“A PROSPECTIVE RANDOMISED STUDY COMPARING DIFFERENT APPROACHES TO INTRAOPERATIVE MANAGEMENT OF DIABETES MELLITUS – THE VELLORE REGIMEN VS INTERMITTENT IV BOLUS REGIMEN”

Dissertation submitted to

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfillment for the award of the degree of

DOCTOR OF MEDICINE

IN

ANAESTHESIOLOGY

BRANCH X

APRIL 2016

INSTITUTE OF ANAESTHESIOLOGY AND CRITICAL CARE

MADRAS MEDICAL COLLEGE

CHENNAI- 600 003.

CERTIFICATE

This is to certify that the dissertation entitled, **"A PROSPECTIVE RANDOMISED STUDY COMPARING DIFFERENT APPROACHES TO INTRAOPERATIVE MANAGEMENT OF DIABETES MELLITUS– THE VELLORE REGIMEN VS INTERMITTENT IV BOLUS REGIMEN"** submitted by **Dr. GLADWIN J FERNANDES,** in partial fulfilment for the award of the degree of Doctor of Medicine in Anaesthesiology by the Tamil Nadu Dr. M.G.R. Medical University, Chennai, is a bonafide record of the work done by him in the INSTITUTE OF ANAESTHESIOLOGY AND CRITICAL CARE, Madras Medical College and government hospital, during the academic year 2013-2016.

Prof. DR. B.KALA M.D., D.A.,
PROFESSOR AND DIRECTOR,
INSTITUTE OF ANAESTHESIOLOGY
&AND CRITICAL CARE
MADRAS MEDICAL COLLEGE,
CHENNAI-600003

DR. R.VIMALA M.D.
DEAN,
MADRAS MEDICAL COLLEGE
GOVT. GENERAL HOSPITAL
CHENNAI-600 003

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled, "**A PROSPECTIVE RANDOMISED STUDY COMPARING DIFFERENT APPROACHES TO INTRAOPERATIVE MANAGEMENT OF DIABETES MELLITUS– THE VELLORE REGIMEN VS INTERMITTENT IV BOLUS REGIMEN"** submitted by **Dr. GLADWIN J FERNANDES,** in partial fulfilment for the award of the degree of Doctor of Medicine in Anaesthesiology by the Tamil Nadu Dr. M.G.R. Medical University, Chennai., is a bonafide record of the work done by him in the INSTITUTE OF ANAESTHESIOLOGY AND CRITICAL CARE, Madras Medical College and government hospital, during the academic year 2013-2016.

PROF. DR . V .PANKAJAVALLI, M.D, D.A,
Professor of Anaesthesiology,
INSTITUTE OF ANAESTHESIOLOGY AND CRITICAL CARE,
RAJIV GANDHI GOVT. GENERAL HOSPITAL,
MADRAS MEDICAL COLLEGE,
CHENNAI – 600 003.

DECLARATION

I hereby, solemnly declare that this dissertation entitled **"A PROSPECTIVE RANDOMISED STUDY COMPARING DIFFERENT APPROACHES TO INTRAOPERATIVE MANAGEMENT OF DIABETES MELLITUS – THE VELLORE REGIMEN VS INTERMITTENT IV BOLUS REGIMEN"** is a bonafide record of the work done by me in the Institute of Anaesthesiology and Critical Care, Madras Medical College and Government General Hospital, Chennai, during the period of 2013 – 2016 under the guidance of **DR . PROF .V .PANKAJAVALLI, M.D, D.A,** Professor of anaesthesiology, Institute of Anaesthesiology and Critical Care, Madras Medical College, Chennai – 3 and submitted to **The Tamil Nadu Dr. M.G.R. Medical University, Guindy, Chennai – 32**, in partial fulfilment for the requirements for the award of the degree of M.D. Anaesthesiology (Branch X), examinations to be held on April 2016.

I have not submitted this dissertation previously to any university for the award of degree or diploma.

Place: Chennai **Dr .GLADWIN J FERNANDES**

Date :

ACKNOWLEDGEMENT

I am extremely thankful to **DR.R.VIMALA M.D.,** Dean, Madras Medical College & Rajiv Gandhi Govt. General Hospital, for her permission to carry out this study.

I am immensely grateful to **Prof .DR. B.KALA, M.D., D.A.,** Director, Institute of Anaesthesiology and Critical Care, for her concern and support in conducting this study.

I am extremely grateful and indebted to my guide, **Prof. DR.V. PANKAJAVALLI, M.D, D.A,** Professor of Anaesthesiology, Institute of Anaesthesiology & Critical Care, for her concern, inspiration, meticulous guidance, expert advice and constant encouragement in preparing this dissertation.

I am very grateful to express my sincere gratitude to the Professors, Dr. ESTHER SUDHARSHINI RAJKUMAR M.D.D.A., Dr. S.ANANTHAPPAN M.D.D.A., Dr. SAMUEL PRABAKARAN M.D. D.A. and Dr.M.VELLINGIRI M.D., D.A.., Institute of Anaesthesiology & Critical Care, for their constant motivation and valuable suggestions.

I express my hearty thanks to my co-guide DR.CATHERINE RATHNASAMY M.D Senior Assistant Professor for the constant monitoring and guidance throughout the course of this study.

I express my humble thanks to my teachers, DR MIRIAM SHIRIN, Senior Assistant Professor, DR.KANTHIMATHY M.D., D.A Senior Assistant

Professor, DR.G.K.KUMAR M.D., Professor, DR.SUGANTHALAKSHMI M.D., Assistant Professor, DR.SUMATHI M.D., Assistant Professor, DR.GANESH M.D., Assistant Professor, DR.SHANMUGAPRIYA M.D., Assistant Professor for their continuous support during the period of study.

I express my deepest gratitude to all my department colleagues who have helped me for following up the patients from assessment room, operation theatre up to the post-operative ward without which this study would not have been possible.

I am thankful to the Institutional Ethical Committee for their guidance and approval for this study.

My sincere thanks to the statistician, who has played an important role during my study.

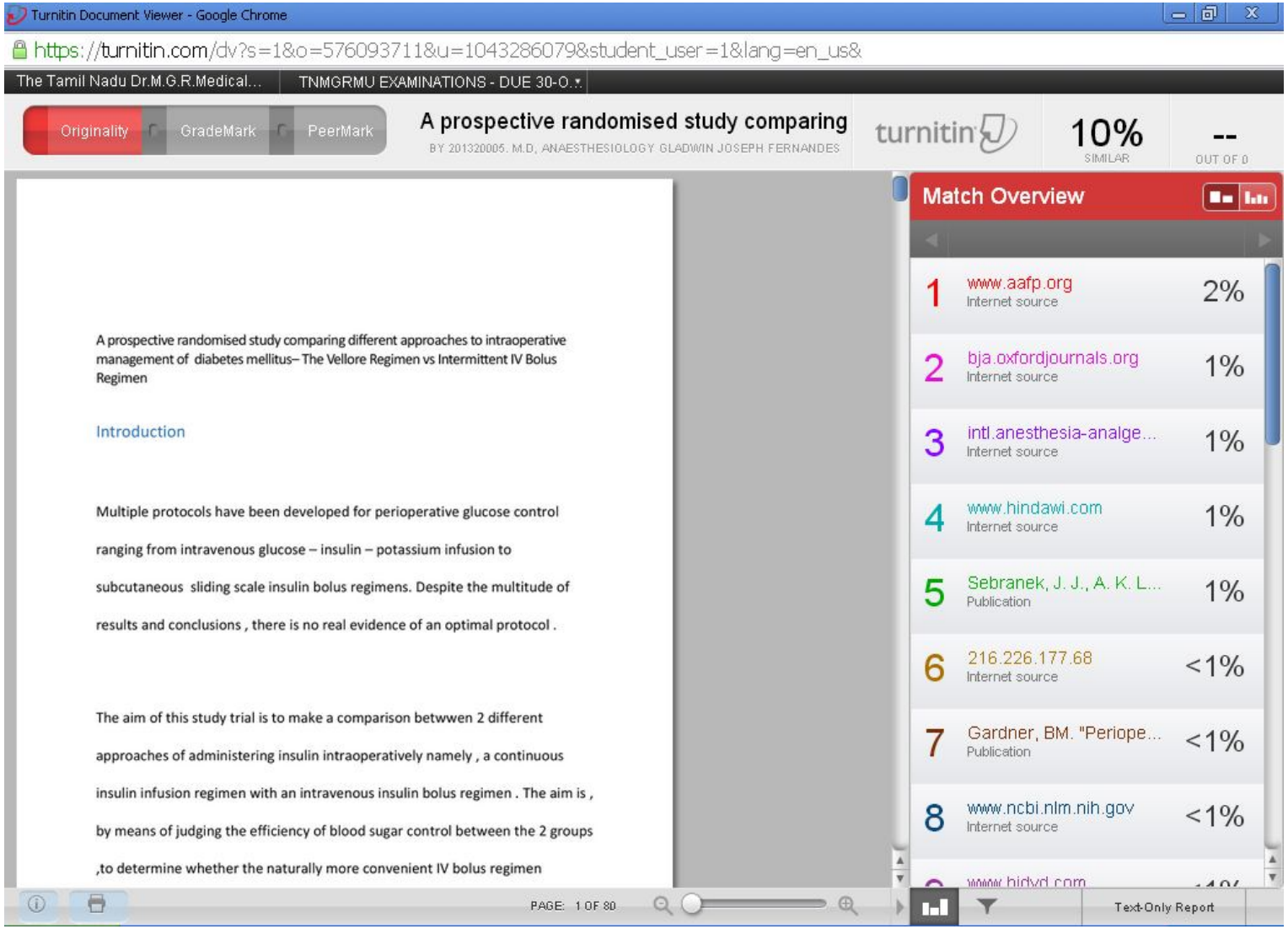
I am thankful to all my colleagues, family and friends for their moral support, help and advice in carrying out this dissertation.

Last but not the least; I thank all the patients for willingly submitting themselves for this study.

Above all I give thanks to the Lord Almighty for blessing me to complete this work.

ABBREVIATIONS

FBS	–	Fasting Blood Sugar
PPBS	–	Post Prandial Blood Sugar
DM	–	Diabetes Mellitus
IV	–	Intravenous
CXR	–	Chest Xray
RFT	–	Renal Function Tests
LFT	–	Liver Function Tests
Hb	–	Haemoglobin
BS0	–	Blood Sugar at hour 0
INS0	–	Insulin Dose at hour 0
GA	–	General Anaesthesia
RA	–	Regional Anaesthesia
DKA	–	Diabetic Keto Acidosis
OHA	–	Oral Hypoglycaemic Agent
NS	–	Normal Saline
D5W	–	5% Dextrose in Water

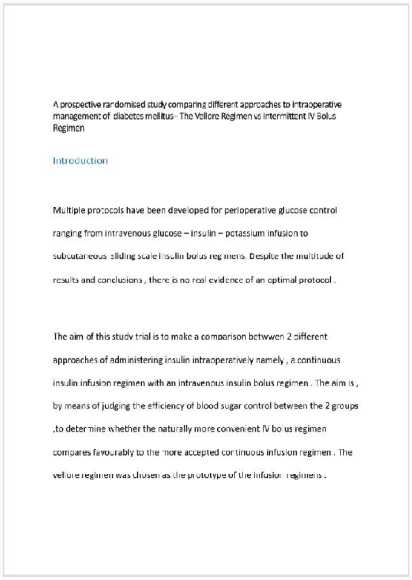

Turnitin Document Viewer - Google Chrome
https://turnitin.com/dv?s=1&o=576093711&u=1043286079&student_user=1&lang=en_us&
The Tamil Nadu Dr.M.G.R.Medical...
TNMGRMU EXAMINATIONS - DUE 30-0...
Originality
GradeMark
PeerMark
A prospective randomised study comparing
BY 201320005. M.D, ANAESTHESIOLOGY GLADWIN JOSEPH FERNANDES
turnitin
10%
SIMILAR
--
OUT OF 0
A prospective randomised study comparing different approaches to intraoperative management of diabetes mellitus– The Vellore Regimen vs Intermittent IV Bolus Regimen
Introduction
Multiple protocols have been developed for perioperative glucose control ranging from intravenous glucose – insulin – potassium infusion to subcutaneous sliding scale insulin bolus regimens. Despite the multitude of results and conclusions , there is no real evidence of an optimal protocol .
The aim of this study trial is to make a comparison betwwen 2 different approaches of administering insulin intraoperatively namely , a continuous insulin infusion regimen with an intravenous insulin bolus regimen . The aim is , by means of judging the efficiency of blood sugar control between the 2 groups ,to determine whether the naturally more convenient IV bolus regimen
PAGE: 1 OF 80
Match Overview
1 www.aafp.org Internet source 2%
2 bja.oxfordjournals.org Internet source 1%
3 intl.anesthesia-analge... Internet source 1%
4 www.hindawi.com Internet source 1%
5 Sebranek, J. J., A. K. L... Publication 1%
6 216.226.177.68 Internet source <1%
7 Gardner, BM. "Periope... Publication <1%
8 www.ncbi.nlm.nih.gov Internet source <1%
Text-Only Report

Digital Receipt

This receipt acknowledges that Turnitin received your paper. Below you will find the receipt information regarding your submission.

The first page of your submissions is displayed below.

Submission author:	201320005. M.d, Anaesthesiology G.
Assignment title:	TNMGRMU EXAMINATIONS
Submission title:	A prospective randomised study co..
File name:	thesisgj.docx
File size:	348.46K
Page count:	80
Word count:	12,981
Character count:	64,144
Submission date:	30-Sep-2015 12:34AM
Submission ID:	576093711



A prospective randomised study comparing different approaches to intraoperative management of diabetes mallitus - The Vellore Regimen vs Intermittent IV Bolus Regimen

Introduction

Multiple protocols have been developed for perioperative glucose control ranging from intravenous glucose – insulin – potassium infusion to subcutaneous sliding scale insulin bolus regimens. Despite the multitude of results and conclusions, there is no real evidence of an optimal protocol.

The aim of this study trial is to make a comparison between 2 different approaches of administering insulin intraoperatively namely, a continuous insulin infusion regimen with an intravenous insulin bolus regimen. The aim is, by means of judging the efficiency of blood sugar control between the 2 groups ,to determine whether the naturally more convenient IV bolus regimen compares favourably to the more accepted continuous infusion regimen. The vellore regimen was chosen as the prototype of the infusion regimens.

TABLE OF CONTENTS

ABSTRACT

"A prospective randomised study comparing different approaches to intraoperative management of diabetes mellitus – The Vellore Regimen vs Intermittent IV Bolus Regimen"

Background:

Diabetes mellitus is a common metabolic disorder with relevant anaesthetic implications. The large number of trials aiming to arrive at an ideal protocol for intraoperative management of the disease have so far not lead to a widely accepted and agreeable solution. This might be due, in part, to poor adherence because of inconvenient strategies.

In this study, I aim to conclude whether the simple and easy intermittent intravenous insulin bolus regimen can stand up to the mostly followed Vellore regimen in efficiency and safety.

Method:

This was a unicentric randomised prospective trial in vascular surgery patients who have type 2 diabetes mellitus. 70 patients were chosen based on predefined criteria and randomly divided into 2 groups .Patients from each group were subjected to hourly intraoperative monitoring and insulin dosing depending on the group .Statistical approach- Primary outcome measures- The mean with standard deviation of glycaemic readings of each hour were calculated within each group and then compared across the groups for statistical significance .Secondary outcome measures -The difference in the percentage of people with uncontrolled sugars (defined as blood glucose values outside 100 - 200 mg %) between hour 0 and hour 3 was calculated and compared across both the groups. Tertiary outcome measure-The approach used for primary outcome measure was applied only to patients with poor pre operative glycaemic control.

