Prospective randomized study of role of Inj. adrenocorticotropic 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 lower segment cesaerian section.

Material and Methods

Place of study: Maruti Hospital Trichy,

Time of study: 2016-2018 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: 80% 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. Adrenocorticotropic 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 anesthesia, particularly for surgery below umbilicus. The main advantage attributed to this technique is 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 [4], 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.
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
- Headache 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 lscs 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.
The table III shows that both groups are comparable with respect to intraoperative events there is no statistically significant difference between these two groups

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

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

The table V shows the mean headache score of the both 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 at 72 hour.

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

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.

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

The table VII 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

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.

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

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

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

| Group | Preoperative Condition | Fluid Infused | Intraoperative Condition |
|-------|------------------------|---------------|--------------------------|
|       | Preop BP (Map)         | Preop HR      | MI                       | 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                   |

*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 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**

| 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 headache 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**

| HOUR | 0     | 2     | 6     | 12    | 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±3.9 | 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**

| 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**

| 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.

**Side effects**

The side effects observed in the both groups of the patients

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

*P<0.005* - comparison of two groups. P value is very significant
There are four patients in the Acth group who had pedal edema and in placebo group about two patients. 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 anesthesia develops post dural puncture headache. Though the incidence has decreased significantly by taking preventive measures of using smaller bore needle[14] & differently designed needle[15] (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 find its efficacy in reducing the severity of the headache following spinal puncture in non obstetric[13] and non surgical cases.

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