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Study on the effect of intravenous dexmedetomidine in females undergoing lower segment cesarean section under general anesthesia

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Abstract
Awareness and recall causing posttraumatic stress disorder are the major hazards of General Anaesthesia in cesarean section because of exclusion of Benzodiazepines and opioids in the anaesthetic management before baby delivery. Hence based on above findings the present study was planned for Clinical Evaluation of Administration of Intravenous dexmedetomidine in Females Undergoing Lower Segment Cesarean Section under General Anesthesia.
The present study was conducted in Department of Anesthesia, Government Medical College, Bettiah, Bihar, India. The 30 cases of the patients undergone the caesarean section under General Anesthesia were included in the present study. The 15 cased were enrolled in the Group I as Cases administered with the 1mcg/kg IV dexmedetomidine 10 minutes before induction. The Group II cases were control cases without dexmedetomidine.
The data generated from the present study concludes that loading dose of IV dexmeditomedine 1mcg/kg is effective in aborting awareness without affecting Apgar score. Dexmedetomidine, when given as a pre-anaesthetic medication and intraoperative infusion, decreases stress response to various noxious stimuli and maintains haemodynamic stability.

Keywords: cesarean section, dexmedetomidine, general anaesthesia, Apgar score, etc

Introduction
A lower (uterine) segment Caesarean section (LSCS) is the most commonly used type of Caesarean section [1]. It includes a transverse cut 1-2 centimetres above the attachment of the urinary bladder to the uterus, called the Pfannenstiel incision in the lower segment. This type of incision results in less blood loss and is easier to repair than other types of Caesarean sections.
It may be transverse (the usual) or vertical in the following conditions [2]. presence of lateral varicosities; constriction ring to cut through it; deeply engaged head.
The location of an LSCS is beneficial for the following reasons: peritoneum is more loosely attached to the uterus; contraction is less than in upper part of uterus; healing is more efficient; sutures are intact (less problem with suture loosening). Most bleeding takes place from the angles of the incision, and forceps can be applied to control it. Green Armytage forceps are specifically designed for this purpose [3].
Although the incision is made using a sharp scalpel, care must be taken not to injure the foetus, especially if the membranes are ruptured, or in emergencies like abruption. The incision can be extended to either sides using a scissor or by blunt dissection using hands. While using the scissors, the surgeon should ensure that a finger is placed underneath the uterus so that the foetus in protected from unintentional injury. If blunt dissection is done, intraoperative blood loss can be minimized. In cases where Pfannenstiel incision cannot be done (such as large baby), Kronig incision (low vertical incision) [4], classical (midline), J [5] or T shaped incisions [6] may be used to incise the uterus [7].
The German gynecologist Hermann Johannes Pfannenstiel (1862–1909) invented the technique [8]. In the United Kingdom, the surgery was first popularised by Dr. Monroe Kerr, who first used it in 1911, so in English speaking countries it is sometimes called the Kerr incision or the Pfannenstiel-Kerr incision. Kerr published the results in 1920, proposing that this method would cause less damage to the vascularized areas of uterus than the classical operation. He claimed that it was better than the longitudinal uterine incision in terms of chances for scar rupture and injury to vessels [9].
Cesarean delivery is defined as the delivery of a fetus through surgical incisions made through the abdominal wall (laparotomy) and the uterine wall (hysterotomy). In 2014, 32.2% of women who gave birth in the United States did so by cesarean delivery [10]. The rapid increase in cesarean birth rates from 1996 to 2014 without clear evidence of concomitant decreases in maternal or neonatal morbidity or mortality raises significant concern that cesarean delivery is overused. The most common indications for primary cesarean delivery include labor dystocia, abnormal or indeterminate fetal heart rate tracing, fetal malpresentation, multiple gestation, and suspected fetal macrosomia. Safe reduction of the primary cesarean delivery rate will require different approaches for these indications, as well as others. Increasing women's access to nonmedical interventions during labor has also been shown to reduce cesarean birth rates. External cephalic version for breech presentation and a trial of labor for women with twin gestations when the first twin is in cephalic presentation are examples of interventions that can help to safely lower the primary cesarean delivery rate [11]. A practice bulletin from the American College of Obstetricians and Gynecologists (ACOG) recommends that all eligible women with breech presentations who are near term should be offered external cephalic version (ECV) to decrease the overall rate of cesarean delivery [12, 13].