Results:

The groups were well balanced for baseline characteristics except for the slightly higher mean PPBS in the intermittent iv bolus group. Since the FBS in both groups was comparable, the confounding factor of preoperative blood glucose control can be taken as insignificant in this case. It was seen that the decreased mean blood glucose measurement in Vellore Regimen Group compared to the Insulin Bolus Regimen Group is statistically significant as the p value is 0.0367 at 2 hours and 0.0383 at 3 hours intraoperatively as per unpaired t- test indicating a true difference among study groups.For the secondary outcome , in comparing the difference between the number of patients who were outside the target range at hour 0 and hour 3 between both the groups every hour , we find that for the Vellore regimen , the percentage dropped from 63% to 0% , while for the insulin bolus regimen it decreased from 17 % to 5 % . Although the Vellore Regimen takes the upper hand here, the finding was not found to be statistically significant .Coming to the tertiary outcome, In patients belonging to Insulin Bolus Regimen Group, the mean Blood Glucose Monitoring of Patients who had Poor Control at Assessment (FBS≥126, PPBS≥200) ranged from 211 mg/dl at baseline to 160.60 mg/dl at the end of hour 3. The comparison turned out to be insignificant although it was in favour of the Vellore regimen

Conclusion:

Based on the above findings, I conclude that the Vellore regimen is marginally more efficacious as well as safer than the intermittent intravenous insulin bolus regimen.

INTRODUCTION

"A PROSPECTIVE RANDOMISED STUDY COMPARING DIFFERENT APPROACHES TO INTRAOPERATIVE MANAGEMENT OF DIABETESMELLITUS – THE VELLORE REGIMEN VS INTERMITTENT IV BOLUS REGIMEN"

Multiple protocols have been developed for perioperative glucose control, ranging from intravenous glucose – insulin – potassium infusion regimens to subcutaneous sliding scale insulin bolus regimens. Despite the multitude of results and conclusions, there is no real evidence of an optimal protocol.

The aim of this study is to make a comparison between 2 different approaches of administering insulin intraoperatively namely, a continuous insulin infusion regimen with an intravenous insulin bolus regimen. The aim is, by means of judging the efficiency of blood sugar control between the 2 groups, to determine whether the naturally more convenient IV bolus regimen compares favourably to the more accepted continuous infusion regimen. The Vellore regimen was chosen as the prototype of the infusion regimens.

AIM

To compare the effectiveness of intra operative control of blood glucose of The Vellore Regimen vs Intermittent IV Bolus Regimen

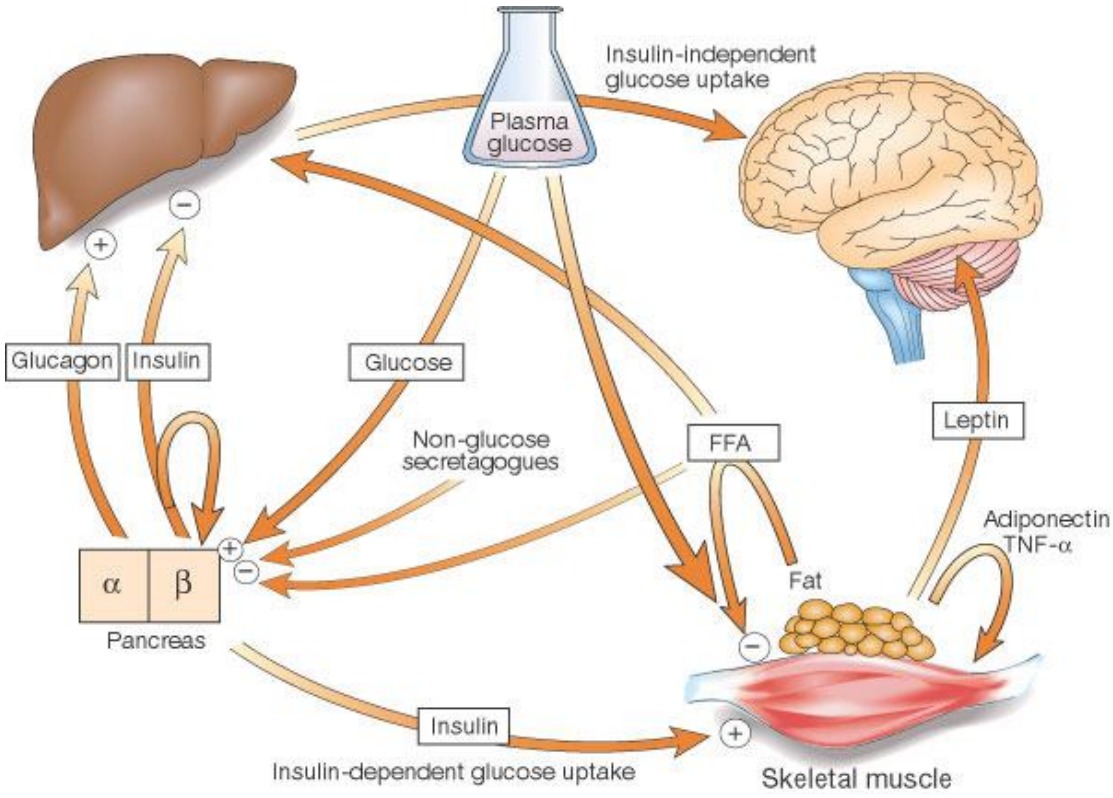
BACKGROUND

Diabetes mellitus has gained much prominence in the present age, not least due to modern lifestyle. This metabolic disorder affecting multiple systems is of great importance to physicians and is a significant risk factor for some of the major causes of death like heart attack and stroke. The silent disease, with an initial non dramatic course of events is even more notorious for the wide range of morbidities it inflicts upon it's sufferers. Causing entities such as diabetic retinopathy, diabetic nephropathy, peripheral neuropathy, diabetic foot and increased susceptibility to a host of infections, it affects almost every organ from head to toe. Anaesthesiologists, being perioperative physicians, should be equally concerned of it's effects as it has a bearing upon case optimization, management and post operative recovery.

To offer a brief synopsis of the pathophysiology, the disease is a common endocrinopathy. The normal metabolism of glucose involves a balance between the use of glucose and it's production within the body or delivery by diet. The primary source of endogenous glucose production is the liver. This happens by means of glycogenolysis and gluconeogenesis. The postprandial surge in blood glucose levels stimulates a rise in plasma insulin secretion from the basal level,in order to effect utilisation of glucose.

About 2-4 hours after a meal, glucose utilisation surpasses endogenous production and hence it becomes necessary to increase the endogenous production to maintain normal levels of blood glucose. During this period, a great proportion of glucose released hepatically is metabolised by insulin independent tissues like the brain, RBCs and GIT, which are not sensitive to insulin and hence the insulin secretion is at a low.

Hormones like glucagon, epinephrine, growth hormone and cortisol act to increase the blood glucose levels and support production. The primary one of these is glucagon which stimulates glycogenolysis and gluconeogenesis and inhibits glycolysis.



Diabetes mellitus is the result of either or both of

1. Reduced insulin supply
2. Insulin resistance

The result is a high blood sugar level which ultimately causes the numerous complications we have come to expect from the disease.

Diabetes mellitus occurs in 2 major forms

1. Type 1 diabetes, a disease involving destruction of beta cells in the pancreas, which is brought about by T cells. The disease is mostly diagnosed in young adults before the age of 40 years. The exact aetiology is not well known and a variety of factors are implicated in causing the disease –environmental triggers eg. Enteroviruses, dietary proteins, or drugs or chemicals that may set the pathological processes in motion in genetically susceptible individuals. About, 80-90 % of beta cell function is lost over a preclinical period of 9 – 12 years before symptoms set in. A marker of the disease is the circulating antibodies. It is distinguished by sudden and severe presentation with hyperglycaemia, weight loss, polyuria, polydipsia, blurring of vision and dehydration.

2. Type 2 diabetes, the most common variant accounting for 90 % of the worldwide occurrence of DM. The subtle disease tends to happen more in overweight people living a sedentary lifestyle. It is characterised by relative insufficiency of beta cells and resistance to insulin. The initial insensitivity to insulin in tissues leads to an increase in insulin secretion by the pancreas, to keep normal plasma glucose levels. As the disease moves on cells of the pancreas get exhausted and are not able to compensate, due to which the blood glucose levels rise. The situation is characterised by 3 important aspects

    A. inefficient use of glucose by peripheral tissues.

    B. impaired basal and stimulated insulin secretion.

    C. increase in the rate of hepatic glucose release.

Insulin resistance is attributed to many factors like abnormal insulin molecule, free fatty acids, circulating insulin antagonists, anti insulin and insulin receptor antibodies, cytokines, target tissue defects. It is also thought that the resistance may be an inherited component, while obesity and sedentary lifestyle are acquired ones. Metabolic syndrome, also called insulin resistance syndrome, is a group of biochemical and clinical features mostly seen in patients who suffer from or are likely to develop type 2 diabetes mellitus. It includes insulin resistance,

hypertension, obesity, procoagulant state, dyslipidaemia, premature atherosclerosis and cardiovascular disease.

Diagnosis

According to the standards of medical care in diabetes 2015, by The American Diabetes Association the revised diagnostic criteria are as follows

Glycosylated Hb≥.5%.
Or
Fasting plasma glucose≥126 mg/dl. Fasting is characterised by lack of caloric intake for at least 8 hours. *
Or
Post prandial plasma glucose≥200 mg/dl during an oral glucose tolerance test. The test must be done as described by the WHO, using a load of glucose containing the equivalent of 75 g anhydrous glucose dissolved in water.*
Or
A patient who has classic symptoms of raised blood sugars or hyperglycaemic crisis with a random plasma glucose ≥200 mg/dl.
*if in doubt the tests should be repeated

Perioperative blood glucose control in diabetic patients

Diabetes mellitus, being a disorder that affects multiple systems, requires the anaesthesiologist to conduct a thorough pre operative evaluation for complications, control, therapy and airway assessment. The management strategy differs,accordingly.

In addition, it is imperative to keep blood glucose values in a certain range so that we can prevent disastrous add- on complications including poor surgical outcome. A situation of insulin hypo secretion (which should be seen as relative) and resistance to insulin can be caused by anaesthesia as well as surgery, due to release of hormones which act to oppose insulin. The counter regulatory hormones are glucocorticoids, growth hormone, glucagon and catecholamines. The degree of counterregulatory activity varies with individuals. It is associated with various surgical factors as well as the outcome after surgery. The hyperglycaemia associated with surgery is proportional to the stress, duration and type of surgery[2]. The hyperglycaemic response to these factors may be attenuated by the lack of caloric intake during and immediately after surgery, making the final glycaemic balance difficult to predict. The degree of rise of blood sugar may be reduced by not having intake of calories perioperatively, which, however makes the balance of blood sugar difficult to foresee.

Raised sugars during surgery can cause dangerous states of dehydration like diabetic ketoacidosis and hyperosmolar hyperglycaemia which can be lethal. Type 2 diabetic patients are specially prone to the latter. Electrolyte abnormalities are quick to occur in the above discussed problems, bringing their own set of complications to the scene. Persistently high blood sugars are also attributed to impaired wound healing, endothelial dysfunction, sepsis and cerebral ischaemia.

Blood glucose levels are also often likely to plummet, especially in cases with poor pre operative control, long fasting duration and receiving of immediate pre op doses of insulin or oral hypoglycaemic agent. A reduced blood glucose of say less than 40 – 50 mg% for a few minutes can cause damage in the form of arrhythmias or problems with higher functions. A more prolonged insult may result in hypoglycaemic coma due to irreversible brain damage. Hypoglycaemia and subsequent neuro-glucopaenia are hard to make out in sleeping patients, after surgery.

The target intra operative levels of blood glucose is a matter of ongoing studies and discussions. From what we know, tight control of sugar i.e. Levels between 108 mg% - 144 mg% are suggested for major surgeries like vascular surgeries, cardiac surgeries and neurological surgeries, though these often result in hypoglycaemia. There are studies

which do not advocate the above approach. General surgeries mostly see an approach of moderate control i.e 140 mg% - 180mg%.

Patients with controlled blood glucose levels through diet and exercise

For these patients, if undergoing minor surgery, no special treatment is recommended except for early morning monitoring and intraoperative monitoring of blood glucose if the duration of the procedure exceeds an hour. If the procedure is a major one, then an active intervention is needed.

Patients on oral hypoglycaemic drugs

A major surgery, where the patient is not going to resume eating soon after surgery, requires a changeover to insulin 2 days prior. If the surgery is a minor one no such shift is needed. Long acting sulfonylureas are withheld 1 day prior. Chlorpropamide should be stopped2-3 days prior to surgery. Metformin, 48-72 hours prior. It can be restarted after 48-72 hours of surgery once renal function tests have been shown to be normal. Short acting oral hypoglycaemic drugs can be continued up to the day of surgery. Some advice skipping the morning dose.

Patients on insulin therapy

For minor surgery, patients on long acting insulin should be changed to insulin which acts for an intermediate duration 24 – 48 hours prior to surgery[11]. Checking blood sugar around the surgical period is very much necessary and a glucose insulin infusion is best started before the surgery itself. Post operatively, the infusion must be halted[11] and the regularly followed subcutaneous regimen should be followed once the patient commences eating. Intraoperative control is of course with intravenous insulin and glucose.

In case of major surgery, the patient is to be admitted to hospital 2-3 days prior to the surgery. Surgery is carried out once the patient's sugars are at least sub optimised [22].

1) Haemoglobin A1c <8%
2) Before meals values of 80–120 mg%
3) Before sleep values of 100–140mg%

Insulin

There exist numerous intraoperative regimen for administering insulin – intravenous infusion, infusion bolus, subcutaneous and various subcategories within.

Subcutaneous insulin is mostly shunned for perioperative glucose control as it is marked by erratic absorption and unsatisfactory control. Among the many intravenous regimen the most commonly followed are the combined glucose and insulin infusion of Alberti and Thomas and the insulin infusion regimens of Watts et al where the glucose runs separate from insulin[3]. Administration of glucose is necessary to provide for the basal glucose requirement, which is 1.2 mg/kg/min (roughly 5 g/h). Many of the regimens add potassium to the mix to account for the translocation of potassium into cells in response to insulin.

REVIEW OF LITERATURE

Anaesthetic management of patients with diabetes mellitus[6]

G. R. McAnulty, H. J. Robertshaw and G. M. Hall

Oxford Journals Medicine & Health BJA Volume 85, Issue 1Pp. 80-90 British journal of anaesthesia 85 (1) : 80-90 (2000)

This review discusses some of the latest developments in the field of diabetes mellitus. Over the past few years evidence has been gathered that improving blood glycaemic control in both the short and long term improves the outcome of surgery. Attention to detail in the everyday management of the disease and it's associated conditions, such as hypertension, decreases the devastating consequences of microvascular and macrovascular complications. Additionally, a more aggressive approach to glycaemic control in the perioperative period results in better wound healing, reduced morbidity and a shorter duration of hospital stays. The days when anaesthetists could tolerate 'permissive hyperglycaemia' with the thought that this approach was in the patient's best interest, are gone. Tight metabolic control in the perioperative period is necessary and is a goal which is attainable in most patients.

