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A Systematic Review of Literature on Effect of Clonidine Premedication on Glucose Level in Type 1 Diabetic Patients (IDDM) During Ophthalmic Surgery

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ABSTRACT: Hormonal fluctuations are causing changes in the cardiovascular, respiratory system and metabolism that would be problematic in a group of patients. One of the most important hormones in this way is catecholamines in patients with cardiovascular problems-especially patients with ischemic heart will impose adverse effects. Since in addition to patient safety, reduction of complications is among the most important goals of anesthesiologist, if could be offered a way to minimize the effects it will facilitate the achievement of this goal somewhat. This study sought to examine the studies in this area which their consequences could provide an overall view of the field of research for the researchers.

Keywords: Type 1 Diabetes, Clonidine, Randomized Clinical Trials, Vitrectomy, Hyperglycemia

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INTRODUCTION

Generally looking for any kind of stress, including induction and maintenance of anesthesia and surgery process, a set of responses under stress response is evoked in which different body systems including the nervous system, endocrine, immunological as well as biochemical changes have been contributed to the cell surface (Cepeda and Carr, 1996). In the meantime, the endocrine system leading to activation of both hypothalamic- hypothesis-adrenocortical and sympathoadrenal pathways also result the increase or decrease in the number of hormones. These hormonal fluctuations, causing changes in the cardiovascular, respiratory system and metabolism that would be problematic in a group of patients.

One of the most important hormones in this way is catecholamines in patients with cardiovascular problems-especially patients with ischemic heart will impose adverse effects. On the other hand, in the result of contrasts the effects of various hormones (reducing insulin against the increase in glucagon, catecholamines, cortisol and growth hormone), which increases blood sugar interface control blood sugar levels in diabetics during surgery (Dierdorf, 2002).

Since in addition to patient safety, reduction of complications is among the most important goals of anesthesiologist, if could be offered a way to minimize the effects it will facilitate the achievement of this goal somewhat. Given the high prevalence of type 1 Insulin Dependent Diabetes Mellitus in the population and given the prevalence of the disease in adolescence, and there is 80 to 90% of diabetic retinopathy in IDDM patients with a history of over 20 years (Yam and Kwok, 2007). From this group of patients most of them need to eye surgery such as vitrectomy (Moitra VK, Meiler, 2006).

Thus it can be stated diabetes is the leading causes of eye disease that will require surgery. If the blood sugar of these patients can be controlled during vitrectomy it can be prevented complications such as hyperglycemia, ketoacidosis, dehydration and electrolyte abnormalities (Rehman and Mohammed, 2003).

In stressful situations, especially in patients with diabetes mellitus, release the epinephrine and norepinephrine causes a double hyperglycemia. This role of catecholamines results from glycogenolytic and lipolytic effects, inhibits insulin activity, and stimulates the pituitary-adrenal axis (Weissman, 1990). Catecholamines produced by liver increase the glucose level and it is response to increase in tissue sensitivity to catecholamines has been exacerbated in diabetic patients (Shamoon, 1983). Cortisol stimulates by gluconeogenesis and increases resistance to insulin leading to prolong and reinforce the effects of hyperglycemia of the catecholamines (Weissman, 1990).

In patients who undergo surgery, therapeutic strategy should imitate the normal metabolism as far as possible. Exogenous insulin prescription which inhibits production of endogenous glucose (both glycogenolysis and gluconeogenesis) and stimulates use of glucose intervenes with metabolic effects of hormonal changes of surgical stresses. However, insulin therapy may increase the risk of hypoglycemia in these patients whose occurrence between 5 to 10% has been reported in different studies (Raucoules-Aimé, 1994). Blood glucose may be controlled by adrenoreceptor agonists and decrease sympathetic tone to release of norepinephrine from nerve terminals (Barker et al., 1995). This mechanism results from central α2 agonists that inhibit catecholamines release during activation of inhibitory α2 adreno receptors

