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RESEARCH ARTICLE

EFFECT OF 4% GELATIN AND DEXTRAN-40 ON BLOOD GLUCOSE LEVELS DURING SURGERY UNDER SUBARACHNOID BLOCK

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ABSTRACT

Background & Aims: Stress response to surgery induces hyperglycemia to limited extent. An additive hyperglycemic response, secondary to the metabolism of intravenous fluids, can thus prove detrimental to the well-being of the patient, if ignored.

Our study aimed to examine and compare the effects of 4% gelatin and dextran-40 on blood glucose levels during surgery under subarachnoid block and their potential to induce hyperglycemia.

Methods: Sixty ASA grade I and II patients were randomized into two groups, 30 patients in each. Group 1 patients were preloaded with 4% Gelatin (10ml/kg) and Group 2 patients were preloaded with Dextran-40 in normal saline (10ml/kg), over a period of 30 minutes (min). Just prior to preloading, base line capillary blood glucose (CBG) level was noted this is followed by subsequent readings at 20 min interval until 100 min from base line reading. All patients received normal saline (0.9%) as a maintenance fluid. Under strict aseptic precautions, subarachnoid block using 15 mg of hyperbaric bupivacaine at L3-L4 or L4-L5 level was given after preloading.

Results: Both groups are comparable in age, weight, sex and age wise distribution. The CBG levels in both the groups were within physiological limits. In group 2, the maximum mean blood glucose level of 94.53 ± 14.57 mg/dL was found at 60 min from onset of preloading, which was found to be statistically significant ($p=0.017$), when compared with corresponding blood glucose level (86.50 ± 10.44mg/dL) in group 1.

Conclusion: Preloading the patients prior to subarachnoid block with 4% gelatin or dextran 40 do not raise CBG levels significantly above the physiological limits.

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INTRODUCTION

Colloids are widely used in fluid resuscitation for hypovolaemic shock as an integral part of the acute medical management in critically ill patients in intensive care unit or inside an operating room (Boldt, 2000). Colloids are also used as preloading fluids prophylactically, to limit complications following sympathetic blockade in central neuraxial blockade, especially subarachnoid block (Buggy *et al*., 1997). Stress response to surgery and catecholamine release following it, is itself known to induce some amount of hyperglycemia, but this remains confined to limited extent. An additive hyperglycemic response, secondary to the metabolism of infused intravenous colloids, especially starches can thus prove detrimental to the well-being of the patient, if ignored (Murty *et al*., 2004). Hyperglycemia is known to potentiate neurological changes and ischemia to the brain spinal cord, heart (McAlister *et al*., 2003) and kidneys (Judith, 1999).

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It also impairs wound healing, by interfering with white blood cells (Nohé *et al*., 2005). These effects could prove to be even more harmful influid resuscitation of uncontrolled diabetes, during neurosurgical proceduresand in the event of cardiopulmonary resuscitation. Dextrans and hydroxyethyl starches produce significant levels of free glucose residues following metabolism. Dextrans are polysaccharides that are normally broken down completely to carbon dioxide and water by the enzyme dextranase, at a rate approaching 70 mg/kg, every 24 hours. However, under stressful conditions, or as a result of catecholamine response to shock, these Dextrans are likely to elevate blood glucose levels to potentially harmful limits following intravenous administration, as a response to the rapid degradation of the glucose polymers to free glucose residues (Kirby and Colloids, 1994; AbhiruchiPatki, 2010). Similar to Dextrans, Hydroxyethyl starches, which are made up of large ethylated starch or glucose polymers, are metabolised by serum amylases to produce smaller molecules of starch polymers and free glucose residues. Even these carry a potential to accelerate blood glucose levels, subsequent to intravenous administration, under stressful conditions (Murty *et al*., 2004). Considering these potential ill-effects of hyperglycemia, in the peri-operative period, on well-being of patients and on the outcome of surgery, we carried out the following study, with an objective to examine and compare the effects of 4% gelatin and dextran-40 on blood sugar levels during subarachnoid block.

MATERIALS AND METHODS

A prospective, randomized non blinded study was conducted after approval from Institutional Ethics and Dissertation committee in the department of Anaesthesiology and Critical Care from July 2012 to June 2013 to compare the effect of 4% gelatin and dextran-40 on blood glucose levels during surgery under subarachnoid block. Informed written consent was obtained from each patient participating in the study. Sixty patients of American Society of Anesthesiologists (ASA) physical status I and II, non diabetic patients, 20-60 years of age, weighing between 40-70 kgs and undergoing elective lower limb or lower abdominal surgical procedures, which were anticipated to last for at least one hour were included in the study.