With the introduction of new innovations in monitoring, exact measurement of capillary as well as blood sugars is possible at hospital

level. According to recent findings the measurement of circulating beta hydroxyl butyrate concentrations can be of use in complicated diabetes mellitus and will be much facilitated with the development of a device for the same which can be used at bed side. The article also states that measurement of glycosylated haemoglobin has little value in the perioperative period. However, it is definitely of great value in assessing the blood glucose control over a long time.

Intensive Insulin Therapy in Critically Ill Patients[23]

The New England Journal of Medicine

Van den Berghe: N Engl J Med, Volume 345(19).November 8, 2001.1359-1367 Van den Berghe et al

The trial aimed at finding a significant association between intensive blood sugar control by insulin therapy and decrease in deaths in the ICU, which was till then a barely treaded area of management.

Methods -A prospective, controlled and randomised study was performed on adult patients requiring positive pressure ventilation in the surgical ICU. Assignment to groups receiving narrow range insulin treatment (maintenance of glycaemic level in a range of 80 and 110 mg/dl) or conventional treatment (providing insulin in the case that blood

sugar level crosses 215 mg/dl and keeping the glucose at a level in a range of 180 and 200 mg/dl) was random.

Results: After a study of 12 months, with a total of 1548 sample size, it was found that intensive insulin therapy decreased mortality in the course of intensive care from 8.0 percent with conventional treatment to 4.6 percent The benefit of strict blood sugar control could be attributed to its effect on death in the group of patients who were in the ICU for beyond 5 days (20.2 percent with conventional treatment, as compared with 10.6 percent with intensive insulin therapy; P=0.005). The highest decrease in death comprised of deaths due to sepsis and associated MODS. Strict control of blood glucose also lessened the overall number of deaths in the hospital setup by a measure of 34 percent, infections in the blood by 46 percent, ARF in need of dialysis or hemofiltration by a measure of 41 percent, the number of PRBC transfusions by a measure of 50 percent, and critical-illness polyneuropathy of critical illness by a measure of 44 percent. The above patients were also found to be weanable faster from the ventilator and requiring lesser duration of special care.

The study trial concluded that keeping the glycaemic levels less than, or equal to 110 mg% was linked to lesser number of deaths and

faster recovery in the study population which comprised of ICU patients belonging to the department of surgery.

Perioperative Management of Diabetes[16]

Jennifer B. Marks, M.D., University of Miami School of Medicine, Miami, Florida Am Fam Physician. 2003 Jan 1;67(1):93-100.

Even though opinions vary, and there is very little information to say that so and so protocol or approach to handling diabetic patients during surgery is superior, it is obvious that if the control of blood sugars is maintained tightly during the perioperative period, the end result of the surgery will be satisfactory in terms of wound healing and avoidance of sepsis. The anaesthetist should be well acquainted with the medications being used by the patient, the quality of control of the disease and any other factors that might influence the sugar levels during surgery.

In the opinion of the author, if there exists any doubt as to whether to give insulin or not or how much of insulin to give, it is more prudent administer it rather than withhold because hypoglycaemia can be easily avoided by co administering glucose with insulin but the complications of hyperglycaemia are difficult to deal with. DKA and hyperglycaemic hyperosmolar conditions take up a lot of energy and time to treat, which could be better spent on dealing with the more demanding anaesthetic

aspects of managing major surgeries. One has to focus on certain factors on a priority basis if the plan of action for dealing with diabetes is to be successful. Checking the blood glucose values often and likewise assessing the levels of electrolytes, volemic status, and pH are some of these. With diligent handling of the glycaemic status of the patient many post operative complications of surgery can be successfully avoided.

A Simple Glucose Insulin Regimen for Perioperative Blood Glucose Control: The Vellore Regimen[3]

Ann Miriam, MD, and Grace Korula, MD Department of Anaesthesia, Christian Medical College Hospital, Vellore, India

(AnesthAnalg2004; 99: 598–602)

The study aimed at finding a convenient way of controlling blood sugar intra operatively. The Vellore regimen, was created to combine the advantages of a combined glucose insulin regimen like the Alberti regimen as well as variable rate infusion e.g. Watt's regimen. Thus the cumbersome technique of the former, and the sophisticated equipment and the risks of the latter were done away with. For every 1-50 mg% rise in blood glucose concentration > 100mg/dl, a single unit of insulin was put through the injection port of the burette containing 100 ml of 5 % dextrose. The blood glucose values were checked every hour. 204

patients were randomly put into 2 groups, 98 in the group for the Vellore regimen, 106 in a group where the anaesthetist was free to choose a technique of his choice. The blood sugar values were then compared. The mean ± SD blood glucose value of the study group was 156 ± 35mg%, while the value of the second group was 189 ± 64 mg/d (P=0.003). With the new regimen the percentage of patients whose sugars were not well in control decreased from 51% to 28 %as compared to the control group which saw it rise from 49 % to 73 %. (P =0.013). It was concluded that the Vellore regimen is easy and convenient for blood glucose control during surgery.

Continuous Perioperative Insulin Infusion Decreases Major Cardiovascular Events in Patients Undergoing Vascular Surgery[5]

A Prospective, Randomized Trial Balachundhar Subramaniam, M.B.B.S., M.D et al Copyright © 2009, the American Society of Anesthesiologists Anesthesiology 2009; 110:970–7

The prospective study trial compared a continuous intraoperative insulin regimen with a regimen of intermittent iv bolus based on a sliding scale within a group of 236 patients who were undergoing vascular surgery, and came to the conclusion that intravenous administration of insulin when given continuously, will mostly cause less change in blood sugar concentrations when contrasted with either bolus subcutaneous or

bolus intravenous insulin dosage. Reduced change of glycaemic levels may explain the fact that the standard deviation of glucose levels was less in the continuous infusion group, in contrast to the bolus insulin group, from 8 h after surgery until 24 h. Although, there was no significant difference in the mean for both the groups. Also, the incidence of major cardiovascular events postoperatively was found to be more in the second group. In conclusion, continuous insulin infusion was found to reduce perioperative myocardial infarction after vascular surgery.

Perioperative Blood Glucose Monitoring in the General Surgical Population[22]

Tejal A. Raju, M.D., Marc C. Torjman, Ph.D., and Michael E. Goldberg, M.D.

J Diabetes Sci Technol. 2009 Nov; 3(6): 1282–1287. Published online 2009 Nov. PMCID: PMC2787027

An association between poor surgical results and diabetes mellitus which is not under control, has been shown to exist, more so in major surgeries like cardiac and brain. However a significant study also found out that maintaining blood sugar levels within a narrow range of 80-110 mg% was actually harmful and caused increased deaths. Based on several other controlled studies it was concluded that maintaining glycaemic

levels between 140 – 180 mg % was better for the patient. Among the many factors that affect blood glucose levels perioperatively, are the manner of use of blood sugar reducing medications preoperatively, titration of insulin intraoperatively and the type of surgery and anaesthesia used. It is advised that the damage can be reduced by not allowing wide fluctuations in the blood sugar levels perioperatively.

Perioperative blood glucose monitoring and control in major vascular surgery patients[12]

J.P.Vankuijk, O. Schouten, W. J. Flu, C.A.denUil, J.J.Bax, D. Poldermans

Eur J VascEndovascSurg (2009) 38, 627-634

The article delves into studies aimed at looking into the effects of intensive blood glucose lowering therapies. It was found out that although earlier studies showed a reduction in morbidity and mortality with such an approach, later studies could not confirm the same. Based on the review of existing literature, they came to the conclusion that narrow range control of glucose, perioperatively, could be harmful in some cases while not causing the intended benefit in many.

Creating a Perioperative Glycemic Control Program[21]

Sara M. Alexanian, Marie E. Mcdonnell, and Shamsuddin Akhtar

Anesthesiology Research and Practice

Volume 2011 (2011), Article ID 465974

The review, while accepting the practitioners' challenge of managing patients with diabetes mellitus during the whole process, also notes that in this time, especially when the patient is treated by multiple faculties, a lot of transitions in care occur between the involved specialities, which can be detrimental in the sense that there is great scope for miscommunication and loss of important information. An option provided is the formation of a team which includes personnel from the various specialities, thus minimising the above mentioned errors. The article also notices that there is no approach that can be generally applied to all the patients uniformly and treatment should be rather individualised. Our understanding of the whole subject is still not in it's advanced stages and much research needs to be done to resolve several disputed issues regarding management. There is no doubt however that the goal will be achieved sooner rather than later, if one considers the rate at which science is progressing.

Diabetes Mellitus in Anaesthesia[13]

JadelisGiquel; Yiliam F Rodriguez- Blanco; Christina Matadial; Keith Candiotti

British Journal of Diabetes and Vascular Disease. 2012;12(2):60-64.

It is too often that one comes across patients suffering from type 2 diabetes mellitus, that too in an uncontrolled state. Undergoing anaesthesia and surgery is not without it's fair share of risks for these patients. Some of them present in advanced stages of damage to vital organs – myocardial ischaemia, infarction, transient ischaemic attacks, diabetic retinopathy, diabetic nephropathy, stroke are but few of the bothersome conditions that plague diabetics, not to mention the suppressed immunity that can undo the purpose of surgery by inviting lecherous infections that are difficult to treat. Having such a huge significance with respect to morbidity and death, it is one of the many conditions that the anaesthesiologist must be thoroughly familiar with. He/she should be able to identify what investigations are needed and not hesitate to order for them.

Glycaemic control in the perioperative period[11]

J. J. Sebranek, A. Kopp Lugli and D. B. Coursin

British Journal of Anaesthesia 111 (S1): i18–i34 (2013)

Doi:10.1093/bja/aet381

According to the review, the preponderance of evidence confirms the undesirable end effects on the patient of pathological glucose metabolism. The anaesthetist is totally responsible for the complete management of DM, right from detection, investigation to appropriate management because of it's effect on so many aspects of anaesthesia and the dire consequences of ignoring it. given the fact that the diabetic group comprises of people of varied nature it is natural that a single regimen won't be applicable to all and every individual must be treated according to his or her specific nature of disease and it' complications. In certainty, if the disease is diagnosed early and it's treatment commenced at the earliest then the anaesthetic as well as surgical risks will be very much reduced. Even though there is no strong consensus about it, the target range of intraoperative blood glucose hangs within the territory bound by intensive control on one extreme and allowance of raised blood sugar levels on the other; the aim being acceptable control and prevention of fall in blood sugars. Future investigations should help identify specific perioperative glucose targets, especially in specialized surgical

populations (i.e. Cardiac, neurosurgical), while advances in monitoring and medications will make it easier to achieve specific glucose targets in individual patients.

MATERIALS AND METHOD

Ethical approval

The protocol of the study was accepted by the medical ethical committee of madras medical college, affiliated to The Tamil Nadu MGR University. The protocol was overseen by the concerned guides and the concerned head of the departments. Approval was also sought from the department of diabetology.

Trial design

A prospective randomised controlled trial in adult patients with type 2 diabetes mellitus coming for vascular surgery, to evaluate the best treatment algorithm to lower blood glucose in the intraoperative setting, utilizing two parallel study arms. One group was allotted for the Vellore regimen while the other had an intermittent intravenous bolus regimen of insulin, based on a sliding scale, chosen for it. Sample size was determined based on the Study -

A Simple Glucose Insulin Regimen for Perioperative Blood Glucose Control: The Vellore Regimen

Authored by Ann Miriam, MD, and Grace Korula, MD

Published in (AnesthAnalg 2004;99:598–602)

In this study group's value was 189 63 mg/dL (P 0.003) the percentage of patients who were poorly controlled (outside 100 to 200-mg/dL range) decreased from 51% to 28% (no patient less than 60 mg/dL) with this regimen as compared with the control group in which it increased from 49% to 72% (10 patients less than 60 mg/dL) (P 0.0013).

Description:

- The confidence level is estimated at 95%
- with a z value of 1.96
- the confidence interval or margin of error is estimated at +/-10
- Assuming that 23 percent of the sample will have the specified attribute p% =23.00 and q%=77.00

$n = p\% \times q\% \times [z/e\%]^2$

$n = 23 \times 77 \times [1.96/5]^2$

$n = 68.03$

Therefore 68 is the minimum sample size required for the study(n=34 in intervention arm and n=34 in control arm)

Inclusion criteria

1. Signed informed consent
2. Known case of type 2 diabetes mellitus
3. On treatment with insulin, either chronically or switched over perioperatively
4. Scheduled for elective vascular surgery
5. Surgery lasting for more than 2 hours
6. Age between 25 – 60 years
7. ASA PS 2, 3, 4
8. Anaesthesia – regional / general

Exclusion criteria

1. Not satisfying inclusion criteria
2. Moribund patients
3. Emergency surgery
4. Patients on steroids
5. Diabetic ketoacidosis
6. Well controlled diabetes not requiring insulin

After obtaining ethical committee approval and informed consent from patients, I studied 70 patients, divided into the 2 study groups. The patients were recruited during a preassessment visit at the department of anaesthesiology. Here, oral information about the study was provided to prospective subjects, following which written consent for participation in the trial was obtained. The chosen patients were randomised into one of the 2 study arms in a 1:1 ratio. The sample size was chosen based on calculated statistically significant sample size using previous similar studies. The study intended to take into account the stress factor involved in surgery and its effect on the comparisons that were to be made. Hence the subgroup of patients undergoing vascular surgery was chosen.

The capillary blood sugar measures taken using the same glucometer were considered standard for the trial. The relation between blood glucose values between the lab and glucometer was noted. Patients from both the groups underwent fasting from midnight before the day of surgery. clear fluids were allowed only till 6 hours before surgery. The night dose of long acting insulin was reduced to half in all patients. All study patients were preferably scheduled for surgery in the morning at 9 AM. These patients did not receive the morning dose of short acting insulin. For patients whose surgery was delayed till afternoon, a glucose insulin infusion was started along with hourly blood sugar monitoring. If

the blood sugar was found to be less than 70mg%, 100 ml of 5%dextrose was rushed and blood glucose was repeated till the value reached above 70. For a blood glucose level above 70 mg% but below 100 mg%, 100 ml of 5%dextrose was given over 1 hour. All other patients having a blood glucose level above 100 mg%, received a mixture of 8 IU regular insulin in 500 ml 5% dextrose at 100 ml per hour.

The readings recorded for the statistics were taken at 0, 1, 2, 3 hours. The 0 reading was taken before induction of anaesthesia, while the remaining readings were taken at respective intervals from the commencement of anaesthesia, till the patient left the recovery room. After returning to the ward the patient was treated for diabetes as per ward protocols.

The Vellore regimen

For each 1 – 50 mg/dl rise in blood sugar greater than 100mg/dl, 1U insulin was put into the burette via the port at the side by means of an insulin syringe. As 100 ml of 5% dextrose was infused in one hour, the level of blood glucose was checked after it. Before starting the infusion, 1 IU of insulin was put into the burette with 50 millilitres of 5%dextrose solution, shaken thoroughly and let run through and out, in order to make up for the initial absorption of insulin by the material of the infusion set[3].

For blood sugar between 70 - 100mg%, only 100ml of plain 5%dextrose solution was infused over one hour.

If the blood glucose was found to be less than 70 mg % at any point, then 100ml of 55dextrose was rushed and the sugar was rechecked after 15 minutes.

The intermittent intravenous bolus regimen

This method was based on a sliding scale used in a similar study conducted by the PILGRIM trial[16]. The scale can be demonstrated as a table with a column of succeeding higher ranges of blood glucose against a column of recommended doses of insulin for the respective blood sugar ranges. If the consecutive blood glucose value measured at the end of the hour was greater than the last reading then the last column of doses was abandoned for a new column carrying higher doses. If not, the column used for the last dosing was reused.