The American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine (SMFM) released joint guidelines for the safe prevention of primary cesarean delivery [14, 15].

Cesarean deliveries were initially performed to separate the mother and the fetus in an attempt to save the fetus of a moribund patient. They subsequently developed to resolve maternal or fetal complications not amenable to vaginal delivery, either for mechanical limitations or to temporize delivery for maternal or fetal benefit. The leading indications for cesarean delivery (85%) are previous cesarean delivery, breech presentation, dystocia, and fetal distress [16].

Controversy exists regarding elective cesarean delivery on maternal request (CDMR). The 2013 American College of Obstetricians and Gynecologists (ACOG) Committee on Obstetric Practice [17] and 2006 National Institutes of Health (NIH) consensus committee [18] determined that the evidence supporting this concept was not conclusive and that more research is needed.

Cesarean delivery is defined as the delivery of a fetus through surgical incisions made through the abdominal wall (laparotomy) and the uterine wall (hysterotomy). Because the words "cesarean" and "section" are both derived from verbs that mean to cut, the phrase "cesarean section" is a tautology. Consequently, the terms "cesarean delivery" and "cesarean birth" are preferable.

Cesarean deliveries were initially performed to separate the mother and the fetus in an attempt to save the fetus of a moribund patient. This operation subsequently developed into a surgical procedure to resolve maternal or fetal complications not amenable to vaginal delivery, either for mechanical limitations or to temporize delivery for maternal or fetal benefit.

The cesarean delivery has evolved from a vain attempt performed to save the fetus to one in which physician and patient both participate in the decision-making process, striving to achieve the most benefit for the patient and her unborn child.

Currently, cesarean deliveries are performed for a variety of fetal and maternal indications (see Indications). The indications have expanded to consider the patient's wishes and preferences. Controversy surrounds the current rates of cesarean delivery in developed countries and its use for indications other than medical necessity. Go to Perimortem Cesarean Delivery and Vaginal Birth after Cesarean Delivery for complete information on these topics.

The anesthesiologist will review regional anesthetic techniques. Regional anesthesia is used for 95% of planned cesarean deliveries in the United States. The 3 main regional anesthetic techniques are spinal, epidural, and combined spinal epidural [19]. Every patient is evaluated for general anesthesia in case an emergency should arise and establishment of an airway becomes necessary.

A review by Afolabi *et al* found that patients undergoing local anesthetic techniques were found to have a significantly lower difference between preoperative and postoperative hematocrit levels when compared with patients undergoing general anesthesia. Women having either an epidural anesthesia or spinal have a lower estimated maternal blood loss [20].

After placement of the regional anesthetic, monitor the fetus until an adequate surgical level has been achieved. When the level of anesthesia is adequate, the skin can be prepared either with an iodine scrub or with 4% chlorhexidine. Before making the initial incision, grasp the patient's skin bilaterally with an instrument such as an Allis clamp at the level of and above the incision to confirm anesthesia up to the level of T4. This ensures that the anesthetic level is appropriate.

The dermatomal level of anesthesia required for cesarean delivery is higher than that required for labor analgesia. A sensory block to the 10th thoracic dermatome is sufficient to achieve analgesia for labor, but for cesarean, the anesthetic level must be extended cephalad to at least the fourth thoracic dermatome to prevent nociceptive input from the peritoneal manipulation.

In patients who require a cesarean delivery secondary to a problem arising during labor, the preparation follows essentially the same steps previously outlined. The only major variation occurs if a patient requires general anesthesia prior to the procedure. In that situation, before intubation, the patient should be prepped and draped and the surgical team should be ready to begin as soon as the patient's airway is secured.

Perinatal outcome is influenced by gestational age at delivery, the presence of congenital abnormalities and growth abnormalities, and the indication for delivery itself. Improvement in perinatal outcome has been greatly enhanced by improved technology available to neonatologists and by improvements in prenatal care (eg, identification of patients at high risk, ultrasonography, and increased usage of antenatal steroids, progesterone, and most recently magnesium sulfate cerebral palsy prophylaxis in those at risk for preterm delivery [21, 22].