Patients on drugs that cause hyperglycemia (steroids,…), patients who are diabetic, those requiring blood transfusion, low haematocrit (packed cell volume <30), patients who develop allergic reactions to study fluids, uncontrolled hypertension, pregnant women and lactating mothers, patients with renal and hepatic diseases, patients who are not willing to participate in the study were excluded from study. Randomization sequence was generated before the start of the study. Patients were selected and randomized by computer and opaque sealed envelope technique, into 2 groups i.e., Group 1 and 2, thirty patients in each group. Group 1 patients were preloaded with 4% Gelatin [Gelofusine-4%] (10ml/kg) and Group 2 patients were preloaded with Dextran-40 in normal saline [Microspan-40] (10ml/kg), over a period of 30 min, prior to spinal anaesthesia, through an 18 –gauge intravenous cannula. Preloading was done under vigilant monitoring of vital parameters-Heart rate, Blood pressure and SPO_2 at 10 minute (min) interval. Preloading was immediately interrupted on evidence of any allergic reaction and symptomatic treatment was given and the patient was excluded from the study.

Throughout the procedure, capillary blood glucose levels were measured at 20 min intervals using a SD-CHECK GOLD glucometer [Accuchek] (CAT NO-01GM10). Glucometer reading was validated against peripheral venous blood glucose measurement periodically once in 60 tests. Just prior to preloading, base line capillary blood glucose level was noted and followed by subsequent readings at 20,40,60,80 and 100 min from base line reading. Following preloading, all the patients received normal saline (0.9%) as a maintenance fluid.
Under strict aseptic precautions, subarachnoid block using 15 mg of hyperbaric (0.5%) bupivacaine at L3-L4 or L4-L5 level was administered immediately after completion of the preloading. Sensory block was noted after fixation of the drug. Hypotension was defined as more than 25% fall in mean arterial pressure and was treated with fluid boluses (normal saline) and injection ephedrine 6mg IV.

Bradycardia was defined as heart rate less than 50 beats/min and treated with injection atropine 0.6mg IV. Patient data variables were summarized as mean and standard deviation (SD).Comparison between two groups with respect to continuous variables such as age, weight, duration of surgery, maximum level of sensory blockade were compared with student t-test (t). Categorical variables like gender distribution and type of surgical procedures were analyzed by chi-square test ($\chi2$).

Intra group variables were analyzed with Analysis of variance (ANOVA) test (F)) with Bonferroni's post-hoc test. All statistical analysis was done by using EPI INFO 3.5.4 version (Epidemiological Information) software. P (Probability) value of < 0.05 was considered as statistically significant.

RESULTS

Sixty two patients were recruited in to the study. Two cases were excluded from study, one case was excluded due to failed spinal and other due to inadequate level of block. In our study, no anaphylactic reactions were observed to study fluids (4% Gelatin and Dextran-40).All the patients were haemodynamically stable during preloading and intraoperative period. The patients in both groups were compared in respect to age, sex, weight, duration of surgery, maximum sensory blockade level and type of surgical procedure carried out in the study.

Table 1. Comparison of demographic data

Characteristic	Gelatin (1) group	Dextran (2) Group	Statistical significance
No. of cases(n)	30	30	---
Age (Years)	42.16 ± 9.69	46.45 ± 9.58	t = 1.75; P=0.08
Sex M: F	19 : 11	23 : 7	$\chi2$ = 0.68; P=0.40
Weight (kg)	57.96 ± 8.55	60.32 ± 6.79	t = 1.19; P=0.23

(t-student unpaired t test ; $\chi2$-chi-square test ,n-number of cases,M-male, F- female, P-probability)
Data entered as Mean (± Standard Deviation).Group 1 = Gelatin group, Group 2= Dextran group.
Ages in both groups are comparable (P value= 0.08). Weights in both groups are comparable (P value= 0.23).
Gender distribution in both groups are comparable (P value =0.40)

Table 2. Comparison of surgical procedures in two groups

Surgical procedure	Gelatin (1) group	Dextran (2) Group	Statistical significance
Urology	10	10	$\chi2$ = 0.07; P=0.78
General surgery	20	20	
Total	30	30	

The types of surgical procedures carried out in two groups were comparable

There is no significant (p>0.05) difference in mean age, mean weight and sex distribution (Table 1).