The Vellore regimen[3]

Blood glucose levels	Treatment regimen
Below 70mg%	Stop insulin if on infusion. Rapid infusion of 100 ml of D5W. Measure blood glucose after 15 min
71-100 mg%	Stop insulin. Infuse DW5at 100 ml/hr
101-150mg%	1U of insulin+100 ml D5W/hr
151-200 mg%	2U of insulin+100 ml D5W/hr
201-250 Mg%	3U of insulin+100 ml D5W/hr
251-300 Mg%	4U of insulin+100 ml D5W/hr
Above 300 mg%	1U insulin for every 1-50 mg above 100mg% + 100ml NS/hr

Intermittent intravenous bolus regimen[16]

Glucose measurement	1st insulin bolus	If glucose rises after 1st bolus	If glucose rises after 2nd bolus
72-144 mg%			
144-162 mg%	2U	4U	6U
162-180 mg%	3U	5U	7U
180-198 mg%	4U	8U	12U
198-216 mg%	5U	9U	13U
216-234 mg%	6U	12U	18U
234-252 mg%	7U	13U	19U
252-270 mg%	8U	15U	20U
270-288 mg%	9U	16U	21U
ABOVE 288 mg%	10U	17U	22U

It is also necessary to explain here the anaesthetic techniques used as it has a bearing upon the results. Either general anaesthesia or regional anaesthesia was used depending on the type of surgery. The regional anaesthesia given was spinal block, along with epidural anaesthesia. All patients received the standard premedications – tab alprazolam 0.25 mg, tab perinorm 10 mg and tab ranitidine 150 mg one hour before surgery. GA was induced with injection thiopentone and maintained with a gas mixture of 35% oxygen in N2O with 1.5 – 2 % of sevoflurane. Analgesia was provided with epidural catheter and with intravenous fentanyl 2 microgram / kg body weight. The maintenance dose used was 20 micrograms every hour. Patients requiring extensive blood transfusion were excluded from the study. Serum potassium was checked every 2 hours and correction was given if necessary.

Statistical Approach

Primary outcome measures

The mean with standard deviation of glycaemic readings of each hour were calculated within each group and then compared across the groups for statistical significance.

Secondary outcome measures

The difference in the percentage of people with uncontrolled sugars (defined as blood glucose values outside 100 -200 mg %) between hour 0 and hour 3 was calculated and compared across both the groups.

Tertiary outcome measures

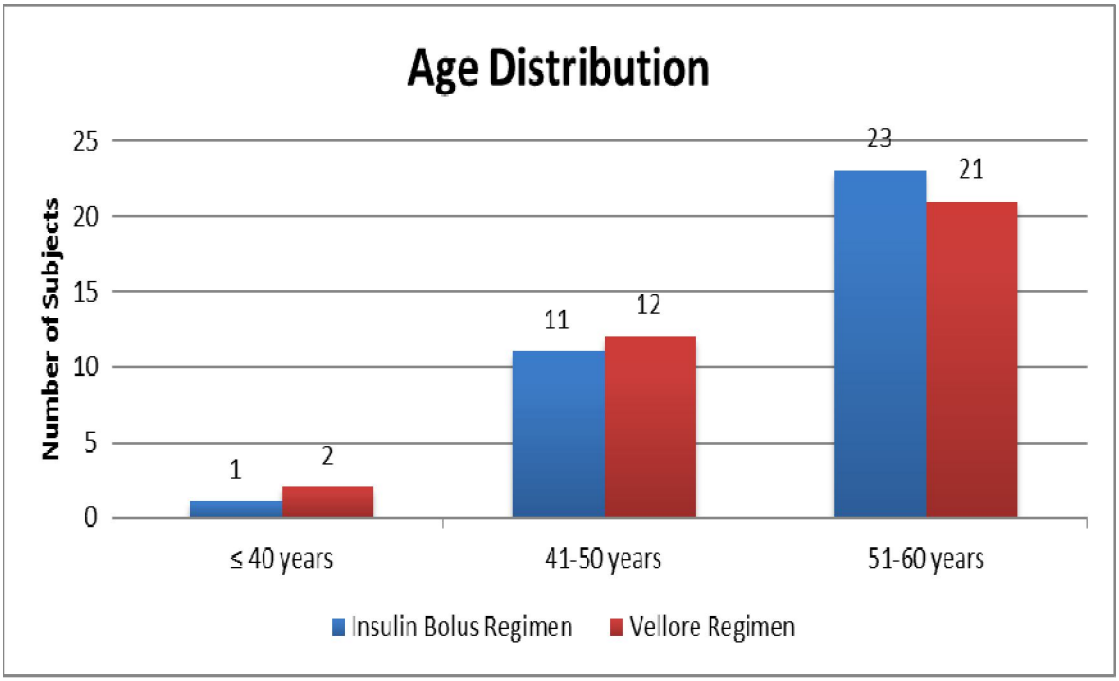
The approach used for primary outcome measure was applied only to patients with poor pre operative glycaemic control

RESULTS

The randomised study involved comparison of 2 groups, each with a sample size of 35 vascular surgery patients. Descriptive statistics was done for all data and were reported in terms of mean values and percentages. Suitable statistical tests of comparison were done. Continuous variables were analysed with the unpaired t test. Categorical variables were analysed with the X2 Test and Fisher Exact Test. Statistical significance was taken as $P < 0.05$. The data was analysed using SPSS version 16 and Microsoft Excel 2007.

Before getting down to compare the two groups for the aforementioned outcomes, it was necessary to make sure that influence of confounding factors was kept to a minimum.

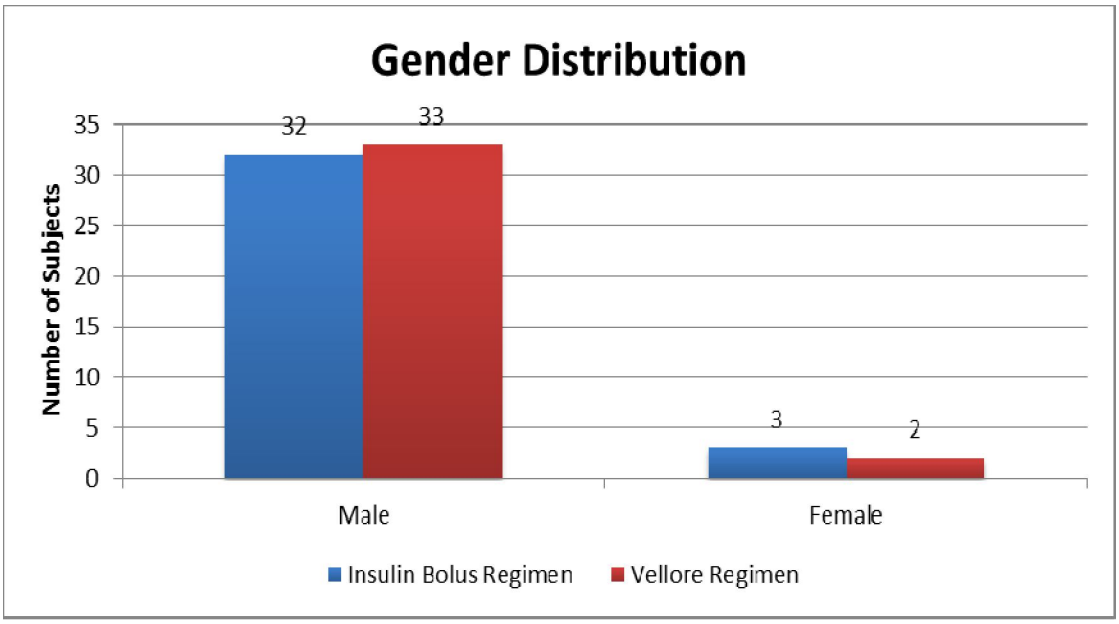
Comparison of factors like age, sex, type of anaesthesia and pre operative glucose control were done.



Age Distribution	Insulin Bolus Regimen	%	Vellore Regimen	%
≤ 40 years	1	2.86	2	5.71
41-50 years	11	31.43	12	34.29
51-60 years	23	65.71	21	60.00
0	0	0.00	0	0.00
Total	35	100	35	100

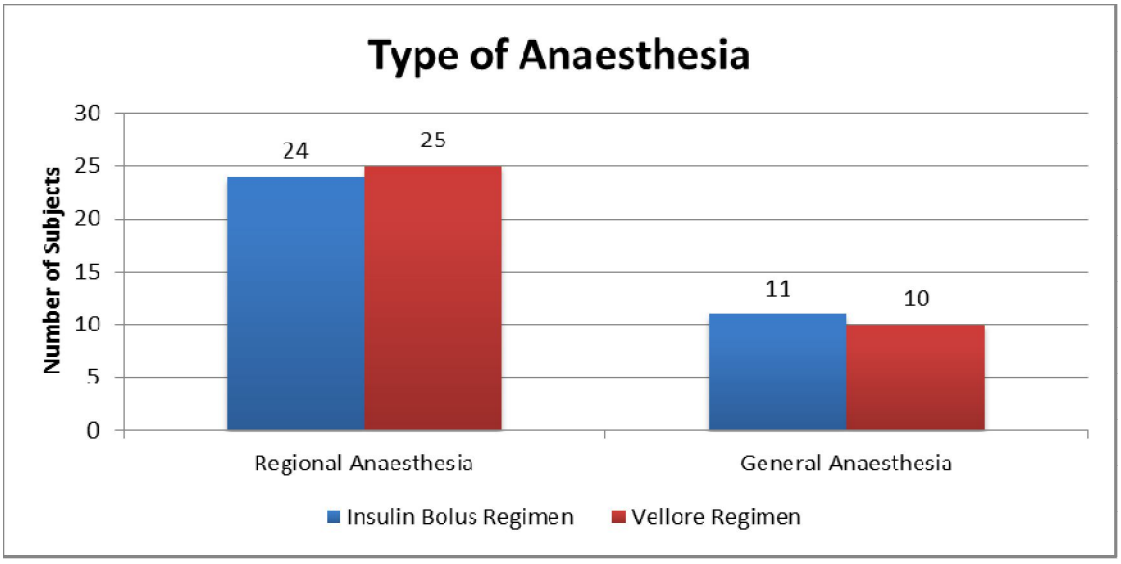
Age Distribution	Insulin Bolus Regimen	Vellore Regimen
N	35	35
Mean	51.89	51.14
SD	5.45	6.16
P value Unpaired t Test		0.5950

Majority of the Insulin Bolus Regimen Group patients belonged to the 51-60 years age class interval (n=23, 65.71%) with a mean age of 51.89 years. In the Vellore Regimen Group patients, majority belonged to the same age class interval (n=21, 60%) with a mean age of 51.14 years. The association between the intervention groups and age distribution is considered to be not statistically significant since $p > 0.05$ as per unpaired t test.



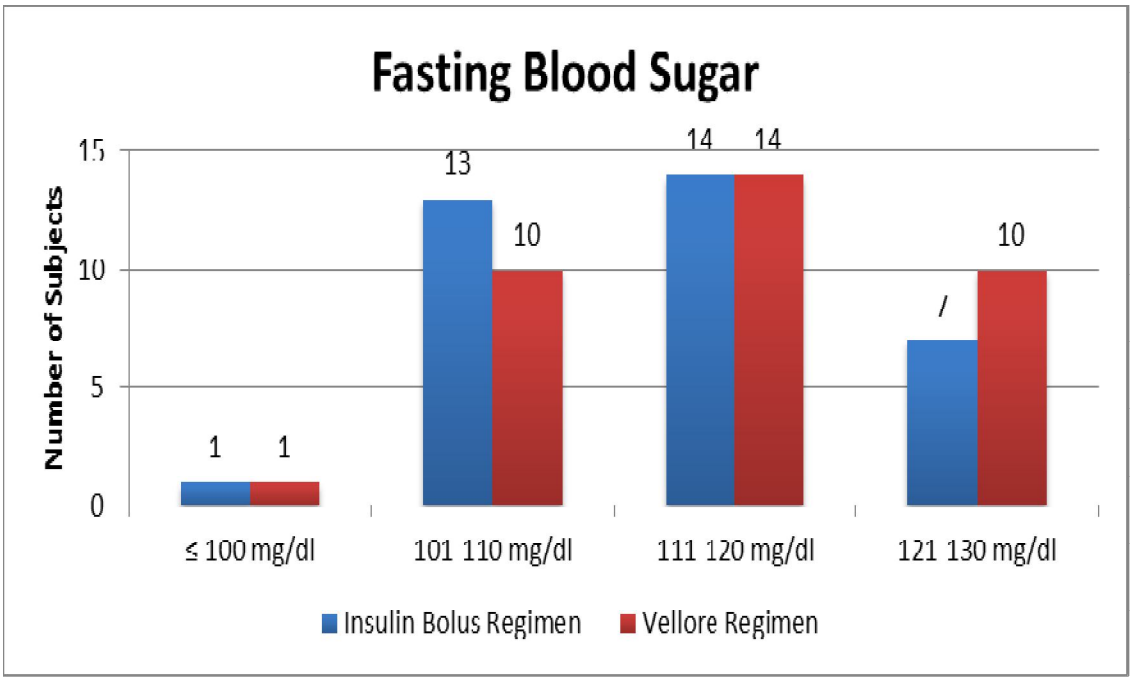
Gender Distribution	Insulin Bolus Regimen	%	Vellore Regimen	%
Male	32	91.43	33	94.29
Female	3	8.57	2	5.71
Total	35	100	35	100
P value Fishers Exact Test			0.6782	

Majority of the Insulin Bolus Regimen Group patients belonged to the male gender class interval (n=32, 91.43%). In the Vellore Regimen Group patients, majority belonged to the same gender class interval (n=33, 94.29%). The association between the intervention groups and gender distribution is considered to be not statistically significant since p > 0.05 as per fisher's exact test.



Type of Anaesthesia	Insulin Bolus Regimen	%	Vellore Regimen	%
Regional Anaesthesia	24	68.57	25	71.43
General Anaesthesia	11	31.43	10	28.57
Total	35	100	35	100
P value Fishers Exact Test			0.8013	

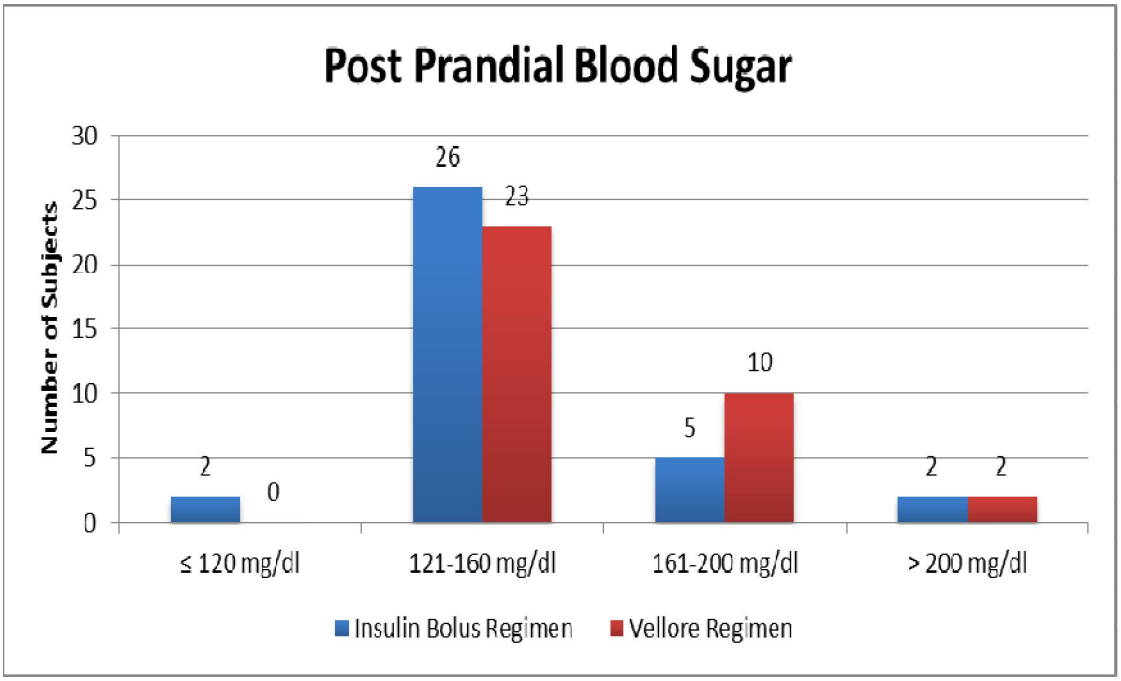
Majority of the Insulin Bolus Regimen Group patients underwent regional anaesthesia (n=21, 68.57%). In the Vellore Regimen Group patients, majority similarly underwent regional anaesthesia (n=25, 71.42%). The association between the intervention groups and type of anaesthesia is considered to be not statistically significant since $p > 0.05$ as per fishers exact test.



