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Comparative efficacy of camylofin dihydrochloride and drotaverine hydrochloride on cervical dilatation in active labour

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Abstract
Aim: This study was conducted among pregnant females between gestational age of 38 weeks and 40 weeks to compare and evaluate the rate of cervical dilatation and duration of active phase of labour in patients receiving drugs Camylofin dihydrochloride and Drotaverine hydrochloride.
Methodology: Prospective interventional studywas conducted from October 2020 to September 2021 among 100 antenatal patients who were randomly divided into two groups, 50 patients in each group. Group I consisted of Camylofin and group II of Drotaverine.
Results: Mean Duration of active phase of labour was shorter in group I than in group II which is statistically significant. Mean cervical dilatation rate was significantly more in group I than group II. Mean Induction delivery interval was significantly more in group II than in group I.
Conclusion: Drotaverine hydrochloride and Camylofin dihydrochloride is effective in shortening the duration of first stage of labour by virtue of faster cervical dilatation there by helping in augmentation of labour. Camylofin dihydrochloride is a superior cervical dilatation agent as compared to Drotaverine hydrochloride and also it seems to be more effective in augmentation of labour.

Keywords: drotaverine, camylofin dihydrochloride, labour, augmentation

Introduction
Labour is characterized by effective steady regular uterine contractions that leads to cervical dilation and descent of the baby in birth canal. Dystocia is one of the major complications that affect more than 50% of spontaneous labour which leads to increased maternal morbidity and perinatal compromise. Introduction of Standardised Labour management has decreased the rate of cesarean due to dystocia [1]. It includes artificial rupture of membranes and Oxytocin usage along with use of antispasmodic agents like Camylofin, Drotaverine, Valethamate and Hyoscine [1].

Labour is a complex process and is characterized by the onset of effective uterine contractions leading to the progressive effacement and dilatation of cervix resulting in the delivery of the fetus, placenta and the membranes [2].

There is extensive preparations in both the uterus and cervix long before this. During the initial 36-38 weeks of gestation, the uterus is in an unresponsive preparatory phase. Concurrently the cervix begins an early stage of remodeling termed softening-yet maintains structural integrity.

The onset of labour represents the culmination of a series of biochemical changes in both the cervix and uterus [1].

Camylofin dihydrochloride
Chemical description Camylofin dihydrochloride is an effective synthetic spasmolytic that was first introduced by Brock in 1950.

Camylofin dihydrochloride is 3-methyl butyl 2-(2-diethyl amino ethyl amino)-2-phenyl acetate hydrochloride. It belongs to the group of spasmolytic, anticholinergic, and gastrointestinal sedative drugs.

Molecular formula: C19H32N2O2.2HCl molecular weight of 393.4.
Its structure is depicted in Figure.1:

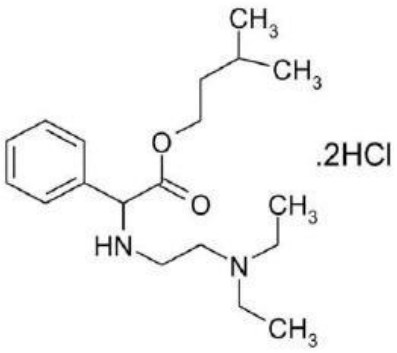

Fig 1: Structure of Camylofin dihydrochloride ($C_{19}H_{32}N_2O_2$, 2HCl)

Composition [3]

Camylofin is available as a 2ml ampoule and a 20ml vial for injection.

Each ml of the product contains:

- Camylofin dihydrochloride: 25 mg
- Benzyl Alcohol (as preservative) IP: 2% w/v
- Water for injection IP: q.s

Mode of action of camylofin in cervical dilation for augmentation of labour

Action of camylofin is unique since, it is a preferential cervical dilator, i.e. it has no interference on the uterine contractions. Although camylofin possesses a musculotropic action, it does not interfere with uterine contractility due to its phosphodiesterase IV iso-enzyme selectivity. Hence camylofin can be recommended for use in accelerating the first stage of labour [4, 5].

Onset of action

After a single intramuscular injection of 50mg of camylofin dihydrochloride, the onset of action begins in 15 to 20 minutes. Intramuscular administration provides relatively slower onset of action compared to intravenous administration. Due to very limited experience with the use of camylofin in the intravenous route, intramuscular route is preferred [5].

Duration of action

The action lasts for 4-5 hours. In clinical studies evaluating acceleration of labour, camylofin showed superior results with just a single dose compared to other molecules like drotaverine, hyoscine and valethamate, where multiple (2-3) doses are required, sometimes at hourly intervals [5].

Metabolism and elimination

Most of the tissues (highest in liver), with the exception of the gastrointestinal tract (least), possess an esterase enzyme which cleaves camylofin into two pharmacologically weak metabolites (isoamyl alcohol and alpha-N-(beta-diethyl aminoethyl) D-amino-phenylacetic acid. Camylofin is rapidly metabolized and only a small amount of it is excreted into the urine [5].

