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Prospective randomized study of role of Inj. adrenocorticotrophic hormone (Inj. Acth) in post dural puncture headache of the patients undergone lower segment cesaerian section

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Abstract

Aim: Evaluate the efficacy, hemodynamic effects and other side effects of inj. ACTH in the treatment of post dural puncture headache of the patients undergone.

Material and Methods

Place of study: Maruti Hospital Trichy,

Time of study: 2016-to -2018 80 patients undergone lower segment cesarean section (LSCS) of ASA status I & II, aged between 20-40 years, who developed post spinal headache after spinal anaesthesia are included in our study They were assigned into any of the two groups – on the randomized basis. Group a patients were assigned to receive INJ. ACTH 25 IU im and group p patients an injection of placebo 0.3ml Normal saline in two doses in 24 hour interval.

Observation: It has been observed that the patients in both groups had similar demographic datas in respect to age, height, weight, distribution and also duration of the surgery and similar perioperative events. In Acth group within two hour of the injection, patients got significant relief and with the second dose of the injection complete relief occurred in majority of the patients at 72 hours in placebo group no such reduction in the headache score seen even after receiving tab. paracetamol.

Conclusion: 86% of the patients in acth group have got complete relief from the headache at 72 hours compared to the 64% in the placebo group. There is some mild increase in the mean arterial pressure in the inj. Acth group and no change in pulse rate or respiratory rate between these two groups. There is virtually no side effects with the use of inj. Acth in post dural puncture headache.

Keywords: ACTH, Post dural puncture headache, lower caeserian section, Inj. Adrenocorticotrophic hormone

Introduction

Spinal anaesthesia developed in the late 1800s with the work of Wynter, Quincke and Corning ^[1]. However, it was the German surgeon, Karl August Bier in 1898, who introduced spinal analgesia in clinical practice ^[2]. Since then, the technique has been widely practiced to provide anaesthesia, particularly for surgery below umbilicus. The main advantage attributed to this technique are its simplicity, its ease of performance, requirement of minimum apparatus, has minimal effect on blood biochemistry. It ensures optimum level of arterial blood gases, patient's remains conscious during surgery and maintains airway, requires minimal instrumentation, post operative care and post operative analgesia.

Since the introduction of spinal analgesia, headache has remained a well-recognized complication. Even Dr. Bier also gained first hand experience of disabling headache related to the dural puncture. He and his assistant experience severe headache for several days. He correctly surmised that headache was related to the excessive loss of cerebrospinal fluid ^[2].

Even 100 years after the first spinal anaesthesia, the correct etiology for the post dural puncture headache is not clearly understood. therefore the treatment for the post dural headache is also not very satisfactory.

Now there are several modalities treatment available for the treatment of post dural puncture headache. Of these the most notable one is epidural blood patch ^[3], which is considered to be gold standard for PDPH. But it effects are less than 100%. So the search continues for newer and better treatment for PDPH.

Over the years Inj. Caffeine benzoate ^[3], inj. vasopresin ^[4], inj. Sumtrptan ^[5], Inj. Hydrocortisone ^[6], inj. Methergin ^[7], inj. ACTH ^[8] and Fibrin glue ^[9] have been uses with varying results inj. ACTH is the newer drug being studied recently.

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The first reported incidence appear in the literature BJA 1994 by Collins ^[10]. It gives excellent recovery from PDPH from several case reports published recently. Up to this time very few studies are done in role of Inj. ACTH in the post dural puncture headache.

So our present study was undertaken to evaluate the effect of inj. ACTH in the post dural puncture headache.

As the incidence of post dural headache is more in young female patient particularly parturient ^[11]. So we investigated in patients undergone LSCS who developed post dural puncture headache after spinal anesthesia.

Aim and objective

1. To evaluate the efficacy of inj. ACTH in the post dural puncture headache of patients undergone lscs
2. Dose and duration required for the complete relief of headache
3. Hemodynamic effects of inj. ACTH and
4. Side effects of inj. ACTH if any

Material and methods

The present study was the Prospective randomized, double blind, placebo controlled as well as dose response clinical study during 2016 to 2018 at Maruti Hospital Trichy.