Fasting Blood Sugar	Insulin Bolus Regimen	%	Vellore Regimen	%
≤ 100 mg/dl	1	2.86	1	2.86
101-110 mg/dl	13	37.14	10	28.57
111-120 mg/dl	14	40.00	14	40.00
121-130 mg/dl	7	20.00	10	28.57
Total	35	100	35	100

Fasting Blood Sugar	Insulin Bolus Regimen	Vellore Regimen
N	35	35
Mean	114.26	115.80
SD	7.79	8.17
P value Unpaired t Test		0.4216

Majority of the Insulin Bolus Regimen Group patients had fasting blood sugar levels in the 111-120 mg/dl class interval (n=14, 40%) with a mean FBS of 114.26 mg/dl.. In the Vellore Regimen Group patients, majority had fasting blood sugar levels in the 111-120 mg/dl class interval (n=14, 40%) with a mean FBS of 115.80 mg/dl. The association between the intervention groups and fasting blood sugar measurements is considered to be not statistically significant since $p > 0.05$ as per unpaired t test



Post Prandial Blood Sugar	Insulin Bolus Regimen	%	Vellore Regimen	%
≤ 120 mg/dl	2	5.71	0	0.00
121-160 mg/dl	26	74.29	23	65.71
161-200 mg/dl	5	14.29	10	28.57
> 200 mg/dl	2	5.71	2	5.71
Total	35	100	35	100

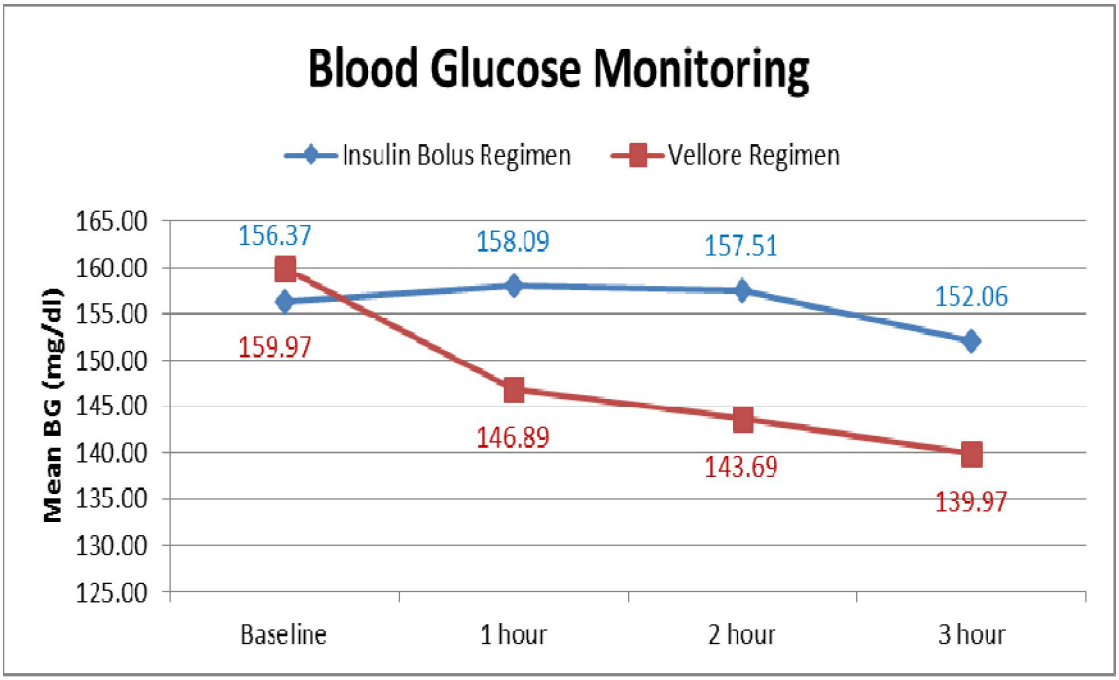
Post Prandial Blood Sugar	Insulin Bolus Regimen	Vellore Regimen
N	35	35
Mean	148.51	161.71
SD	24.89	22.06
P value Unpaired t Test		0.0218

In patients belonging to Insulin Bolus Regimen Group, the mean PPBS measurement is 148.51 mg/dl. In Vellore Regimen Group, the mean PPBS measurement is 161.71 mg/dl. The increased mean PPBS measurement in Vellore Regimen Group compared to the Insulin Bolus Regimen Group is statistically significant as the p value is 0.0219 as per unpaired t- test indicating a true difference among study groups.

However, the post prandial blood sugar is only one of the many variables used in assessing the quality of blood glucose control and since the fasting blood glucose values analysis did not show any significant difference between the two groups, it is safe to consider that the 2 groups did not significantly differ in terms of preoperative blood glucose control.

Primary Outcome Measure

Blood glucose monitoring at hourly intervals in both the groups



Blood Glucose Monitoring		Baseline	1 hour	2 hour	3 hour
Insulin Bolus Regimen	N	35	35	35	35
	Mean	156.37	158.09	157.51	152.06
	SD	34.09	37.17	34.23	30.22
Vellore Regimen	N	35	35	35	35
	Mean	159.97	146.89	143.69	139.97
	SD	35.00	35.16	17.54	18.17
P value Unpaired t Test		0.6643	0.1997	0.0367	0.0383

Results

In patients belonging to Insulin Bolus Regimen Group, the mean blood sugar measurement ranged from 156.37 mg/dl at baseline to 152.06 mg/dl at the end of 3 hours. Similarly in the Vellore Regimen Group, the mean blood glucose measurement ranged from 159.97 mg/dl at baseline to 139.97 mg/dl at the end of 3 hours. The mean blood glucose measurement at each hour was compared in both the groups. The decreased mean blood glucose measurement in Vellore Regimen Group compared to the Insulin Bolus Regimen Group is statistically significant as the p value is 0.0367 at 2 hours and 0.0383 at 3 hours intraoperatively as per unpaired t- test indicating a true difference among study groups.

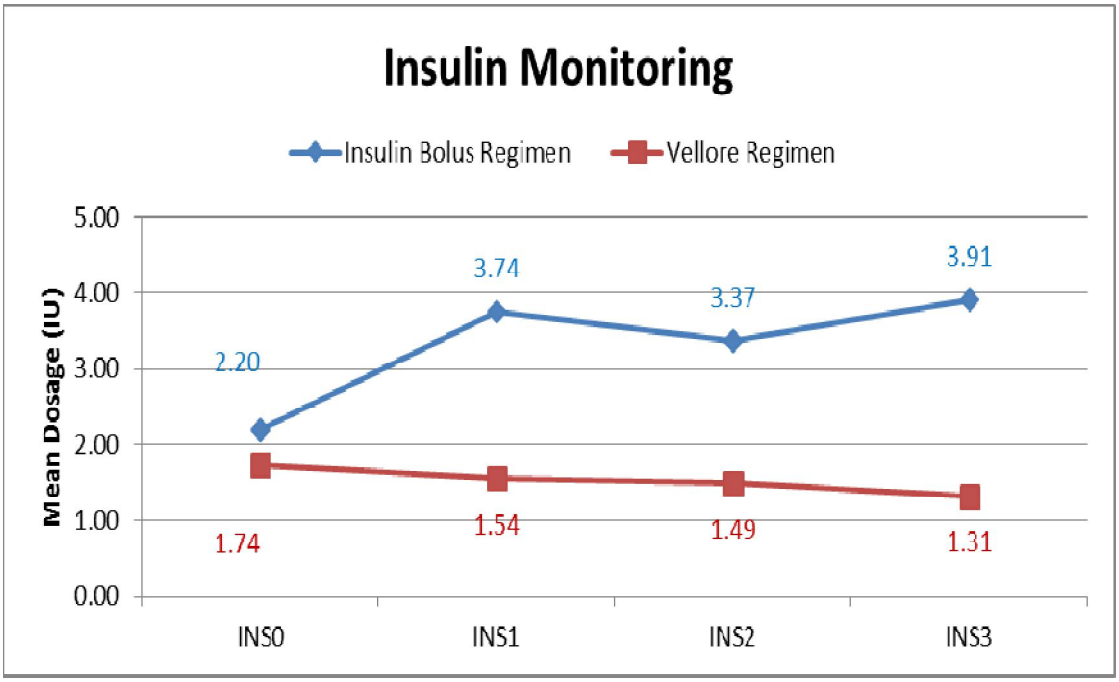
Discussion

The mean BS measurement intraoperatively at 2-3 hours was meaningfully less in Vellore Regimen Group compared to the Insulin Bolus Regimen Group by 12.96 mg/dl. This significant difference of 8% decrease in mean blood glucose measurement intraoperatively in Vellore Regimen Group compared to the Insulin Bolus Regimen Group is true and has not occurred by chance.

Conclusion

In this study we can safely conclude that mean post prandial blood sugar measurement was significantly and consistently lower intraoperatively in Vellore Regimen Group compared to the Insulin Bolus Regimen Group when used to manage intraoperative blood sugar levels.

Insulin requirement



Insulin Monitoring		INS0	INS1	INS2	INS3
Insulin Bolus Regimen	N	35	35	35	34
	Mean	2.20	3.74	3.37	3.91
	SD	1.98	4.01	3.92	4.86
Vellore Regimen	N	35	35	35	35
	Mean	1.74	1.54	1.49	1.31
	SD	0.78	0.61	0.56	0.47
P value Unpaired t Test		0.2109	0.0028	0.0079	0.0039

Results

In patients belonging to Insulin Bolus Regimen Group, the mean insulin dosage ranged from 2.2 IU at baseline to 3.91 IU at the end of 3 hours. Similarly in the Vellore Regimen Group, the mean insulin dosage ranged from 1.74 IU at baseline to 1.31 IU at the end of 3 hours. The decreased mean insulin dosage in Vellore Regimen Group compared to the Insulin Bolus Regimen Group is statistically significant as the p value is 0.0028 at 1 hour, 0.0079 at 2 hours and 0.0039 at 3 hours intraoperatively as per unpaired t- test indicating a true difference among study groups.

Discussion

The mean insulin dosage intraoperatively between 1-3 hours was meaningfully less in Vellore Regimen Group compared to the Insulin Bolus Regimen Group by 2.24 IU. This significant difference of 62% decrease in mean insulin dosage intraoperatively in Vellore Regimen Group compared to the Insulin Bolus Regimen Group is true and has not occurred by chance.

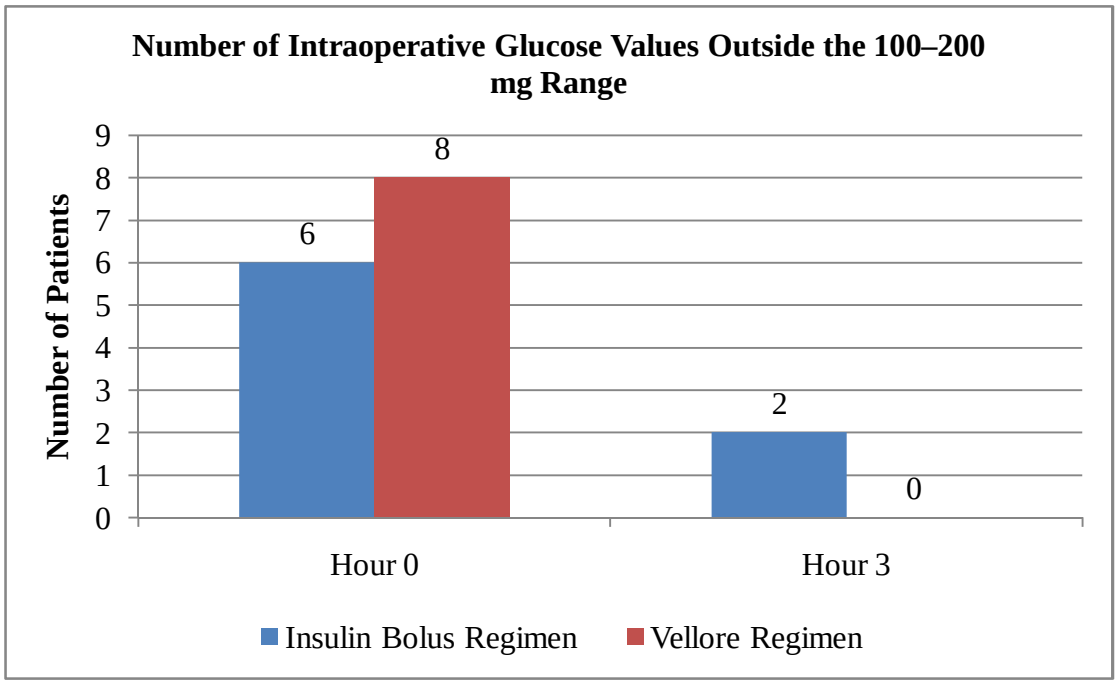
Conclusion

In this study we can safely conclude that mean insulin dosage was significantly and consistently

Lower intraoperatively in Vellore Regimen Group compared to the Insulin Bolus Regimen Group when used to manage intraoperative blood sugar levels

Secondary Outcome Measure

Number of Intraoperative Glucose Values outside the 100–200 mg Range



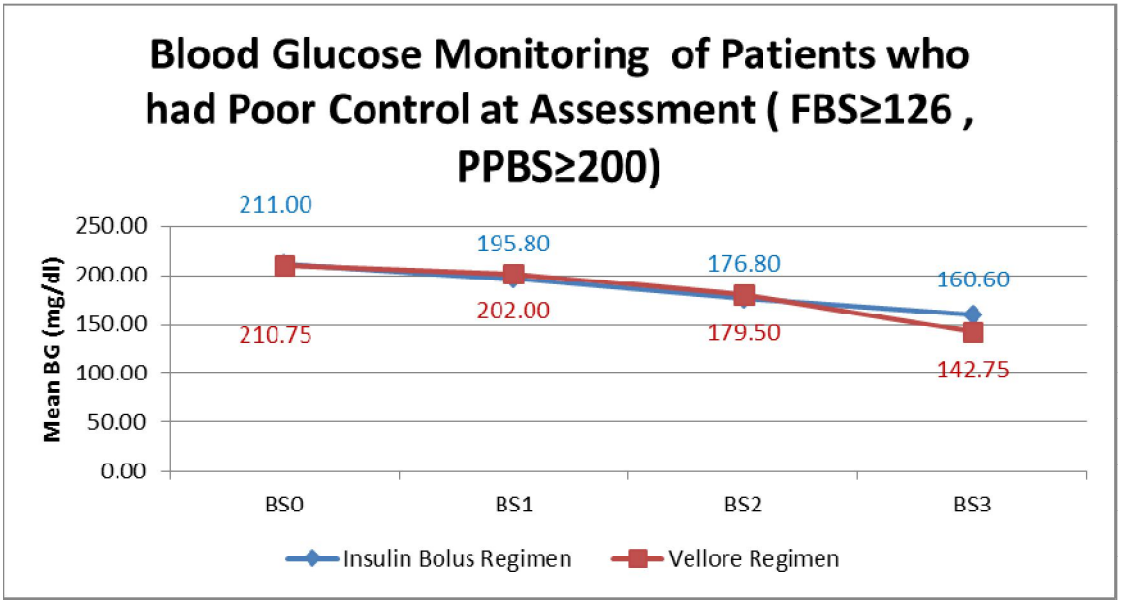
Number of Intraoperative Glucose Values outside the 100–200 mg Range	Hour 0	%	Hour 3	%
Insulin Bolus Regimen	6	17.1	2	5.7
Vellore Regimen	8	22.8	0	0%
P value Fishers Exact Test			0.2333	

In patients belonging to Vellore Regimen Group, the number of intraoperative glucose levels external to the 100–200 mg range between hour 0 is 42.86% (n=6). In patients belonging to Insulin Bolus Regimen Group, the number of intraoperative glucose values external to the 100–200 mg range hour 3 is 100% (n=2). The increased the number of intraoperative glucose levels external to the 100–200 mg range between hour 0-3 in Vellore Regimen Group at hour 0 and at hour3 in Insulin Bolus Regimen Group is statistically not significant as the p value is > 0.05 as per unpaired t- test.