Drotaverine hydrochloride

Drotaverine, a benzylisoquinoline derivative, is an effective antispasmodic drug, structurally related to papaverine [6].

Chemistry

Chemical name: (Z)-1-(3, 4-diethoxybenzylidene)-6, 7-diethoxy-1, 2, 3,4-tetrahydroisoquinoline.

Molecular formula: C24H31NO4.

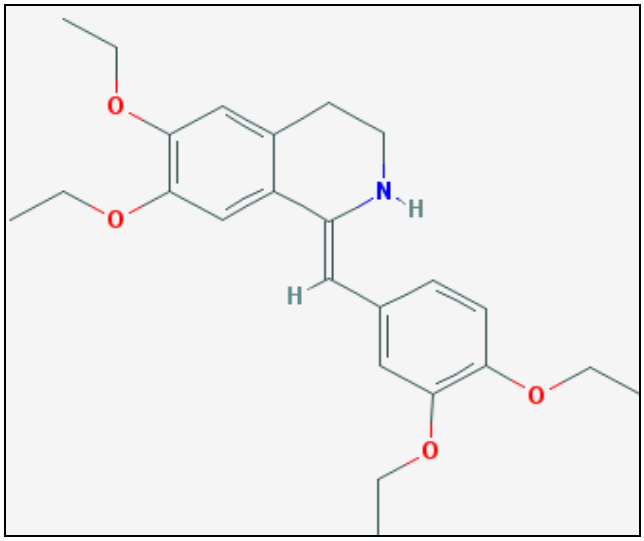

Fig 2: Chemical structure of Drotaverine Hydrochloride

Mechanism of action

Drotaverine is an inhibitor of type IV phosphodiesterase leading to increase in intracellular cyclic AMP and cyclic GMP. It has mild calcium channel blocking effect with a direct action on smooth muscle thereby relieving smooth muscle spasm and cervical dilatation [7]. It has no anticholinergic effects.

Pharmacokinetics

Absorption and distribution

After intravenous administration the drug distributes rapidly into every organ. It is 80-95% bound to plasma proteins. The half-life is 7 to 12 hrs. 3-60% of the dose was in the bile collected during 5 hours. 12 It does not cross the human placenta hence has no significant fetal adverse effect.

Metabolism and elimination

The metabolism is mainly hepatic by demethylation. The drug is excreted mainly by non-renal route in the bile as beta-glucuronide. During 96 hours of observation, 67% of the radioactivity administered was found in the stools while only 20% of it was eliminated with urine. 12 Its metabolites are more potent than drotaverine itself.

Adverse effects

Headache, vomiting, nausea, tachycardia [7].

Contraindications

Severe renal/hepatic/cardiac dysfunction [6].

Drug reactions

May attenuate the action of levodopa [6].

Preparation used

Each ampoule contains 40mg of drotaverine hydrochloride in 2 mL aqueous solution.

Materials & Methodology

Type of study: Prospective interventional comparative study

Time frame of study: October 2020 to September 2021

Study population: This study will be conducted among random population of pregnant females in the Rajah Muthiah Medical College, Annamalai University.

Inclusion criteria

- Term pregnancy inactive labour-initial cervical dilatation of 3-4cm.
- Vertex presentation.
- Labour accelerated with Oxytocin whenever needed.
- Spontaneous and induced labour.
- Age 18-35 years.

Exclusion criteria

- Medical disorders complicating pregnancy.
- Obstetric complications.
- Malpresentation.
- Women with previous caesarean section.
- Known drug allergy.

Results

Table 1: Comparison of duration of labour between groups studied at different stage (I, II, III)

Parameter	Group	N	Mean	SD	t value	P Value
Duration I Stage	Camylofin dihydrochloride	50	297.90	92.85	2.552	0.012 *
	Drotaverine hydrochloride	50	345.10	92.07		
Duration II Stage	Camylofin dihydrochloride	50	38.20	11.41	2.060	0.042 *
	Drotaverine hydrochloride	50	34.00	8.80		
Duration III Stage	Camylofin dihydrochloride	50	5.30	1.19	1.875	0.064 NS
	Drotaverine hydrochloride	50	5.90	1.91		
Total Duration	Camylofin dihydrochloride	50	343.20	98.24	2.257	0.026 *
	Drotaverine hydrochloride	50	386.84	95.12		