Selection of Cases

80 lower segment cesarean section (LSCS) patients of ASA status I & II, aged between 20-40 years, who developed post spinal headache after spinal anesthesia

Exclusion criteria

1. patient who refused to give consent
2. Patients with hepatic, renal, cardiovascular and endocrine disorder.
3. history of previous headache and family history of headache
4. fever or wound infection
5. intraoperative or post operative undue events

In the post operative follow up all patients were allowed to nurse the their baby and received inj. Diclofenac sodium 3 ml IM on sos basis. Those patients who complained the headache were re examined and PDPH was established using our headache criteria.

They were assigned into any of the two groups – on the randomized basis

GROUP A they were assigned to receive INJ. ACTH and GROUP P placebo injection.

In addition all the patients are advised to take plenty of oral fluids or IV fluid, take supine position, movement restriction and analgesic.

In A group of patients 25 IU of inj. ACTH given intramuscularly two doses in 24 hours interval.

In P group of patients placebo injection given intramuscularly two doses in 24 hours interval.

Every patient observed closely for about one hour after injection for any possible hypersensitive reaction.

Headache score

Headache score is given to assess the severity and also

responsiveness to treatment. It is based on the score devised by crocker in 1976 ^[11].

It is assessed before giving drug and after every one hour for first six hour and then every four hour for next three days. Score

- No headache
- Mild headache which permit longer period of staying upright
- Moderate headache which makes difficult for stay upright for more than half an hour
- Intense headache ^[9] immediately upon from getting up from bed
- Head ache which occur even while lying horizontal in bed

Statistical test

All datas are collected, recorded, tabulated and analysed using statistical test.

Statistical test

Head ache score was analysed by mann whitney test Demographic data and hemodynamic variables are analysed by unpaired t test.

$P < 0.05$ is considered to be statistically significant

$P < 0.001$ is considered to be very significant

Observation

The present study the role of inj. Adrenocorticotrophic hormone in the post dural puncture headache of the patients undergone lower segment cesarean section ^[5], conducted in 80 patients who developed postdural puncture headache after undergone lscs under spinal anesthesia table I.

Table 1: Demographic data

Group	Age [yrs]	Weight [kg]	Height [cm]
ACTH n=42	26.7+5.2	52.4+5.9	155.8+4.8
PLACEBO n=38	27.4+5.7	53.3+6.1	156.1+4.3

The table I shows the demographic data of the patients, with respect to age, weight and height. Thus both the groups are comparable and no statistically significant difference between the two groups was observed.

Table 2: Distribution of the patients with the indication for emergency lscs

Indication	ACTH group N=42	Placebo group N=38
Failed progress	14	15
Prom	7	6
Fetal distress	10	9
Previous lscs	8	6
Placenta previa	3	2

The table II shows that no significant difference in the indications for the emergency lscs⁴ between two groups.

All the patient included in the study had similar intraoperative course with respect to mean BP. Mean HR, fluid infused, incidence of hypotension, mean spo₂, and duration of Surgery.

Table 3.

Group	Preoperative Condition		Fluid Infused MI	Intraoperative Condition			
	Preop BP (Map)	Preop HR		Incidence of Hypotension	Mean Spo2	Mean HR	Duration of Surgery Mins
ACTH	86±6	90±15	2400±200	9	96±3	80±20	60±15
Placebo	84±7	88±14	2350±250	10	95±2	76±24	56±18

The table III shows that both groups are comparable with respect to intraoperative events there is no statistically significant difference between these two groups

The table IV shows number of patients in both groups with different headache score before giving an inj. Acth or placebo. P value is statistically not significant between these groups

Table 4: Number of patient with headache score with two groups

	Acth	Placebo
Score 1	15	15
Score 2	13	11
Score 3	9	8
Score 4	5	4
Total	42	38

Mean headache score of both group of patients

The table V shows the mean headache score of the patient in both the groups after administration of inj. ACTH or placebo in 72 hours.