In comparing the difference between the number of patients who were outside the target range at hour 0 and hour 3 between both the groups every hour, we find that for the Vellore regimen, the percentage dropped from 63% to 0%, while for the insulin bolus regimen it decreased from 17 % to 5 %.

Tertiary Outcome Measure

Blood glucose monitoring of patients who had poor control at assessment



Blood Glucose Monitoring of Patients who had Poor Control at Assessment (FBS≥126, PPBS≥200)		**BS0**	**BS1**	**BS2**	**BS3**
Insulin Bolus Regimen	N	5	5	5	5
	Mean	211.00	195.80	176.80	160.60
	SD	9.85	31.25	54.03	41.03
Vellore Regimen	N	4	4	4	4
	Mean	210.75	202.00	179.50	142.75
	SD	8.62	37.27	37.68	20.12
P value Unpaired t Test		0.9688	0.7992	0.9323	0.4262

In patients belonging to Insulin Bolus Regimen Group, the mean Blood Glucose Monitoring of Patients who had Poor Control at Assessment (FBS≥126, PPBS≥200) ranged from 211 mg% at baseline to 160.60 mg% in the culmination of 3 hours. Similarly in the Vellore Regimen Group, the mean BS measurement ranged from 210.75 mg/dl at baseline to 142.75 mg/dl at the end of 3 hours. The decreased mean Blood Glucose Monitoring of Patients who had Poor Control at Assessment (FBS≥126, PPBS≥200) in Vellore Regimen Group compared to the Insulin Bolus Regimen Group is statistically not significant as the p value is > 0.05 as per unpaired t- test.

Comparison of the number of patients whose blood glucose values crossed below 60 mg % and above 225 mg% in the course of the study in both the groups

Comparison between the two groups for the number of patients found to be having blood glucose levels < 60 mg% and > 225mg%. There was no instance of drop in blood sugar below 60 mg% in the Vellore regimen group while there was one such episode in the insulin bolus regimen group. The patient was treated with rapid infusion of 100 ml of 5 % dextrose over 15 minutes and reassessed. Further treatment was continued as per the respective regimen. Also the number of people with blood sugars above 225mg% was 3 in the Vellore regimen group while the intermittent iv bolus regimen had 8 such patients.

	H0	**H1**	**H2**	**H3**
Vellore regimen	<60 0 >225 0	<60 0 >225 2	<60 0 >225 1	<60 0 >225 0
Insulin bolus	<60 0 >225 0	<60 0 >225 4	<60 1 >225 2	<60 0 >225 2

DISCUSSION

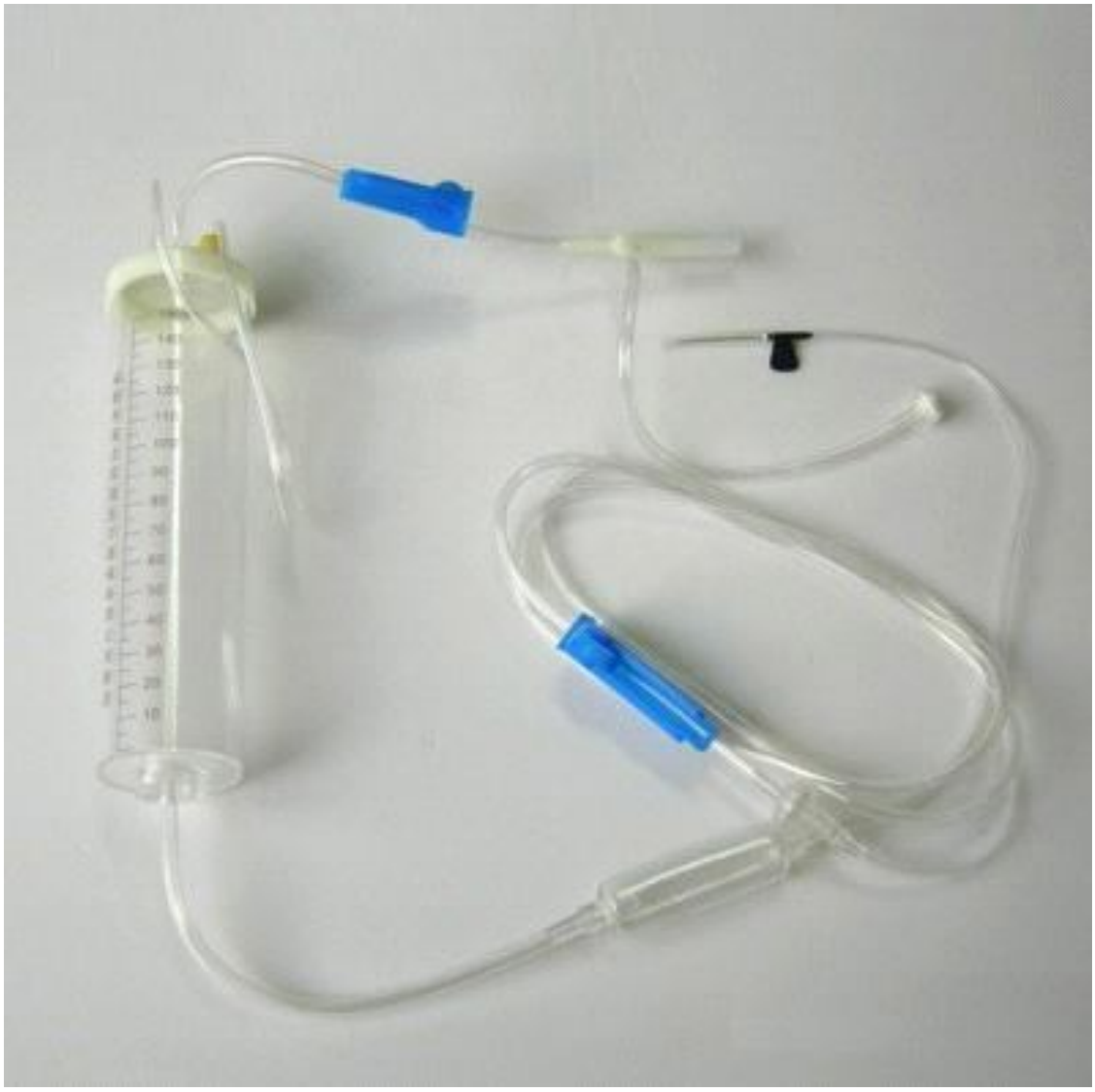
Blood glucose control in the diabetic patient undergoing major surgery is of utmost importance. Control of blood sugars is imperative for the proper management of diabetic patients and is shown to reduce the occurrence of not only microvascular complications but also the neurological ones that are common. However, evidence doesn't show the expected fall in the occurrence of macrovascular damages, which are likely linked to associated conditions like hypertension, smoking and poor dietary / lifestyle choices[6].The latter finding is supported by the observation that patients suffering from both DM as well as hypertension show reductions in risk of complications of DM and death due to macrovascular damages and ocular damage if they are managed with ACE inhibitors or beta blockers. Type 2 DM patients who are undergoing minor surgery need not be started on insulin if the planned surgery is a minor one. All DM patients who are about to undergo major surgery and are either on oral hypoglycaemic drugs or on insulin must definitely start receiving insulin before surgery. Using a continuous intravenous infusion of insulin is a better option compared to intermittent subcutaneous bolus regimens and may be associated with better end results. Intermittent intravenous bolus regimens are also accepted and are in use[6]. However, the protocol used to the end result should be simple and convenient, as

time and concentration has to be devoted to so many other major anaesthetic challenges one faces in such cases. The Vellore regimen was devised to suit the above concern and has been quite accepted in our daily practice. In doing this trial, I intend to ascertain whether the even more convenient intermittent intravenous bolus regimen, based on a sliding scale, provides glycaemic control benefits comparable to the usually followed insulin infusion regimen.

In our institute, we don't follow a single regimen for the purpose of blood glucose control. The method adopted depends on the anaesthesiologist, and can vary from giving subcutaneous insulin to resorting to insulin only in instances of hyperglycaemia. Convenience is necessary for any regimen to be successful.

The insulin used was regular human insulin. The rationale of supplying insulin in dextrose is that the body needs glucose for baseline energy requirements which is around 1.2 mg/kg/min i.e. 5 g/hour, as narrated by Hirsh[10], Meyer and White. As discussed earlier, the body needs glucose for it's, basal metabolic requirements. These studies have also shown that most of the times patients can be kept within the blood sugar range of 120-180 mg% using an insulin

Infusion rate between 1 -2 IU per hour[16]. The insulin dose was mixed with water prior to introducing it into the burette so that no drug was wasted.



There is a tendency for considerable quantities of insulin to adsorb on infusion sets, especially if the sets are long, consequently decreasing the starting velocity of delivery of insulin if the protocol that is used has a

solution with more volume compared to the insulin dose[21]. Person et al found that a washout of about fifty ml with a solution containing twenty five IU of regular insulin in five hundred ml of normal saline allows seventy five percent of expected drug for the first 50 ml of the infusion and hundred percent after that. I put one ml of the drug into ten ml of dextrose solution, rinsed the burette and threw it out prior to commencing the infusion, in an attempt to minimise

The above described effect of adsorption. A detailed look at the master chart shows the blood sugars stabilising well in the latter hours, which may be attributed to the wearing off of the adsorption effect[3].

Potassium was not included in the Vellore regimen because unlike the Alberti regimen where 10% dextrose was used, the Vellore regimen used 5% dextrose and hence the demand for insulin was reduced[3]. However, monitoring of serum Potassium was done at least 2 hourly intraoperatively, especially in very long duration procedures, and appropriate treatment was promptly instituted.

The target range for blood glucose control was chosen as 100-200mg%[3]. In this whole exercise it is of prime importance that hypoglycaemia is avoided at all costs, as the complications are potentially disastrous, the worst case scenario being hypoglycaemic coma and

cardiac arrest. It is also not so easy to suspect hypoglycaemia in a patient under general anaesthesia.

The purpose of this study trial was to converge on an appropriate regimen that was both effective as well as convenient. While the Vellore regimen has proven it's efficiency in some previous trials, there are very few studies undertaken to make a comparison of it with the more popular but controversial intermittent intravenous bolus regimen of insulin. The study was conducted in vascular surgery patients, who have a very common association with the disease.

For analysing the statistics, our outcome measures were as follows

1. Primary – comparison between the two groups of mean +- standard deviation of intraoperative blood glucose on an hourly basis.
2. Secondary – comparing the difference between the number of patients who were outside the target range(100mg% - 200mg%) at hour 0 and hour 3 between both the groups
3. Tertiary – comparison between the two groups of mean+- standard deviation of intraoperative blood glucose on an hourly basis, only for those patients who had poor preoperative blood glucose control (FBS>126 mg%, PPBS>200mg%)

Based on the analyses, the following were the findings

The primary outcome showed a significant difference between the two regimen, in favour of the Vellore regimen. The mean blood glucose measurement at each hour was compared in both the groups. The decreased mean blood glucose measurement in Vellore Regimen Group compared to the Insulin Bolus Regimen Group is statistically significant as the p value is 0.0367 at 2 hours and 0.0383 at 3 hours intraoperatively as per unpaired t- test indicating a true difference among study groups.

For the secondary outcome, in comparing the difference between the number of patients who were outside the target range at hour 0 and hour 3 between both the groups every hour, we find that for the Vellore regimen, the percentage dropped from 63% to 0%, while for the insulin bolus regimen it decreased from 17 % to 5 %. Although the Vellore Regimen takes the upper hand here, the finding was not found to be statistically significant.

Coming to the tertiary outcome, In patients belonging to Insulin Bolus Regimen Group, the mean Blood Glucose Monitoring of Patients who had

Poor Control at Assessment (FBS≥126, PPBS≥200) ranged from 211 mg/dl at baseline to 160.60 mg/dl at the end of hour 3. The comparison turned out to be insignificant although it was in favour of the

Vellore regimen. The mean blood glucose measurement varied from 210.75 mg/dl at baseline to 142.75 mg/dl at the end of hour 3. The decreased mean Blood Glucose Monitoring of Patients who had Poor Control at Assessment (FBS≥126, PPBS≥200) in Vellore Regimen Group compared to the Insulin Bolus Regimen Group is statistically not significant as the p value is > 0.05 as per unpaired t- test.

An overview of the complications that occurred during the surgery is also important to take into consideration the safety of each of the regimen Therefore, I also undertook a comparison between the two groups for the number of patients found to be having blood glucose levels < 60 mg% and > 225mg%. There was no instance of drop in blood sugar below 60 mg% in the Vellore regimen group while there was one such episode in the insulin bolus regimen group. The patient was treated with rapid infusion of 100 ml of 5 % dextrose over 15 minutes and reassessed. Further treatment was continued as per the respective regimen. Also the number of people with blood sugars above 225mg% was 3 in the Vellore regimen group while the intermittent iv bolus regimen had 8 such patients. The comparison attests to the safety of the Vellore regimen.

As a side note, it was also observed that the Vellore regimen consumed less insulin to give better control over blood sugars than the intermittent iv bolus regimen.