Unfortunately, despite the dramatic rise in the rate of cesarean delivery, the overall rate of cerebral palsy has not decreased. The only perinatal intervention for which strong evidence shows a beneficial effect on both mortality and the risk of cerebral palsy is antenatal treatment of the mother with glucocorticoids [23].

A minority of cesarean deliveries are performed for fetal distress, where fetal heart rate tracings are clearly associated with an increased risk of fetal hypoxia and acidosis. Fetal heart rate monitoring has not decreased the overall rate of cerebral palsy; rather, it has decreased the threshold to perform cesarean deliveries for nonreassuring fetal status.

Unfortunately, many obstetricians admit that their practice of medicine has become more defensive. Given the fear of inquiry regarding how a particular patient's labor was managed, many obstetricians may have a lower threshold to perform a cesarean delivery despite the fact that the incidence of neonatal seizures or cerebral palsy has not been affected by increasing cesarean delivery rates [24].

The biochemical mechanism of action of general anaesthetics is not well understood. Theories need to explain the function of anaesthesia in animals and plants. To induce unconsciousness, anaesthetics have myriad sites of action and affect the central nervous system (CNS) at multiple levels. Common areas of the central nervous system whose functions are interrupted or changed during general anaesthesia include the cerebral cortex, thalamus, reticular activating system, and spinal cord. Current theories on the anaesthetized state identify not only target sites in the CNS but also neural networks and loops whose interruption is linked with unconsciousness. Potential pharmacologic targets of general anaesthetics are GABA, glutamate receptors, voltage-gated ion channels, and glycine and

serotonin receptors. Halothane has been found to be a GABA agonist, and ketamine is an NMDA receptor antagonist.

General anaesthesia is usually induced in a medical facility, most commonly in an operating theatre or in a dedicated anaesthetic room adjacent to the theatre. However, it may also be conducted in other locations, such as an endoscopy suite, radiology or cardiology department, emergency department, or ambulance, or at the site of a disaster where extrication of the patient may be impossible or impractical.

Anaesthetic agents may be administered by various routes, including inhalation, injection (intravenous, intramuscular, or subcutaneous), oral, and rectal. Once they enter the circulatory system, the agents are transported to their biochemical sites of action in the central and autonomic nervous systems.

Most general anaesthetics are induced either intravenously or by inhalation. Intravenous injection works faster than inhalation, taking about 10–20 seconds to induce total unconsciousness. This minimizes the excitatory phase (Stage 2) and thus reduces complications related to the induction of anaesthesia. [Citation needed] Commonly used intravenous induction agents include propofol, sodium thiopental, etomidate, methohexital, and ketamine. Inhalational anaesthesia may be chosen when intravenous access is difficult to obtain (e.g., children), when difficulty maintaining the airway is anticipated, or when the patient prefers it. Sevoflurane is the most commonly used agent for inhalational induction, because it is less irritating to the tracheobronchial tree than other agents.

Dexmedetomidine is most often used in the intensive care setting for light to moderate sedation. It is not recommended for long-term deep sedation. A feature of dexmedetomidine is that it has analgesic properties in addition to its role as a hypnotic, but is opioid sparing; thus, it is not associated with significant respiratory depression (unlike propofol).

Many studies suggest dexmedetomidine for sedation in mechanically ventilated adults may reduce time to extubation and ICU stay. People on dexmedetomidine can be rousable and cooperative, a benefit in some procedures.

Compared with other sedatives, some studies suggest dexmedetomidine may be associated with less delirium. However, this finding is not consistent across multiple studies. At the very least, when aggregating many study results together, use of dexmedetomidine appears to be associated with less neurocognitive dysfunction compared to other sedatives. Whether this observation has a beneficial psychological impact is unclear. From an economic perspective, dexmedetomidine is associated with lower ICU costs, largely due to a shorter time to extubation.

Awareness and recall causing posttraumatic stress disorder are the major hazards of General Anaesthesia in cesarean section because of exclusion of Benzodiazepines and opioids in the anaesthetic management before baby delivery. Hence based on above findings the present study was planned for Clinical Evaluation of Administration of Intravenous dexmedetomidine in Females Undergoing Lower Segment Cesarean Section under General Anesthesia.

