in the range of 0-5 (average 1.37) out of these 24 patients 16 patients (88.8%) had vaginal delivery while 8 cases had caesarean section, indication being foetal distress in 2 cases while prolonged labour with rupture of membrane > 24 hours in 4 cases while failed induction in 2 cases.

Discussion

Comparative evaluation of different parameters in carboprost and buctocin series has proved that carboprost is a far superior drug for induction of labour and effacement of cervix. In carboprost series all 100 patients delivered within 36 hours (success rate 100%) while with buctocin 11 out of 36 cases in induction group and all 29 of augmentation group (100%) delivered within 36 hours and overall success rate in induction series is 61.53% (12.5% in primigravida and 66.6% in multigravida). While using desamino-oxytocin Bhatt *et al* (1976) recorded 89.1% success in their series of 55 patients while Gupta *et al*, recorded success rate of 92.5%.

According to Craig *et al* (1971) success rate was 99% and this high percentage of success reflects the efficacy of induction dosage scheme (upto 4 tablets ½ hourly was given in trial). The main drawback in our series was the limitation of maximum number of tablets to be used; one cannot give more than 10-12 tablets in one course (as written on the literature of the drug) and also it becomes more expensive.

In our series 33.3% of primigravidas and 37.5% of multigravida in induction series delivered within 12 hours. These figures are not in accorrdance with the figure of Craig *et al* (1971) where 85% of primigravidas and 96% of multigravida delivered within this period. Overall including induction as well as augmentation cases 80% of the total patients delivered within 12 hours. These results agree with the results of Gupta *et al* 95.5% of patients delivered within 12 hours.

Induction delivery interval for induction is 14 hours 29 minutes, while for augmentation it is 10 hours 11 minutes. Bhatt *et al* (1976) recorded 11½ hours IDI in induction series and 4½ hours in augmentation series. The difference can be explained on the basis of more patients with low score in our series.

In the present study in carboprost

series 92% patients had vaginal delivery and 8% had lower segment caesarean section while in buctocin series 97.5% had vaginal delivery 2.5% had caesarean section. In Craig *et al* (1971) series 99% patients had vaginal delivery, 1% had caesarean section, in Gupta *et al* series vaginal delivery occurred in 93.5% and caesarean section in 7% and in Bhatt *et al* series 90%, had vaginal delivery.

There were no side effects or 3rd stage complications except 3 cases of mild PPH. This was in accord with all other authors.

We did not find any study conducted on carboprost for induction of labour in literature. In our opinion this PGF alpha salt can be used safely with controlled dosage schedule. It would be unfair to condemn carboprost in favour of PGE_2 compounds for induction of labour.

Conclusion

There is no doubt that buctocin is an excellent drug where labour has already begun and if combined with anatomy duration of labour is still shorter but as far as efficacy of carboprost is concerned nothing to compare, especially in low bishop score.

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