Comparing my study with similar studies done previously, I found that the results were similar, being in favour of insulin infusion regimens for intra operative glycaemic control. The trail on which my study was primarily based was 'A Simple Glucose Insulin Regimen for Perioperative Blood Glucose Control: The Vellore Regimen 'conducted at CMC, Vellore. It compared the Vellore regimen in the study group with many commonly used regimens in the control group[3]. Another trial' Continuous Perioperative Insulin Infusion Decreases Major Cardiovascular Events in Patients Undergoing Vascular Surgery' did a similar comparison between continuous and intermittent approaches of insulin administration and found the former to be superior[5]. The PILGRIM trial is currently conducting a study comparing the GIK regimen, the intermittent IV insulin bolus regimen and GPL pre-treatment with liraglutide[16].

Preoperative Evaluation

All diabetic patients should undergo a thorough evaluation of all aspects of the disease right from a detailed history covering the onset, duration progress, medications and complications to examination and investigations. The assessment for complications should focus on all expected affected systems. The cardiac system may not show symptoms

of myocardial ischaemia due to peripheral neuropathy, hence a baseline ECG is a must[16]. On further suspicion one may proceed with stress testing, ECHO, angiography.

Renal evaluation is also important and includes seeking history of facial puffiness, signs of water retention, hypertensionetc. Renal function tests are necessary[16]. Serum creatinine isn't very reliable as an indicator of renal dysfunction because values remain normal till at least half the nephron function is lost. A twenty four hour urine creatinine estimation is a more sensitive indicator. Proteinuria and defective creatinine clearance in a diabetic patient could signal chances for occurrence of ARF perioperatively.

Orthostatic hypotension is another concern which may foreshadow intraoperative haemodynamic instability. Other signs of autonomic neuropathy such as resting tachycardia and loss of normal respiratory-heart rate variability must be sought. The patient should then be optimised by approaching those problems that can be corrected like for example, the blood sugar levels, the acid base status and electrolyte abnormalities. The above measures play a crucial role in the final outcome of the surgery [16].

Glycaemic control

Most patients, especially those undergoing major surgery, are hospitalised 2 -3 days before surgery for optimising glucose control.

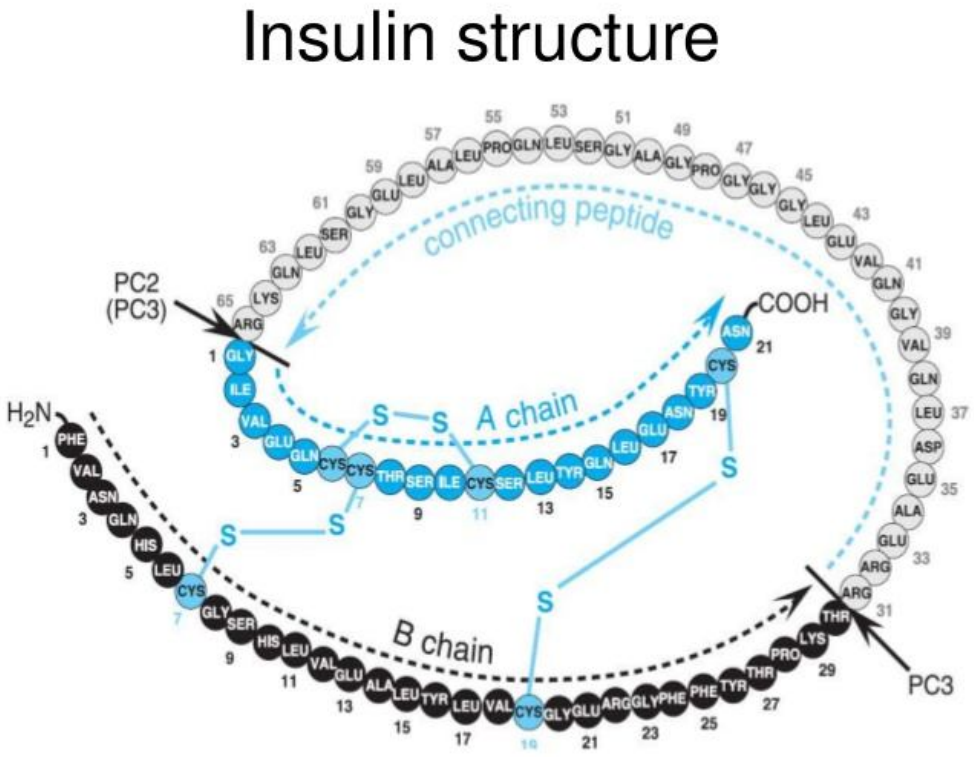
In order to achieve quality control we need to check blood glucose levels quite often and adjust the dosages on insulin accordingly. This is shown to achieve stability in the glycaemic levels. The recommendations of timings in which to carry out the monitoring, include before meals, post meals and before sleep. In patients on insulin, the long acting insulin must be withheld 24-48 hours prior to surgery. The alternative would be giving a combination of intermediate acting insulin with a short acting one, twice a day or giving short acting insulin prior to all meals. However, on the day before surgery, long-acting insulin may be used throughout the day if the patient's control is fine, especially if the patient is on glargine. Because this recently introduced insulin analogue keeps a steady concentration in the course of the day, more experience with its utilisation may perhaps show its safety as a basal insulin in the course of the surgical period[16].

Oral agents are generally stopped before surgery, except for minor procedures where the patient is going to start eating soon after surgery, and changed to insulin. Long-acting OHA’s are stopped two to three days before surgery, while short-acting sulfonylureas, other insulin

secretagogues, and metformin should be withheld the night before or the day of surgery[16]. There exist no suggestions for use of thiazolidinediones prior to surgery; their prolonged duration of action is a good enough reason to avoid them perioperatively.

Intraoperative Management

Insulin



The word insulin derives from the Latin word insula which means island and is called so because it is produced by the island like beta cells of the pancreas. it is an anabolic hormone that is involved in such crucial metabolic activities as

1. Skeletal muscle and fat absorption of glucose from blood,
2. Storage of fat and inhibition of lipolysis,
3. Inhibition of gluconeogenesis

Normally, constant baseline levels of insulin are released into blood, to control blood glucose levels. Glucose, which is the main fuel for life can also be destructive in higher concentrations. Whenever glycaemic levels reduce beyond a certain extent, the body utilises glycogen as an energy source via the process of breakdown of glycogen, which involves breaks down the glycogen stored in the liver and muscles into glucose, so that it can be used as a fuel

Patients with type 1 diabetes have their source of insulin destroyed due to autonomic complications and therefore depend on externally provided insulin for life.

Patients with type 2 DM on the other hand, initially develop insulin resistance due to poorly known factors and later exhaust their source of insulin supply over a period of years due to the persistently high stimulation of the islet cells. These patients in the long run require insulin if lifestyle changes and OHA's fail to get the blood glucose levels under control. A little less than half of the patients with Type 2 diabetes need their blood sugars to be controlled by insulin.

Insulin is thought to be an ancient protein that possibly originated more than a billion years ago. Molecular structures that might be precursors to insulin have been found even in the simplest unicellular organisms. Insulin-like proteins have also been demonstrated in Fungi.

The make up of insulin is not the same in all the species but differs in small ways. as opposed to human insulin, animal insulin has somewhat different effects on the metabolism of carbohydrates on account of the differences in structure. The human insulin resembles porcine insulin very closely.

Gone are the days when we would use animal insulin to inject into humans. Modern medicine uses recombinant DNA technology to create bio synthetic insulin. With this new advent, it was possible to avoid complications of animal insulin like allergy and resistance due to antibody formation.

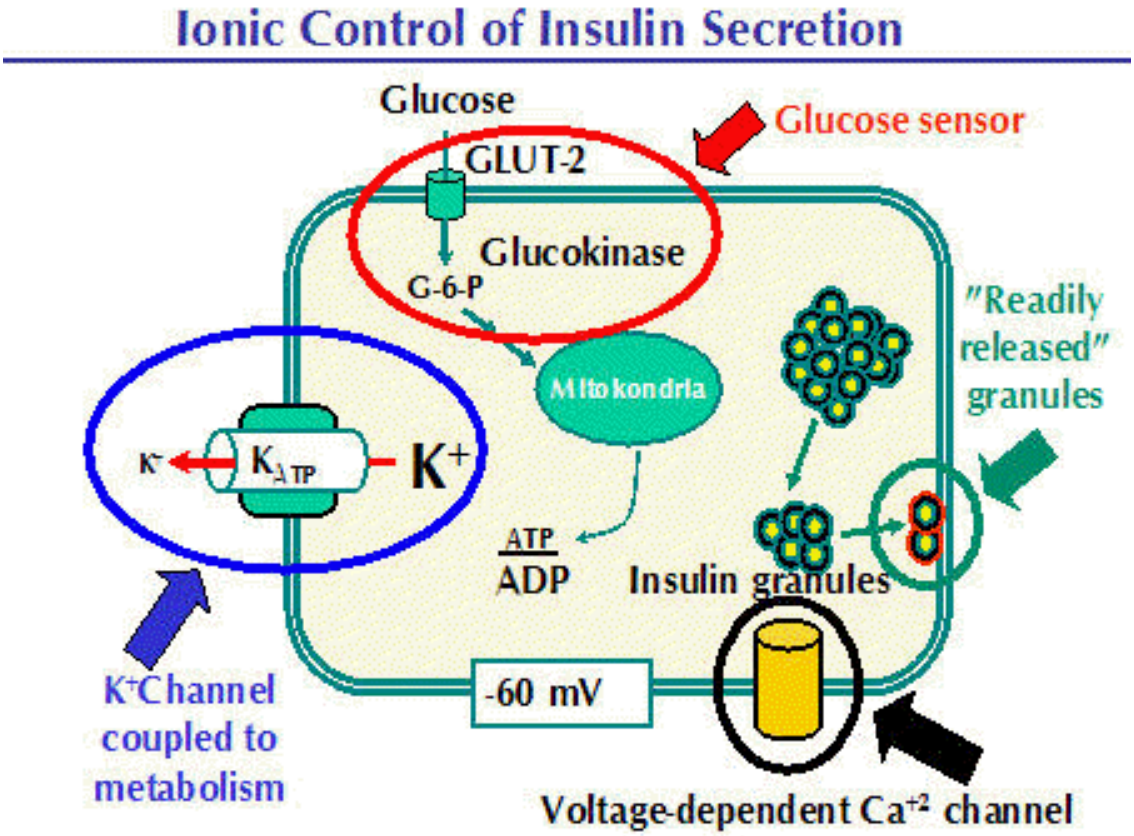
A recent technique of producing insulin involves introducing the human insulin gene in plants e.g. Sunflower to produce insulin, in a technique called bio farming. This is sure to markedly reduce costs.

As of today, there are many analogues of insulin. Insulin analogues are modifications of human insulin that are developed and engineered to cater to specific aspects of desired pharmacokinetics. The first biosynthetic insulin analogue was createdespecially for clinical use at the

time of meals, Humalog (insulin lispro), it starts taking effect at around 15 mins. The route of administration is subcutaneous. It is absorbed into the body much faster than subcutaneously injected regular insulin. Other analogues which act similarly in terms of onset of action are novo rapid and aprida. These have related pharmacokinetic outline. Because of a sequence that decreases the generation of dimers and these insulins are quickly absorbed. Insulins which form monomers are absorbed faster. Fast acting insulins no longerneed to be administered before meals by a certain time interval as it was previously required for human insulin and animal insulins. There also exist insulins that have prolonged periods of action ; the first of the long acting types was Lantus (insulin glargine). Their effect lasts from a period of 18 – 24 hours. the most common route of administration of insulin is the subcutaneous one. The dose is delivered by insulin syringes or pumps or insulin pens that have needles which can be disposed. Technology is advanced to such an extent that insulins which are administered via the inhalational route have now appeared in the market.

Insulin is a protein and hence cannot be taken orally, which if done, it will be broken into amino acids with resultant loss of it’s function. There is testing going on into ways to safeguard insulin within the GIT, making it possible to be administered via the oral or sublingual route.

Although this endeavour is still in it's infancy various of such drugs are being tested in human trials and preparations are on to launch the products.



There still exists no 100% certainty about which method is best for perioperative blood glucose control. Few studiesexplicitlyindicate the supremacy of one protocol over another. Any protocol should

a) Sustain good blood sugar regulation to prevent extreme variations in glycaemic status, which is the main goal of the whole exercise

and is the factor upon which the success of the protocol is dependant

b) Avoid other metabolic and electrolyte interferences that may arise, for example, dangerous hypokalaemia may occur after long duration insulin infusions

c) Be comparatively simple to comprehend. The above quality cannot be overlooked because sugar control is one small component of a much larger anaesthetic management plan.

d) Be usable in a wide range of circumstances.

For any regimen to be successful, it has to be able to promptly find out any changes in metabolic regulation and rectify them in advance of them worsening.

For many years, physicians used the subcutaneous route of delivery of insulin based on sliding scale[16]. This has recently seen a reduction and newer regimens have entered the scene. Recent studies have shown that intravenous insulin infusion is in fact a better alternative, maybe owing to the 100 % bioavailability as compared to the erratic absorption of the subcutaneous route. Of the intravenous infusion regimens also there are many types, one of which is the variable rate glucose insulin type. The glucose and the insulin runs separately so that each can be adjusted independent of the other[24]. This also has it's disadvantage as unnoticed

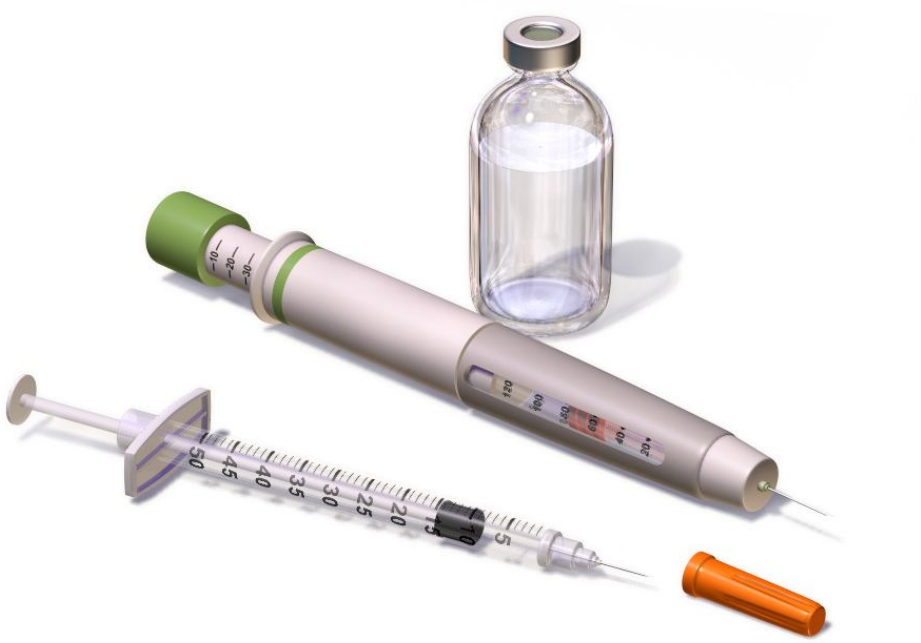
running out of one of the infusions can be catastrophic. IV insulin infusion utilises an easy method to maintain blood sugar regulation over a broad range of insulin needs.

The aim is to keep blood glucose levels within a desired scale (example., 120 to 180 mg% in the course of the surgical period. In a patient with type 1 diabetes, the insulin infusion is started at a rate of 0.5 to 1 U per hour. In a patient with poor control or in one with type 2 diabetes, the starting dose is mostly higher, about 2 to 3 U per hour or more. The infusion rate is adjusted according to a glucose feedback protocol based on hourly glucose readings.