Methodology

The present study was conducted in Department of Anesthesia, Government Medical College, Bettiah, Bihar, India. The 30 cases of the patients undergone the caesarean section under General Anesthesia were included in the present study. The 15 cased were enrolled in the Group I as Cases administered with the 1mcg/kg IV dexmedetomidine 10 minutes before induction. The Group II cases were control cases without dexmedetomidine only administered with saline.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

Inclusion criteria

- Parturients in the age group 18 to 35 years.
- Parturients belonging to ASA Class I and II.
- Height 150-170 cm.

Exclusion criteria

- Known hypersensitivity to local anaesthetics or dexmedetomidine.
- Patients with medical and obstetric complications like anaemia, heart disease, gestational hypertension, gestational diabetes mellitus, shock, septicemia and hypertension.
- Subjects having any absolute contraindications for spinal anaesthesia like raised intracranial pressure, severe hypovolemia, bleeding diathesis, local infection
- Height <150 cm and >170 cm.
- BMI > 30
- Patient refusal.

Results & Discussion

Lower segment caesarean section is a commonly performed surgical procedure usually done under subarachnoid block with 0.5% hyperbaric bupivacaine. It has many advantages like easy to perform, rapid onset of action and good muscle relaxation. Pregnancy is usually associated with difficult airway due to mucosal oedema, friable mucosa, large breasts and worsening of Mallampatti Class. As the mother is awake, it helps in establishing bond between mother and baby. This gives regional anaesthesia a distinct advantage over general anaesthesia.

One of its main disadvantages is the limited duration of action and hence lack of postoperative analgesia. Moreover, surgery on the uterus performed under subarachnoid block is often accompanied by visceral pain. Blockade to the T4 dermatome is necessary to perform caesarean delivery without maternal discomfort. It is commonly associated with hypotension and attendant decreased utero-placental perfusion [25]. Incidence of hypotension can be decreased by reducing the volume of local anaesthetic agent, but it carries a risk of inadequate analgesia [26]. Hence, various adjuvants have been used with local anaesthetics in subarachnoid block to avoid intra-operative visceral and somatic pain and to provide prolonged post-operative analgesia [27].

Alpha-2 (α2) adrenergic receptor agonists like clonidine and dexmedetomidine have been the focus of interest as adjuvants to intrathecal local anaesthetics due to their sedative, analgesic, perioperative sympatholytic and haemodynamic stabilizing properties. Benefits of adding clonidine to intrathecal bupivacaine like faster onset of action and improved intra-operative sensory and motor blockade, prolonged post-operative analgesia and decreased

dosage of local anaesthetic agent have been demonstrated in various studies. Clonidine has also been used intrathecally as an adjuvant with bupivacaine up to a dose of 1 µg/kg without significant maternal and neonatal side-effects6. But, usual dose of clonidine (15-150µg) may be some times associated with bradycardia, hypotension and sedation3.

Table 1: Basic Characteristics

Groups	Group I	Group II
Administration of	**1mcg/kg IV Dexmedetomidine**	**Normal Saline**
No. of Cases	15	15
Age (years)	21 – 28	22 – 27
Weight (kg)	43 – 65	45 – 66
APGAR Score		
1 mins	7	7
5 mins	9	9

Table 2: Monitoring Parameters

Groups	Group I	Group II
Administration of	**1mcg/kg IV Dexmedetomidine**	**Normal Saline**
No. of Cases	15	15
Systolic BP		
Base	86	89
Induction	83	90
Delivery	91	95
Extubation	93	99
Heart Rate		
Base	85	86
Induction	71	75
Delivery	82	91
Extubation	84	94

Table 3: Awareness & Recall Parameter

Groups		Group I	Group II
Administration of		**1mcg/kg IV Dexmedetomidine**	**Normal Saline**
Awareness Parameter			
Intra-operative Sweating	No	1	5
	Yes	14	10
Intra-operative lacrimation	No	2	6
	Yes	13	9
Pupillary Dilatation	No	3	5
	Yes	12	10
Intra-operative Coughing	No	5	8
	Yes	10	7
Intra-operative Jerking	No	2	6
	Yes	13	9
Recall Parameter			
Recall Status			
Early		10	6
Late		5	9