The types of surgical procedures carried out in two groups were comparable (Table 2). The mean duration of surgery, which was taken as time from surgical incision to skin closure were also comparable in two groups (Table 3). Mean of the maximum level of sensory blockade achieved after spinal anaesthesia were T10 in group 1and T8 in group 2 (Table 3). The baseline mean capillary blood glucose levels (mg/dL) at onset of preloading in two groups were 90.58±11.03 in group 1 and 89.45±11.27 in group 2, which were comparable (p=0.69). In group 1 (Gelatin), baseline mean blood glucose level was 90.58±11.03 mg/dL. The maximum mean blood glucose level of 92.76 ± 14.77 mg/dL was found at 100 min from the onset of preloading, which was found to be statistically not significant from baseline mean blood glucose level.

In group 2 (Dextran), baseline mean blood glucose level was 89.45 ± 11.27 mg/dL. The maximum mean blood glucose level of 94.53 ± 14.57 mg/dL was found at 60 min from the onset of preloading, which was found to be statistically significant (p=0.017), when compared with corresponding (60min) blood glucose level in group 1. The mean capillary blood glucose levels at 20, 40 and 80 from onset of preloading, in two groups were comparable and statistically not significant (P<0.05).The mean capillary blood glucose levels at 100 minutes from onset of preloading, in two groups were 92.76 ± 14.77 mg/dL in group 1 and 89.66 ± 14.15 mg/dL in group 2, which were comparable (p=0.41). The capillary blood glucose levels in both the groups were within physiological limit(Table-

DISCUSSION

A prospective, randomized study was conducted in the Department of Anaesthesiology and Critical Care from July

Table 3. Duration of Surgical procedure and level of sensory blockade:

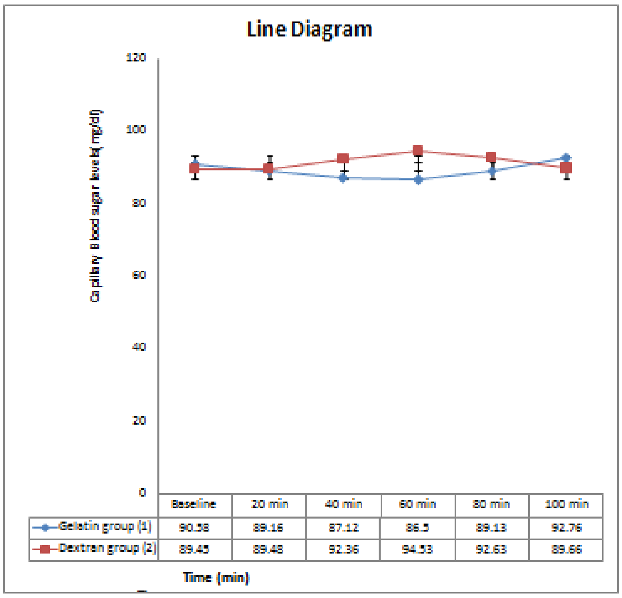
	Gelatin (1) group	Dextran (2) Group	Statistical significance
Duration of surgery [minutes] (Mean ± SD)	85.90 ± 21.10	88.16 ± 22.24	t = 0.40; P=0.68
Maximum level of sensory blockade	T 10	T 8	t = 2.44; P=0.017

The mean duration of surgery, which was taken as time from surgical incision to skin closure were also comparable in two groups. (85.90±2.10 minutes in group 1 and 88.16±22.24 minutes in group 2).Mean of the maximum level of sensory blockade achieved a fter spinal anesthesia were T10±1.34 in group 1 and T8±1.18 in group 2.

Table 4. Differences in Mean capillary blood glucose levels (mg/dl) between two groups

Time (minutes)	Gelatin (1) group	Dextran (2) Group	Statistical significance
Baseline	90.58 ± 11.03	89.45 ± 11.27	t = 0.39; P=0.69
20 min	89.16 ± 9.08	89.48 ± 13.26	t = 0.11; P=0.91
40 min	87.12 ± 11.10	92.36 ± 14.01	t = 1.62; P=0.11
60 min	86.50 ± 10.44	94.53 ± 14.57	t = 2.45; P*=0.017
80 min	89.13 ± 10.02	92.63 ± 16.07	t = 1.01; P=0.31
100 min	92.76 ± 14.77	89.66 ± 14.15	t = 0.82; P=0.41
Statistical significance	F = 1.29; P=0.29	F = 0.72; P=0.60	---

(P*-Statistically significant)The capillary blood glucose levels in both the groups were within physiological limits. In group 2 (Dextran), baseline mean blood glucose level was 89.45 ± 11.27 mg/dl. The maximum mean blood glucose level of 94.53 ± 14.57 mg/dl was found at 60 min from onset of preloading, which was found to be statistically significant (p=0.017), when compared with corresponding (60min) blood glucose level in group 1.



