



ASSESSMENT OF BLOOD GLUCOSE LEVELS AND SEVOFLURANE REQUIREMENT IN PATIENTS ON DEXMEDETOMIDINE INFUSION FOR INTRA-PERITONEAL SURGERIES

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ABSTRACT:

The aim of the present study was to observe the effect of intravenous Dexmedetomidine on levels of blood glucose, which is one among several stress response markers under General Anesthesia (GA) for laparoscopic intra-peritoneal surgeries.

The study was planned in the Department of Anaesthesia in Sri Krishna Medical College and Hospital, Muzaffarpur, from Jan 2016 to Oct 2016. The 30 patients undergoing for laparoscopic intra-peritoneal surgeries of 1-2 hours duration with minimal expected blood loss were enrolled. The approval of the institutional committee was taken prior conduct of study. All the patients were informed consents. The 15 patients in Group A received loading dose of Inj. Dexmedetomidine $1\mu\text{g}/\text{kg}/10\text{min}$ diluted to 50ml with Normal Saline, given before induction, followed by maintenance dose $0.5\mu\text{g}/\text{kg}/\text{hour}$ till the end of surgery. The 15 patients in Group B received Normal Saline in a similar manner.

Dexmedetomidine, a highly selective α_2 -adrenergic receptor agonist has generated lot of interest for its sedative, analgesic, perioperative sympatholytic, anesthetic-sparing, and hemodynamic-stabilizing properties. The data generated in the two study groups in the present study concludes that the use of dexmedetomidine maintains blood glucose levels and favourably influencing the intra operative stress induced blood glucose levels.

Keywords: Dexmedetomidine, Stress induced blood glucose levels, laparoscopic intra-peritoneal surgeries, etc.

INTRODUCTION:

Dexmedetomidine, sold under the trade name Precedex among others, is an anxiety reducing, sedative, and pain medication. Dexmedetomidine is notable for its ability to provide sedation without risk of respiratory

depression (unlike other commonly used sedatives such as propofol, fentanyl, and midazolam) and can provide cooperative or semi-arousable sedation. Similar to clonidine, it is an agonist of α_2 -adrenergic receptors in certain parts of the brain. Dexmedetomidine

hydrochloride is also used in veterinary medicine for dogs and cats.[1]

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.[2] 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.[3]

Dexmedetomidine can also be used for procedural sedation such as during colonoscopy. It can be used as an adjunct with other sedatives like benzodiazepines, opioids, and propofol to enhance sedation and help maintain hemodynamic stability by decreasing the requirement of other sedatives. Dexmedetomidine is also used for procedural sedation in children.[4]

Dexmedetomidine is a highly selective α_2 -adrenergic agonist. Unlike opioids and other sedatives such as propofol, dexmedetomidine is able to achieve its effects without causing respiratory depression. Dexmedetomidine induces sedation by decreasing activity of noradrenergic neurons in the locus ceruleus in the brain stem, thereby increasing the activity of

inhibitory gamma-aminobutyric acid (GABA) neurons in the ventrolateral preoptic nucleus. In contrast [clarification needed], other sedatives like propofol and benzodiazepines directly increase activity of gamma-aminobutyric acid neurons. Sedation by dexmedetomidine mirrors natural sleep. As such, dexmedetomidine provides less amnesia than benzodiazepines. Dexmedetomidine also has analgesic effects at the spinal cord level and other supraspinal sites. Thus, unlike other hypnotic agents like propofol, dexmedetomidine can be used as an adjunct medication to help decrease the opioid requirements of people in pain while still providing similar analgesia. [5]

Intravenous dexmedetomidine exhibits linear pharmacokinetics with a rapid distribution half-life of approximately 6 minutes and a terminal elimination half-life of approximately 2 hours. Plasma protein binding of dexmedetomidine is about 94% (mostly albumin).[6]

Dexmedetomidine is metabolized by the liver via glucuronidation and cytochrome P450. As such, it should be used with caution in people with liver disease.[7] The majority of metabolized dexmedetomidine is excreted in the urine (~95%).