Table 5: Mean headache score of both group

Time	0 hour	2 HOUR	6 HOUR	12 HOUR	24 HOUR	48 HOUR	72 HOUR
ACTH N=42	2.09±1.07	0.38±0.05	0.30±0.51	0.44±0.61	0.54±0.43	0.23±0.43	0.11±0.32
Placebo N=38	2.0±1.01	1.81±1.15**	1.44±1.08**	0.96±0.81*	0.86±0.84*	0.76±0.63*	0.57±0.59*

*p<0.05- comparison of two groups. P value is significant
 **p<0.005- comparison of two groups. P value is very significant

The table V shows the mean headache score of the both the group patient after the intervention either with inj. ACTH or placebo.

In ACTH group after the administration of drug the mean headache score reduced to less than one within two hours. And remained in below one through out 72 hours. But after 12 hour there is some increase in the mean headache score. But with the second dose after 24 hour mean headache score is remain stable within less than 0.5.

In contrary the placebo groups has no such reduction in the headache score. The P value is statistically very significant at 2 hour, at 6 hour and again at 48hr. It is significant at 12 hour and at 72 hour

Table 7.

Headache Score	0 hrs	2 hrs	6 hrs	12 hrs	24 hrs	48 hrs	72 Hrs
ACTH N=13	2	0.3	0.2	0.5	0.6	0.2	0.1
Placebo N=11	2	1.8*	1.6*	1.5*	1.2*	0.8*	0.6*

*p<0.05- comparison of two groups. P value is significant

This graph show the mean trend of headache score two patient after administration of inj. ACTH or placebo. Within two hour mean headache score comes to 0.3 in ACTH group and with the second dose it comes to almost zero in 72 hour. In placebo group it is slowly decreased and even after 72 hour it mean score is around 0.6.

Individual headache score

1. Mean headache score of patients in both group whose initial headache score was one.

3. Mean headache score of the patients of the both group whose initial headache score was three.

Table 6.

Headache score	0	2hrs	6hrs	12hrs	24hrs	48hrs	72hrs
ACTH N=15	1	0.2	0.1	0.1	0.2	0	0
Placebo N=15	1	0.8*	0.7*	0.7*	0.5*	0.3*	0.2*

*p<0.05- comparison of two groups. P value is significant

Table 8.

Headache	0 hrs	2 Hrs	6 hrs	12 hrs	24 hrs	48 hrs	72 Hrs
ACTH N=9	3	0.6	0.5	0.7	0.8	0.4	0.3
Placebo N=8	3	2.8**	2.0**	1.8*	1.4*	1*	0.8*

*p<0.05- comparison of two groups. P value is significant
 **p<0.005- comparison of two groups. P value is very significant

The table VI and the graph (xxx) show changes in the mean headache score of the score one patients. Within two hour of injection of ACTH the headache score coming down to less than 0.2. With second dose it is completely becomes zero within 48 hour.

In placebo group mean headache score is slowly reduced and even after 72 hour it is not comes to zero.

The table VIII shows the mean trend of score 3 group patients. Immediately after injection of inj. ACTH mean headache score comes to less than 1. With the second dose it almost comes to less than 0.5.

But in placebo group it is slowly decreasing even after receiving rescue dose of t.paracetamol. After 72 hour the headache score still remains around 0.8

2. Mean headache score of the patients of the both group whose initial headache score was two.

4. Mean headache score of the patients of the both group whose initial headache score was four.

Table 9.

Headache Score	0 hrs	2 hrs	6 Hrs	12 hrs	24 hrs	48 hrs	72 hrs
ACTH N=5	4	1.2	0.8	1.2	1.4	0.6	0.3
Placebo N=4	4	3.8**	2.7**	2.4*	2.2*	1.6**	1.4**

* $p < 0.05$ - comparison of two groups. P value is significant

** $p < 0.005$ - comparison of two groups. P value is very significant

This graph shows the trend of mean headache score of score 4 group patients after administration of inj. ACTH or

placebo. In ACTH group within two hours the headache score is reduced to around 1 and with second dose it comes to almost nil (0.3 headache score after 72 hour) In placebo group it is remained high inspite of receiving t.paracetamol. And even after 72 hour it score around 1.4 which means still patient have suffering significant headache.

Relief of headache

Table 10.