of central pre-synaptic. One of the drugs frequently used can be referred to clonidine. Clonidine is considered as a receptor agonist of adrenoceptor for improvement in metabolic status of diabetic patients in stressful situations such as surgery (13-14). It is necessary during surgery avoid hyperglycemia because of prolonged hyperglycemia induced by glucose and create an osmotic diuresis which cause water and electrolyte imbalance in patients (McAnulty and Hall, 2003). Increase in serum osmolality caused a hyperosmolar condition that could be causing hyperviscosity, thrombogenic and dysfunction of the central nervous system (Milaskiewicz and Hall, 1992).

In addition, according to findings published indicates that repair and wound tensile strength and phagocytic function may be impaired during hyperglycemia. High levels of free fatty acids concentration increased incidence of cardiac arrhythmias during anesthesia and disrupts a state of hepatic glucagon in patients (Milaskiewicz and Hall, 1992). Given to above mentioned notes, precise control of the metabolic status of the patient during surgery is recommended to reduce morbidity (Hirsch et al., 1991).Insulin infusion with metabolic effects of hormonal changes made during surgery (Raucoules-Aimé et al., 1995) but insulin diets put individuals at risk of hypoglycemia reactions and have no effect on resistance to insulin of released catecholamines (Raucoules-Aimé et al., 1994).

In one study it was shown that despite increase in insulin levels, blood glucose levels are increased in patients undergoing surgery, which it was itself evidence of insulin resistance (McAnulty and Hall, 2003). In this study, clonidine was used to inhibit catecholamines. Use of clonidine inhibits the release of catecholamines and thereby providing an improved blood glucose levels during surgery. The operating mechanism of these effects is because of the central α2 agonists which inhibit the release of catecholamines during activation of inhibitory α2 adrenoceptor of central pre-synaptic. Studies have shown that this reduction was dose dependent and is associated with a decrease in plasma catecholamines after oral administration (Mikawa et al., 1995). Central and peripheral effects of clonidine may be associated with improvements in patient's metabolic control that this problem was shown in one study (McAnulty and Hall, 2003). Clonidine is considered as a receptor agonist of adrenoceptor for this action (Quintin et al., 1991). Yet, there is disagreement on pituitary – adrenal system; however, reduction in release ACTH hormone and cortisol has been reported by clonidine (Gaumann et al., 1991). In non-diabetic patients, the effect of agonist α2 adrenoceptor on blood concentration is variable and depends on the type of surgery (Lyons et al., 1997) and consumed dosage (Nishina et al., 1998). Low doses of clonidine may cause hyperglycemia while 4μg/kg doses (Swislocki et al., 1993) and more (Nishina et al., 1998) may inhibit hyperglycemia response. Use of clonidine in eye surgery improve hemodynamic status during surgery and reduces the intraocular pressure and the requirements of anesthesia is used (Kumar et al., 1992). In a study conducted in 2003, it was found that as a premedication, clonidine reduces the need for insulin and improves blood glucose control during eye surgery. The improved metabolic control is related with lower concentrations of catecholamines (McAnulty and Hall, 2003). This study indicated that higher doses of clonidine adjust glycemic response to surgery (McAnulty and Hall, 2003). There was any hypoglycemic reaction in patients who received 225- 375 μg clonidine.