The metabolic stress response to surgical trauma is characterized by increased serum levels of catecholamines and other steroid hormones.[8] If this stress response is of prolonged duration, the hyper-metabolic state can lead on to decreased resistance, delayed ambulation and increased morbidity and mortality.[9]

Excitation of the hypothalamus during stress results in the secretion of adrenocorticotrophic hormone (ACTH), which in turn initiates sudden increase in cortisol level. The cortisol mobilizes amino acids and fat from the body stores, and makes them available for synthesis of glucose, thus can cause hyperglycemia.[9] Hence, monitoring blood glucose level can reflect the metabolic stress response to surgery and the effect of Dexmedetomidine in blunting this stress response. Several studies have indicated that

administration of IV Dexmedetomidine during general anesthesia can decrease the minimum alveolar anesthetic concentration (MAC) of Sevoflurane. Thus a clinical study was conducted to assess the effect of Dexmedetomidine on Sevoflurane consumption. The infusion of Dexmedetomidine will not significantly affect the recovery from anesthesia as indicated by time for tracheal extubation.

The aim of the present study was to observe the effect of intravenous Dexmedetomidine on levels of blood glucose, which is one among several stress response markers under General Anesthesia (GA) for laparoscopic intra-peritoneal surgeries.

Methodology:

The study was planned in the Department of Anaesthesia in Sri Krishna Medical College and Hospital, Muzaffarpur, from Jan 2016 to Oct 2016. The 30 patients undergoing for laparoscopic intra-peritoneal surgeries of 1-2 hours duration with minimal expected blood loss were enrolled. The approval of the institutional committee was taken prior conduct of study. All the patients were informed consents.

The 15 patients in Group A received loading dose of Inj. Dexmedetomidine 1µg/kg/10min diluted to 50ml with Normal Saline, given before induction, followed by maintenance dose 0.5µ/kg/hour till the end of surgery. The 15 patients in Group B received Normal Saline in a similar manner.

Anaesthesia was maintained with nitrous oxide in oxygen (50:50), at 3Litres/minute, with Inj. Vecuronium bromide 0.1mg/kg as loading dose and 0.025mg/kg as top-up when required (last dose 25minutes before expected completion of surgery) and Sevoflurane titrated to maintain BIS 40-60.

Blood glucose levels were measured from patient’s fresh capillary whole blood using glucose strip test.

Inclusion criteria: Adult patients of either sex of ASA I OR II, falling between the age groups of 20-65 years presenting for surgery laparoscopic intra-peritoneal surgeries were included after obtaining a written informed consent.

Exclusion criteria: Patients with history of asthma; cardiac or hepatic disorders; Taking centrally acting drugs like antidepressants; Diminished mental competence, deafness, visual disturbances which would prevent them to comprehend the Visual analogue scale (VAS); Pregnant or lactating mothers.

Results & Discussion:

The data from the group A and group B were collected and presented as below. The 15 patients in Group A received loading dose of Inj. Dexmedetomidine 1µg/kg/10 min diluted to 50 ml with Normal Saline, given before induction, followed by maintenance dose 0.5µ/kg/hour till the end of surgery. The 15 patients in Group B received Normal Saline in a similar manner.

Table 1: Demographic Details

Parameters	Group A	Group B
No. of Cases	15	15
Administration	Dexmedetomidine 1µg/kg/10 min	Normal Saline
Age	32 – 43 years	29 – 35 years
Weight in kg	53 – 79 kg	58 – 75 kg
ASA I Cases	8	10
ASA II Cases	7	5
Duration of Surgery	90 – 106 mins	92 – 110 mins
Duration of Anaesthesia	115 – 128 mins	109 – 122 mins

Table 2: Blood Glucose Levels

Parameters	Group A	Group B
No. of Cases	15	15
Administration	Dexmedetomidine 1µg/kg/10 min	Normal Saline
Baseline (mg/dl)	105 – 110	107 - 112
30 mins after intubation (mg/dl)	114 – 118	145 -153
Post-Operative 1 hr (mg/dl)	104 – 109	128 – 143
Post-Operative 2 hr (mg/dl)	106 – 109	118 - 123

Table 3: Sevoflurane consumption (ml)

Parameters	Group A	Group B
No. of Cases	15	15
Administration	Dexmedetomidine 1µg/kg/10 min	Normal Saline
1 st Hour	6.5 – 8.4	10.1 - 13.3
2 nd Hour	7.9 – 9.8	11.5 – 12.8