Group	Relief from the headache after 72 hours (% of pt)	No relief from the headache after 72 hours (% of pts)
ACTH 42	36 (86%)	6 (14%)
Placebo 38	24*(64%)	14 (36%)

* $p < 0.05$ - comparison of two groups. P value is significant

The table XI shows that 36 number (86%) of the patients in the acth group had complete relief from the headache⁷ at 72 hrs compared to placebo group which had 24 patients (64%) only complete relief.

Where an after 72 hour only 6 of the patient in the acth

group had no complete relief from the headache whereas in placebo group 14 patients (36%) had not complete relief.

Hemodynamic changes

Change in the mean arterial blood pressure

Table 11.

HOUR	0	2	6	12	24	48	72
ACTH	82.3±5.0	90.4±5.1	88.7±5.4	83.9±4.1	83.6±5.2	84±4.5	83±5.1
Placebo	83.1±6.1	83.5±6.4*	82.4±5.8*	81.4±6.2	83.2±4.3	82.3±5.9	81.7±5.2

* $p < 0.05$ - comparison of two groups. P value is significant

The table XI shows the changes in the mean arterial pressure in the both groups, in ACTH group mean arterial blood pressure is increased significantly immediately after that inj. ACTH. But this increased blood pressure is return to baseline within eight hours.

Thus even though the there is significant increase compared

to the placebo group, the increase is less than 10% from the mean baseline. So it will not cause any problem in healthy patients.

Pulse rate changes

Pulse rate changes in both groups

Table 12.

Time	0	2	6	12	24	48	72
ACTH	75±7	77±8	78±6	75±5	73±6	74±8	72±4
Placebo	73±6	72±6	74±4	74±6	73±5	74±4	72±3

The table XII show the changes in the pulse rate following the administration of inj, ACTH and placebo. There is some mild increase in the pulse rate after the administration of inj. ACTH for upto 6 hours. Then it comes to baseline value.

The increase in the pulse rate is not statistically significant

Changes in the respiratory rate

Respiratory rate changes

Table 13.

Time In Hours	0	2	6	12	24	48	72
ACTH	14.4±1.2	15.8±1.8	16.2±1.3	15.7±1.6	14.2±1.0	14.8±1.2	14.3±1.4
Placebo	14.6±1.6	15.2±1.4	14.3±1.7	14.1±1.2	15.2±1.3	14.8±1.5	14.3±1.6

The table XIII show the mean changes in the respiratory rate of the both group patient following the administration of inj. ACTH or placebo. There is some mild increase in the respiratory rate following the administration of ACTH. But it is not statistically significant.

The table XIII shows that in ACTH group only 5% patient required rescue doses in the form of t. paracetamol. But in placebo group 26% patient received rescue doses.

Side effects

The side effects observed in the both groups of the patients

Rescue medication

Table 14.

	No. of Patient	% of Patient
ACTH	2	5%
PLACEBO	10**	26%**

** $p < 0.005$ - comparison of two groups. P value is very significant

	ACTH Group	Placebo Group
Seizure	0	0
Pedal Edema	4	2
Nausea & Vomiting	1	4*
Pruritus	0	0
Urinary Retenoin	0	0

There are four patient in acth group had pedal edema and in placebo group about two patient.

Nausea and vomiting incidence is more in placebo group (4) compared to the ACTH group may be due to spinal headache ^[8] itself causes vomiting.

Conclusion

Patients receiving spinal anaesthesia develops post dural puncture headache. Though the incidence has decreased significantly by taking preventive measures of using smaller bore needle ^[14] & differently designed needle ^[12] (whitacre needle). but it has not eliminated completely.

The PDPH ^[10] is quite distressing to the many a patients, various methods has been tried to treat the headache without much success. Epidural blood patch ^[14] is considered to be the gold standard treatment. but it has not been universally used because of the invasive nature and patient reluctance to accept a second injection. It has been reserved for the very severe PDPH.

Study concludes

1. The "role of inj. ACTH in the post dural puncture headache ^[15] in the patients undergone LSCS "we have observed inj. acth is quite helpful in reducing the severity of the headache in more than 80% of the patients.
2. We can conclude that inj. Acth should be employed for the treatment of PDPH at an early stage in parturient mothers.
3. We suggest that more studies be undertaken to finds its efficacy in reducing the severity of the headache following spinal puncture in non obstetric ^[13] and non surgical cases.

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