Graph-1 Line diagram showing time in minutes in x axis and capillary bloo d glucose levels in mg/dL in y-axis (standard deviation included)

Graph 1. Line diagram showing mean capillary blood glucose levels in 2 groups

2012 to June 2013 to compare the effect of 4% gelatin and dextran-40 on blood sugar levels during surgery under subarachnoid block. A majority of the studies conducted on starch solutions and dextrans have evaluated their volume expansion properties and their impact on blood coagulation. Very few studies have examined the possibility of starches and dextrans producing hyperglycemia, in spite of their pharmacodynamic potential to cause the same.

In our study, spinal anaesthesia was used as the technique of choice in all the patients, so as to standardize the stress response due to anaesthesia and surgery in two groups. Stress response to surgery and catecholamine release following it, is itself known to induce some amount of hyperglycemia, but this remains confined to limited extent (Desborough, 2000). For similar reasons, only normal saline was used in all the patients, as the subsequent intravenous fluid intra-operatively. Ringer's Lactate, has been shown to possibly cause hyperglycemia, due to the conversion of lactate to glucose via the Cori's cycle (Tayek and Katz, 1997). Murty *et al*. (2004)., in 2004, studied the effects of 6%Hestar-450, Pentastarch 200 and Ringer's Lactate as preloading fluids in spinal anaesthesia, on blood sugar levels. They concluded that both the starches significantly elevated the blood sugar levels ($P < 0.05$), which were within physiological limits and peaks at the end of two hours with Hestar6%-450 and at the end of three hours with pentastarch 6%-200. However, in their study, Ringer's Lactate did not significantly elevate blood sugar level.

Abhiruchipatki *et al.,* 2010, studied effect of 6% hydroxyethyl starch-450 and low molecular weight dextran on blood sugar levels during surgery under subarachnoid block and demonstrated a sustained and statistically significant rise ($P < 0.05$) in blood sugar levels from the baseline, with the infusion of both Ringer's lactate and Hydroxy ethyl starch 6%-450, which peaked at the end of 45minutes and at the end of one hour, respectively. Dextran 40, on the other hand demonstrated a steep and statistically highly significant (above physiological limit) rise ($P < 0.001$) in mean capillary blood glucose levels from the mean baseline reading, which peaked at 45 minutes.

Hofer *et al*., in 1992, studied the effect of hydroxyethyl starch solutions on blood glucose concentrations in diabetic and non diabetic rats and concluded that all though there existed a strong possibility for hydroxyethyl starches to cause hyperglycemia, neither hetastarch nor pentastarch infusions significantly altered blood glucose values over the 3-hr study period, regardless of whether the rats were diabetic or nondiabetic. They assumed that the data collected from the study on rats is transferable to humans and hence they concluded that hydroxyethyl starch solutions could be used in diabetic and non-diabetic patients without raising the blood sugar levels. Our study demonstrated that in group 1 (Gelatin), the maximum mean blood glucose level was found at 100 min from onset of preloading, which was found to be statistically not significant from baseline mean blood glucose level. In group 2 (Dextran), the maximum mean blood glucose level was found at 60 min from onset of preloading, which was found to be statistically significant (P=0.017), when compared with corresponding (60 min) blood glucose level in group 1. The mean capillary blood glucose levels at 100 minutes from onset of preloading, in two groups were comparable (p=0.41). The capillary blood glucose levels in both the groups were within physiological limits.

Conclusion

We conclude, that preloading the patients prior to subarachnoid block with 4% gelatin or dextran 40 in normal saline do not rise capillary blood glucose levels significantly above the physiological limits. Our study has a few limitations, though; we included 4% gelatin and Dextran-40, as study infusions, primarily because of their relatively easier availability in our institution, leaving scope for inclusion of other starches with different molecular weights and different compositions in future studies.

Conflicts of interest: None

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