This surgical population was chosen because the surgery is standardized and common. Laparoscopic surgeries cause major hemodynamic alterations during induction of anaesthesia, creation of pneumoperitoneum, and at extubation. Stress response to surgery encompasses a wide range of endocrinological, immunological, and haematological effects. Endocrine responses to surgery are characterized by increased secretions of pituitary hormones and activation of sympathetic nervous system. Excitation of the hypothalamus during stress results in the secretion of adrenocorticotrophic hormone which in turn initiates sudden increase in cortisol level.[3]

The stress response manifests clinically and metabolically with a wide range of endocrinal, immunological and haematological effects. Some of them include sympathetic nervous system activation, insulin resistance and hyperglycemia, cytokine production with a host of immunological and haematological changes. Blood glucose concentrations increase after surgical incision. The cortisol and catecholamines facilitate glucose production as a result of increased hepatic glycogenolysis and gluconeogenesis. In addition, peripheral use of

glucose is decreased due to insulin resistance. The blood glucose concentrations are related to the intensity of the surgical injury; the changes follow closely the increases in catecholamines. Following cardiac surgery, blood glucose concentrations can increase up to 180-216 mg/dL and remain elevated for up to 24 h after surgery. The changes are less significant with minor surgery.[10]

Neuroendocrinal response, in other words, stress response to surgery is a well addressed problem that can have significant effect on patient outcome. Indirect indicators such as blood sugar are measured to reflect the neuroendocrinal response during surgery, so that the anesthetic technique could be modulated accordingly. Measurement of stress hormones such as cortisol level and catecholamines intraoperatively is non-practical and cumbersome [11]. Blood sugar increases after surgical stimulation with good correlation between the magnitude of rise in blood sugar and the extent of surgical injury to the tissues [12].

The perioperative period is marked by decrease in insulin concentration and significant increase in insulin resistance leading to increased glucose

levels. In our study, when dexmedetomidine groups were compared to control group, blood sugar levels were less after intubation and 2h post extubation. Blood glucose levels values at different time intervals intraoperatively were comparable. Dexmedetomidine when used intramuscularly in dose of 1 mcg/kg, there were no significant differences between the groups in the blood glucose levels.[13] A previous study [14] has showed no significant difference in blood glucose levels and insulin levels. However, one study showed significant difference in blood glucose levels during postoperatively in 1h while there was no significant difference during 30 min postintubation and 6 h postoperatively.[15]

The hypnotic and supraspinal analgesic effects of Dexmedetomidine are mediated by suppression of neuronal firing in the locus coeruleus, resulting in inhibition of norepinephrine release and activity in the descending medullo-spinal noradrenergic pathway.[16-17] This suppression of inhibitory control leads to decreased histamine secretion, resulting in hypnosis similar to natural sleep, without ventilatory depression.[18] The stress response manifests clinically and metabolically with a wide range of endocrinal, immunological and haematological effects. Some of them include sympathetic nervous system activation, insulin resistance and hyperglycemia, cytokine production with a host of immunological and haematological changes.

In Shamim study [19], when dexmedetomidine groups were compared to control group, blood glucose levels were less after intubation, during extubation, and 2 h postextubation. Also, in agreement with the present study, Uyar et al. [20] found that a single bolus dose of dexmedetomidine (1 µg/kg) before induction of anesthesia attenuated the neuroendocrinal responses in patients undergoing craniotomy and there was a notable increase in plasma cortisol and glucose level in the placebo group, than in the dexmedetomidine group. Also, Mukhtar et al. [21] demonstrated that the use of dexmedetomidine in pediatric cardiac surgery with a loading dose of 0.5 µg/kg and a

maintenance dose of 0.5 µg/kg results in reduction in markers of stress response as cortisol, catecholamines, and blood glucose levels.

Conclusion:

Dexmedetomidine, a highly selective α₂-adrenergic receptor agonist has generated lot of interest for its sedative, analgesic, perioperative sympatholytic, anesthetic-sparing, and hemodynamic-stabilizing properties. The data generated in the two study groups in the present study concludes that the use of dexmedetomidine maintains blood glucose levels and favourably influencing the intra operative stress induced blood glucose levels.

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