Results of other studies on the effects of variable clonidine on changes in cortisol serum associated with surgery have been published. These studies have shown that these differences cannot be explained using doses of clonidine variables (Lyons et al., 1997). In other study published by Gaumann et al. (Gaumann et al., 1991), a significant decrease was obtained in cortisol serum associated with surgery. But no samples were collected before administration of oral clonidine and patients who were receiving high doses of steroids were not excluded. On the other hand, there was not observing any different between cortisol serum levels after clonidine premedication in two studies (Lyons et al., 1997). In another study it was shown that exmedetomidine, a potent α2 adrenoreceptor agonist with high selectivity power, it does not inhibit adrenal steroidogenesis (Venn et al., 2001). In the Bahlula et al. study, there was any change in plasma levels of cortisol but the authors on this study stated that their information in this field due to use of flunitrazepam premedication is not interpretable (McAnulty and Hall, 2003). Because the benzodiazepines known as one of the compounds to alter ACTH secretion (Gram et al., 1984). Clonidine stimulates releases of growth hormone and oral clonidine is used in growth hormone stimulation test. It was found in a study that administration of oral clonidine in diabetic patients who undergo eye surgery increases plasma levels of growth hormone but this increase does not influence control of patient' blood glucose (McAnulty and Hall, 2003). This issue may be surprising but destructive effects of increased growth hormone on blood glucose levels in diabetic patients do not probably result from the effects of catecholamines or cortisol during surgery (McAnulty and Hall, 2003). However, this study indicated that increased growth hormone level is relatively short and researchers could not ignore the possibility that postoperative changes in glycemic control of patients occurred due to the growth hormone because growth hormone takes several hours to influence glucose homeostasis (Weissman, 1990). On the other study, it was found that plasma peptide C concentration in patients who received clonidine is lower (McAnulty and Hall, 2003). Several explanations have

been given for this issue. In the first phase, clonidine inhibits insulin release through the effect of peripheral α2 pre-synaptic receptors (Weissman, 1990). The second hypothesis is that lower concentration of blood glucose level results from stimulation of less powerful insulin release (McAnulty and Hall, 2003). The third hypothesis is that clonidine reduces resistance against insulin through inhibition of catecholamines release, thus, it reduces the need to endogenous and exogenous insulin (Weissman, 1990).

Clonidine as a premeditation also improved the stability of the cardio-vascular and used to improve the cardio-vascular responses to laryngoscope, intubation and surgery (Engelman et al., 1989). It also appears that cardiac ischemia clonidine improves before the surgery (McSPI, 1997). These features seem helpful in diabetic patients undergoing eye surgery. This group of patients is affected with a higher prevalence of cardiovascular disorders such as hypertension, ischemic heart disease and impaired ventricular function. In addition to the above, clonidine has been shown to reduce the intraocular pressure and prevent the increase in intraocular pressure induced by acute hypertension that may occur in either local or general anesthesia (Kumar et al., 1992). Due to above mentioned as it appears clonidine may be useful in diabetic patients, especially in eye surgery.Therefore, this study is aimed to design a randomized clinical trial with efficacy of clonidine in comparison with premedication in reducing blood sugar in patients with type 1 diabete who underwent vitrectomy is examined.

DISCUSSION

Generally looking for any kind of stress, including induction and maintenance of anesthesia and surgery process, a set of responses under stress response is evoked in which different body systems, including the nervous system, endocrine, immunological as well as biochemical changes have been contributed to the cell surface (Cepeda and Carr, 1996).

In stressful situations, especially in patients with diabetes mellitus, release the epinephrine and norepinephrine causes a double hyperglycemia. This role of catecholamines results from glycogenolytic and lipolytic effects, inhibits insulin activity, and stimulates the pituitary-adrenal axis (Weissman, 1990).

In diabetic patients who are undergo surgery, therapeutic strategy should imitate the normal metabolism as far as possible. Exogenous insulin prescription which inhibits production of endogenous glucose (both glycogenolysis and gluconeogenesis) and stimulates use of glucose intervenes with metabolic effects of hormonal changes of surgical stresses. However, insulin therapy may increase the risk of hypoglycemia in these patients whose occurrence between 5 to 10% has been reported in different studies (Raucoules-Aimé, 1994). Insulin infusion with metabolic effects of hormonal changes made during surgery (Raucoules-Aimé et al., 1995) but insulin diets put individuals at the risk of hypoglycemia reactions and have no effect on resistance to insulin released of catecholamines (Raucoules-Aimé et al., 1994).

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