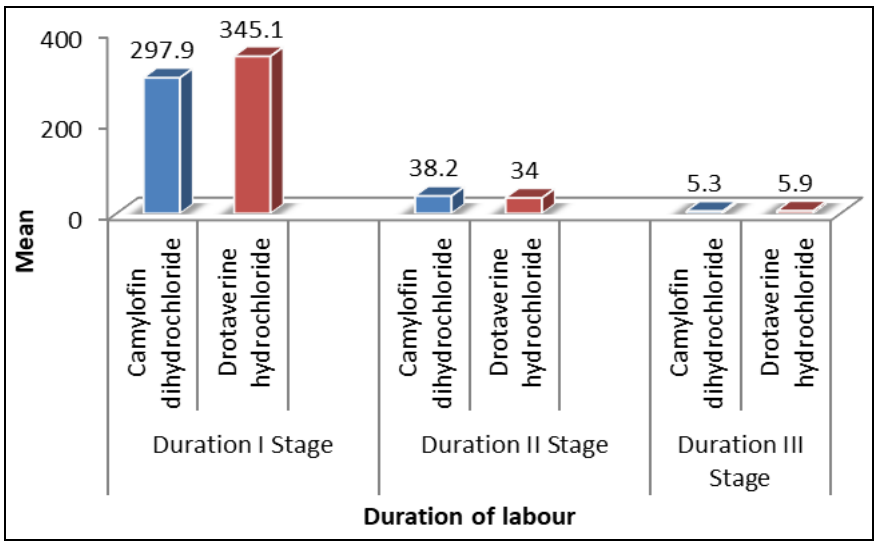

Fig 3: Comparison of duration of labour between groups studied at different stage (I, II, III)

Comparison of duration of labour between groups studied at different stage showed that there was a statistically significant difference found between Camylofin dihydrochloride and Drotaverine hydrochloride groups at stage I ($p<0.05$), stage II ($p<0.05$) and there was no difference found at stage III ($p=0.06$).

Table 2: Comparison of Cervical dilatation between two groups studied

Parameter	Group	N	Mean	SD	t value	P Value
Rate Cervix Dilatation	Camylofin dihydrochloride	50	1.70	0.32	2.013	0.047 *
	Drotaverine hydrochloride	50	1.58	0.28		

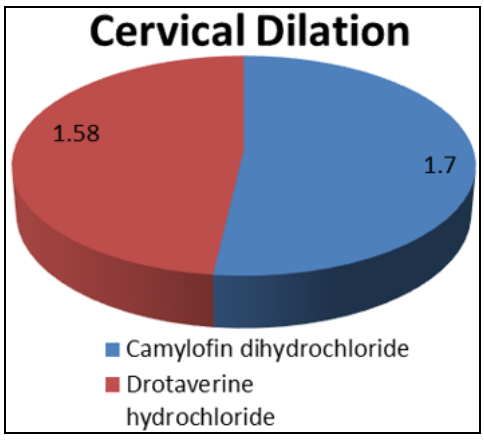

Fig 4: Comparison of Cervical dilatation between two groups studied

Comparison of Cervical dilatation between groups studied showed that there was a statistically significant difference found between Camylofin dihydrochloride and Drotaverine hydrochloride groups $p<0.05$. The rate of cervix dilatation was very good with Camylofin dihydrochloride group.

Discussion

In both groups maximum patients were between 21-30 years (58% in group I and 72% in group II). All patients in both groups had period of gestation between 38-40 weeks. In both groups 93.6% of patients were booked. Distribution of spontaneous labour and induced labour was statistically similar in two groups. Oxytocin acceleration was statistically similar in both the groups of patients. Mean Duration of active phase of first stage of labour was shorter in group Ithan in group II which

is statistically significant. Mean cervical dilatation rate was significantly more in group I than group II. Mean Induction delivery interval was significantly more in group II than in group I. The length of the second stagehand third stage was similar in both groups.

The percentage of third stage complications was statistically similar (4%) in both the groups and were due to the instrumental deliveries in both groups. Some minor side effects like nausea, vomiting and dryness of mouth were seen in group I. Nausea, vomiting, headache, mild hypotension was observed in group II. No serious adverse effects were noted in both the groups. No fetal side effects were observed. 2% in group I and 4% in group II had instrumental deliveries, which is statistically not significant. The most common indication in both groups were failure of maternal forces and fetal distress.

Comparison of Cervical dilatation between groups studied showed that there was a statistically significant difference found between Camylofin dihydrochloride and Drotaverine hydrochloride groups $p<0.05$. The rate of cervix dilatation was very good with Camylofin dihydrochloride group.

Camylofin dihydrochloride and Drotaverine hydrochloride are widely used nowadays for facilitation of cervical dilatation thereby shortening the duration of active phase of labour resulting in augmentation of labour. Various trials have been done in proving the safety and efficacy of both Camylofin dihydrochloride and drotaverine.

The present study inferred thatCamylofin dihydrochloride has caused a significant reduction in the active phase of labour than Drotaverine. This confirms the efficacy of the drug in its usage in augmentation of labour as suggested by various studies done before.

Conclusion

So we can say that in modern obstetrics no women should be allowed to suffer in pain and agony of labour. Labour should be considered as a pleasurable moment in the life of every pregnant women. Drugs which hasten labour should be welcomed by both obstetrician and the labouring mother. Hence the two drugs are effective in shortening the duration of labour.

In our study we observed that intramuscular Camylofin dihydrochloride (Anafortan) was more efficacious than intravenous Drotaverine hydrochloride (Drotin) in shortening the duration of labour.

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