G. E. Kanazi *et al*. (2006) [28] studied the effects of low-dose dexmedetomidine (3 µg) or clonidine (30 µg) on the characteristics of bupivacaine (12 mg) spinal block. The purpose of the study was to compare the onset and duration of sensory and motor block, as well as the hemodynamic changes and level of sedation, following intrathecal bupivacaine supplemented with either dexmedetomidine or clonidine. In this prospective, double-blind study, 60 patients undergoing transurethral resection of prostate or bladder tumor under spinal anesthesia were randomly allocated to one of three groups. Group B received 12 mg of hyperbaric bupivacaine with normal saline, group D received 12 mg of bupivacaine supplemented with 3 µg of dexmedetomidine and group C received 12 mg of bupivacaine supplemented with 30 µg of clonidine (total volume made to 1.9ml in each group). Patients in groups D and C had a significantly shorter onset time of motor block and significantly longer sensory and motor regression times than patients in group B. The mean time of sensory regression to the S1 segment was longer in group D and group C compared to group B. The regression of motor block to Bromage 0 was longer in group D and group C compared to group B The onset and regression times were not significantly different between groups D and C. The mean arterial pressure, heart rate and level of sedation were similar in the three groups intraoperatively and post-operatively. They concluded that Dexmedetomidine (3 µg) or clonidine (30 µg), when added to intrathecal bupivacaine, produces a similar prolongation in the duration of the motor and sensory block with preserved hemodynamic stability and lack of sedation.

Al-Ghanem SM *et al*. (2009) [29] studied the effects of adding dexmedetomidine (5 µg) versus fentanyl (25 µg) to intrathecal isobaric bupivacaine (10 mg) on spinal block characteristics in gynecological procedures. The purpose of the study was to evaluate the onset and duration of sensory and motor block as well as operative analgesia and adverse effects of Dexmetedomidine (DXM) or fentanyl given intrathecally with plain 0.5% bupivacaine for spinal anesthesia. Seventy six patients scheduled for vaginal hysterectomy, vaginal wall repair and tension free vaginal tape were prospectively studied. Patients were randomly allocated to receive intrathecally either 10 mg isobaric bupivacaine plus 5 µg dexmetedomidine (group D n = 38) or 10 mg isobaric bupivacaine plus 25 µg fentanyl (group F n = 38). They observed that patients in group D had significantly longer sensory and motor block times than patients in group F. The onset times to reach T10 dermatome and to reach peak sensory level as well as onset time to reach modified Bromage 3 motor block were not significantly different between the two groups. The mean time of sensory regression to S1 was longer in group D and group F. The regression time of motor block to reach modified Bromage 0 was longer in group D and group F. They concluded that in women undergoing gynecological procedure under spinal analgesia, 10 mg plain bupivacaine supplemented with 5 µg dexmetedomidine produced prolonged motor and sensory block compared to 10 mg plain bupivacaine with 25 µg fentanyl.

Mahdy WR *et al*. (2011) [30] studied the effects of adding DXM (5 µg) versus fentanyl (25 µg) to intrathecal bupivacaine (10 mg) on spinal block characteristics and neonatal outcome in uncomplicated cesarean delivery. Aim of the study was to evaluate the quality of the block, hemodynamic effects, and adverse effects of dexmedetomidine or fentanyl given intrathecally with hyperbaric 0.5% bupivacaine and their effects on the neonate. 90 females scheduled for uncomplicated elective cesarean delivery were assigned into three groups: Control group (n = 30) received intrathecal placebo, with bupivacaine 10 mg in 2.5 ml, Dxm group (n = 30) received intrathecal dexmedetomidine 5 µg with bupivacaine 10 mg in 2.5 ml. and Fent group (n = 30) received intrathecal fentanyl 25µg plus bupivacaine 10 mg. in 2.5 ml. They observed that onset time to reach peak sensory and motor level were shorter in DXM and Fentanyl groups compared with the control group with no significant difference

between DXM and Fentanyl groups. Also DXM group had significantly longer sensory and motor block times than patients in control and Fentanyl group. No adverse effects on mothers or babies were noticed among three groups. They concluded that DXM seemed to be an attractive adjuvant to spinal bupivacaine in cesarean section giving good quality of spinal anesthesia with minimal side effects and no adverse effects on the babies.

I. van Tuijl *et al*, (2006) [31] conducted a randomized trial to study the effects of intrathecal clonidine (75 µg) to hyperbaric bupivacaine 0.5% (2.2 ml) on postoperative pain and morphine requirements after caesarean section. A group of 106 women received spinal anaesthesia using either bupivacaine 0.5% (2.2 ml) heavy with 0.5 ml normal saline 0.9% (B) or bupivacaine 0.5% (2.2 ml) heavy with clonidine (75 µg) in 0.5 ml normal saline (BC). They recorded total morphine consumption in the first 24 hours after surgery, duration of postoperative analgesia, postoperative pain scores, the need for alfentanil during surgery, block regression, clonidine side-effects, morphine side effects and side-effects in newborn were recorded. They observed that time for first analgesic request in the BC group was 129 minutes compared with 55 minutes in the B group. 42% of patients in BC group had complete block 1 hour after surgery compared with 8% of patients in B group. Total morphine consumption was similar in both groups. No clinically relevant maternal or neonatal side-effects were detected. They concluded that addition of clonidine (75 µg) to hyperbaric bupivacaine prolongs spinal anaesthesia after caesarean section and improves early analgesia, but does not reduce the postoperative morphine consumption during the first 24 hours without any maternal or neonatal side effects.

Finding out whether a patient is conscious or awake while undergoing general anesthesia pose a major problem [32]. The limitations of current clinical methods to assess anesthetic adequacy have been well known. Mechanisms in the central nervous system that control higher functions like memory and consciousness may be anesthetized adequately, whereas spinal cord mechanisms that suppress movement to surgical stimulus may not be anaesthetised adequately. A direct method of evaluating consciousness is needed, rather than the current practice of monitoring hemodynamic changes or movement responses. A machine or monitor that measures physiologic changes associated with the conscious state would be an improvement on current methods, which are dependent on responses that only indirectly reflect consciousness.

One of the drawbacks of routinely practiced balanced anaesthesia with nitrous oxide (N2O) is awareness. During balanced anaesthesia, the depth is maintained with 66% N2O in oxygen (O2). Dwyer *et al*. [33] had reported 100% awareness in volunteers anaesthetised with 63% N2O. Russell [32] could demonstrate awareness in 61% patients only receiving 70% N2O. Although higher concentration (above 70%) of N2 O is not routinely administered in clinical practice, it has been demonstrated by different investigators3-6 that it can be used safely and it reduces the intraoperative narcotic requirement drastically. Hence less postoperative respiratory complications induced by narcotic. As the patients are maintained with N2O and lesser doses of narcotic, there may be chances for developing awareness under anaesthesia. But so far the problem of awareness was not evaluated during balanced anaesthesia with higher concentration of N2 O.

Awareness during anesthesia with intraoperative memory occurs when the patient is able to process information and recollect specific responses to several stimuli. Explicit or declarative memory is when the patient remembers facts, events or experiences that occurred during general anesthesia. Implicit or procedural memory is defined as the memory of motor and sensorial capacities and abilities wherein the patient is unable to verbally express his experience during anesthesia, but there are changes in his postoperative behavior, habits and performance in such a way that psychological tests are required to detect the implicit memory. Dreaming is a phase that raises issues regarding the classification of the awareness type. Dreaming is considered to be a transitional state between the explicit and implicit memory. The experience of consciousness is not the same for all patients. These may be collected as memories (hearing perception, tactile sensation, difficulty to move and breath, panic, anxiety, chronic fever, insomnia and recurrent nightmares) or neurosis, also known as post-traumatic stress disorder.

Conclusion

The data generated from the present study concludes that loading dose of IV dexmeditomedine 1mcg/kg is effective in aborting awareness without affecting Apgar score. Dexmedetomidine, when given as a pre-anaesthetic medication and intraoperative infusion, decreases stress response to various noxious stimuli and maintains haemodynamic stability.

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