Another type of insulin infusion is the combined glucose insulin regimen or the glucose-insulin-potassium regimen, wherein glucose and insulin run together in the same line. It can be used for both insulin dependant as well as non insulin dependant diabetic patients [1]. The advantage of this technique is the safety. There is no risk of one drug running out. One of the cons of this method is that it doesn't allow to separately alter the insulin and glucose delivery as may be needed. Every time the ratio of insulin to glucose has to be changed a fresh solution has to be prepared. But once the variations in sugars reach a minimum, the same solution can be used up for the rest of the duration of the

procedure[13]. A new concentration of solution must be prepared if the ratio of insulin to glucose requires changing.

In one intervention trial in patients undergoing cardiac surgery, attempting to achieve intraoperative tight glycaemic control (<100mg %) did not show improvement in outcomes when compared to good glycaemic control (<200mg%). However, in another study by Subramanian et al., involving 236 patients undergoing vascular surgery, subjects randomized preoperatively to a continuous intravenous insulin infusion protocol (goal glucose range 100–150mg%) versus an intermittent intravenous bolus protocol (treatment if >150mg%) had a lower rate of perioperative heart attack[5].



Even though the role of subcutaneous insulin in the intraoperative period is diminished, it is still used by some for perioperative management. Erratic absorption of the subcutaneous dose, which is otherwise a normal problem, becomes more unpredictable in the perioperative period due to altered tissue perfusion, especially in the obese. If for some reason the surgery is unexpectedly extended in time or the case is taken up later than planned then the effect of the subcutaneous dose may not last as long as needed. However, the approach may be of use if the procedure involved is a minor, lasting for a brief duration of time.

In some instances one may find patients who are using continuous infusion pumps which deliver the drugs into the subcutaneous tissue. Such patients receive insulin which only acts for a short period. During surgery is not very difficult to convert the route of administration to intravenous route. If the procedure is very brief of if the case is being done under local anaesthesia then one may continue with the subcutaneous pump instead of changing over to IV insulin[16]

In patients with type 2 DM whose control of blood sugar has been very good through the years it is enough to just measure the blood sugar at least once in every two hours. Insulin needs to be commenced when the glucose values reach 180mg% to 200mg%. However, one must keep in

mind that blood glucose regulation is capable of deteriorating at any instant even in such well managed patients because of surgical. To the stress factor, we can add complications like infection, steroidal drugs.

Glucose, Fluid, And Electrolyte Management

Most physicians advocate administration of glucose at the rate of 5 grams per hour in diabetic patients who are going to be treated with continuous insulin. The rationale being, the body needs a sustained source of glucose as fuel without which catabolism will set in. Fats and protein will be broken down in a process called gluconeogenesis after the glycogen stores near exhaustion. The more stressful the situation the greater the glucose requirement. Also, continuous administration of insulin necessitates glucose infusion because insulin itself suppresses gluconeogenesis and glycogenolysis.

There are various concentrations of dextrose containing solutions to choose from. The selection of the appropriate one is based upon the duration for which one needs to administer and other patient factors. It is preferable to use 5%dextrose in a volume of 100 ml for procedures. As the procedure length increases one can choose a solution containing a higher concentration of glucose so as to restrict the water intake. Other concentrations available are 10 %, 20% and 50%. the replacement and

maintenance of body fluids during surgery should be done through separately infused balanced salt solutions[16].

Changes in concentration of potassium occur more than with other ions in the pathophysiology of diabetes mellitus. Insulin causes Potassium to transfer into cells. DM complications like hyper glycaemia can result in shift of potassium out of cells. The same goes for acidosis occurring in DKA, which leads to exchange of the potassium within cells for hydrogen ions outside. It therefore obvious that potassium level monitoring is an important part of any insulin regimen. However, one must be careful to note that serum potassium levels may not give an accurate picture of the potassium stores of the body. In DM patients whose renal function tests show no abnormality and whose serum potassium levels are within normal limits, one should add 10meq/L – 20meq/L of potassium for every litre of dextrose containing fluid. The dose can increase if serum potassium levels are low. Potassium can be withheld till the values normalise for patients with hyperkalaemia.

Postoperative Management

In the postoperative period it is common to see subcutaneous sliding scale regimens being followed. Many don't recommend this approach because the variability of glycaemic values tend to be high due to the disadvantages associated with the route. Such patients are at high

risk of ending up in DKA due to persistent hyperglycaemia. It is therefore advisable to stay on the safer side by resorting to intravenous insulin regimens until the patient is capable of oral intake.

When food is ready to be started the patient should receive the regular dose of insulin subcutaneously prior to food. Meanwhile, the intravenous administration can continue till two hours later.

There might be patients who did not require insulin intraoperatively but exhibit the need for it in the period after surgery. The subcutaneous route can be used in such cases at a dose of 0.5-0.7 IU/kg body weight, which has to be split into insulin of short duration of action before each meal or a combination of intermediate acting with short acting insulin two times a day before meals or a combination of long acting insulin at bedtime and short acting insulin before each meal.

If the oral intake started is liquid in nature then it is best to continue with the IV regimen instead of opting for the subcutaneous regimen. Liquid diets have varying levels of sugar which may pose them risks of extreme glycaemic values. Liquid diet doesn't follow a pattern of intake and can be consumed at any random time all too frequently, hence an intravenous regimen would do these patients more good[16]. In any case, the insulin infusion should carry one until two hours after commencing the subcutaneous doses.

Previously not much objection existed to allowing mild rises in glycaemic levels during surgery. This attitude arose because anaesthetists felt safer to permit it in unconscious anaesthetised patients who couldn't communicate their symptoms, thus not risking the overseeing of dangerous falls in blood sugar levels. Such thoughts which prevailed then are not pardonable anymore as we have very accurate and easy to use gadgets at our disposal to conveniently monitor blood sugars. Moreover, there is overwhelming evidence in support of strict control of sugars. With recent change in attitudes anaesthetists are often aggressive in their handling of glucose regulation, as described by a study done in the United Kingdoms. But, out of the 172 participants in this survey, twenty two percent still wanted to maintain blood glucose above 180mg% in DM patients and two percent were in favour of a level of above 234mg%. A great proportion of participants managed to regulate sugars in type 1 DM patients with insulin infusions, especially for lengthy procedures. A staggeringly huge proportion of participants did not think it to be imperative, in type 2 DM patients scheduled for smaller surgeries, as they believed that omission of glucose containing crystalloid solutions was enough to reduce the need for hypoglycaemic agents. Astonishingly, nearly twenty percent of experienced anaesthesiologists had a similar plan for type2 DM patients who were going through big operations the amount of money involved and the difficulties may affect ideas about the

rigorousness of glycaemic control and, until recent times, there has not been strong proof in favour of tight glucose control regimens for either perioperative or ICU care.

Even to this day there is no general consensus on what is the ideal protocol for managing diabetic patients, perhaps because there aren't enough studies done in this. Alberti, Hirsch et al, and Gavin recommend that in the perioperative time duration one should maintain glucose levels in the range of 10mg% to 200mg% so as to minimise the ill effects arising out of not doing so. The incidence of morbidity and mortality reduced considerably by doing so[1]. Van Den Berghe found association of decreased death rate with strict insulin treatment in DM patients who were in ICU belonging to the surgery department [23]. According to Jennifer B. Marks, in the article' Perioperative Management of Diabetes' the target range for blood sugar control can be changed according to the demand of the circumstance, if required [14]. Generally blood sugar levels beyond 200mg% or under 100mg% should be evaded to reduce the problems that occur in association with extremes of blood sugar values.

The type of anaesthesia used has a bearing upon the control of blood sugar as pain management differs in regional and general anaesthesia so does the stress factor which influences the anti- insulin processes within the body. No study supports one type of anaesthesia

more than the other when it comes to diabetes mellitus. No evidence suggests that one anaesthetic technique or another affects mortality or morbidity in diabetic patients. Halter & Pflug showed that spinal anaesthesia at the dermatome level of T2–T6caused a lowering in the acute counteraction of insulin to blood sugar, while spinal blockade of lower levels of a dermatome level of T9–T12 did not cause such reduction[13].Also, regional techniques have the plus point of letting the patient stay awake and minimises the stress of the surgery. Regional anaesthesia is also known to reduce blood sugar. The risk of venous thromboembolism is also reduced. All is not rosy for the use of central neuraxial techniques in DM. Already suffering from autonomic neuropathy and cardiovascular ailments, the haemodynamic stability of these patients is at a greater compromise in opting for the technique. The already damaged nerves are more like to suffer additional damage, which may be compounded by poor tissue blood supply.

Regional anaesthesia poses greater risks in the diabetic patient with autonomic neuropathy[13].The variations in blood pressure can adversely affect the previously affected vital organs and worsen their course of deterioration. The altered immunity doesn’t help as the patient is at risk of suffering from epidural abscess, or worse, CNS infections easily. In the event that the peripheral neuropathy worsens following surgery, this may

be blamed upon the anaesthetist as an adverse effect of the regional technique[6].

Induction agents may affect the maintenance of blood sugar levels intraoperatively. The effect of propofol, however is not well known. Thiopentone minimised the potential to prevent the hyperglycaemia effects of a high dose of glucose[15]. Etomidate was found to allow better control of sugars by suppressing the synthesis of cortisol.

Benzodiazepines have two different effect that seem to neutralise each other with regard to blood glucose control. They suppress the secretion od adrenocorticotrophic hormone and thereby, the formation of cortisol in large doses. They also lower stimulation of the sympathetic system. While the above described effects should make it easy to regulate sugars, there is this opposing effect of increased growth hormone secretion. Diabetes related effects are significant for midazolam only when used in high doses or continuously as in an infusion[6].

Opioid anaesthetics, when used in large doses are very effective in suppressing the sympathetic nervous system. They also have an effect on the HPO axis. The result is a relieving degree of haemodynamic as well as glycaemic stability, as expected. One must bear in mind at the same time that the response to these drugs may be amplified in diabetics and should therefore proceed with caution while administering them, giving

low doses at a time[6]. One must consider the renal status of the patient and rule out diabetic nephropathy. If present, the dose of morphine requires reduction as it's active metabolite morphine 6 glucuronide is excreted by the kidney. The metabolite of fentanyl, norfentanyl, is inactive, though it is also excreted by the kidney. Hence, fentanyl doesn't require dose reduction.

Certain neuro muscular blocking drugs need caution in diabetics. Since these patients are more likely to present with hyperkalaemia, the use of suxamethonium should follow after confirmation of serum Potassium levels to be normal. Suxamethoniumcan increase K+ levels, albeit transiently, by 0.5 – 1 meq/L. If starting serum levels of Potassium are high then it is better to trade suxamethonium for non depolarising blockers. Vecuroniummust be used with caution in patients suffering from diabetic nephropathy and the same applies to other drugs depending on the kidney for their elimination.

Halothane, enflurane and isoflurane inhibit the response of insulin to blood sugar in a convertible fashion and depends on the dose, in the body. The consequence of propofol on the secretion of insulin is unknown. DM patients have a diminished capability to empty lipids from the circulation. Although this is not likely to be of much importance during short anaesthetic procedures when only propofol is utilised for

maintenance or as an induction agent, it may have consequences for patients who are administered propofol for long periods of sedation in the ICU[6].

SUMMARY

As already discussed, the primary outcome showed a statistically significant efficiency of the Vellore regimen over the IV insulin bolus regimen. while the secondary and tertiary outcomes, although in favour of the Vellore regimen were not of statistical significance.

The primary outcome showed a significant difference between the two regimen, in favour of the Vellore regimen. The mean blood glucose measurement ranged from 156.37 mg/dl at baseline to 152.06 mg/dl at the end of 3 hours. Similarly in the Vellore Regimen Group, the mean blood glucose measurement ranged from 159.97 mg/dl at baseline to 139.97 mg/dl at the end of 3 hours. The decreased mean blood glucose measurement in Vellore Regimen Group compared to the Insulin Bolus Regimen Group is statistically significant as the p value is 0.0367 at 2 hours and 0.0383 at 3 hours intraoperatively as per unpaired t- test indicating a true difference among study groups.

For the secondary outcome, in comparing the difference between the number of patients who were outside the target range at hour 0 and hour 3 between both the groups every hour, we find that for the Vellore regimen, the percentage dropped from 63% to 0%, while for the insulin bolus regimen it decreased from 17 % to 5 %. Although the Vellore

Regimen takes the upper hand here, the finding was not found to be statistically significant.

Coming to the tertiary outcome, In patients belonging to Insulin Bolus Regimen Group, the mean Blood Glucose Monitoring of Patients who had Poor Control at Assessment (FBS≥126, PPBS≥200) ranged from 211 mg/dl at baseline to 160.60 mg/dl at the end of hour 3. The comparison turned out to be insignificant although it was in favour of the Vellore regimen. The mean blood glucose measurement varied from 210.75 mg/dl at baseline to 142.75 mg/dl at the end of hour 3. The decreased mean Blood Glucose Monitoring of Patients who had Poor Control at Assessment (FBS≥126, PPBS≥200) in Vellore Regimen Group compared to the Insulin Bolus Regimen Group is statistically not significant as the p value is > 0.05 as per unpaired t- test.

CONCLUSION

Based on all the above findings, I come to the conclusion that the Vellore regimen, which is a type of continuous insulin infusion regimen is more convenient as well as superior to the intermittent insulin bolus regimen in terms of both efficiency and safety.

BIBLIOGRAPHY

1) Alberti KGMM, Thomas DJB. The management of diabetes during surgery. Br J Anaesth 1979;51:693–710.

2) Alberti KGMM. Diabetes and surgery. Anesthesiology 1991;74: 209–11.

3) Ann Miriam, MD, and Grace Korula, MD Department of Anaesthesia, Christian Medical College Hospital, Vellore, India. A Simple Glucose Insulin Regimen for Perioperative Blood Glucose Control: The Vellore Regimen. (AnesthAnalg2004;99:598–602)

4) Anushka Patel, M.D., Ph.D., Stephen MacMahon, D.Sc., Ph.D., John Chalmers, M.D., Ph.D., Bruce Neal, M.D., Ph.D., and Laurent Billot, M.Sc., the George Institute for International Health and University of Sydney. Intensive Blood Glucose Control and Vascular Outcomes in Patients with Type 2 Diabetes. N Engl J Med 2008;358:2560-72.

5) BalachundharSubramaniam, M.B.B.S., M.D.,* Peter J. Panzica, M.D.,† Victor Novack, M.D., Ph.D.,‡ Feroze Mahmood, M.D.,† RobinaMatyal, M.B.B.S.,† John D. Mitchell, M.D.,† EswarSundar, M.B.B.S.,† Ruma Bose, M.B.B.S.,† Frank Pomposelli, M.D.,§ Judy R. Kersten, M.D., Daniel S. Talmor, M.D., M.P.H.#.

Continuous Perioperative Insulin Infusion Decreases Major Cardiovascular Events in Patients Undergoing Vascular Surgery. A Prospective, Randomized Trial. Anesthesiology 2009; 110:970–7 Copyright © 2009, the American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins, Inc.

6) G. R. Mcanulty, H. J. Robertshaw and G. M. Hall. Anaesthetic management of patients with diabetes mellitus. Oxford Journals Medicine & Health BJA Volume 85, Issue 1Pp. 80-90. British journal of anaesthesia 85 (1) : 80-90 (2000)

7) Galloway JA, Shuman CR. Diabetes and surgery. Am J Med 1963;34:177–91.

8) GavinLA.Perioperative management of the diabetic patient.In: Karam JH, ed. Endocrinology and metabolism clinics of North America. Philadelphia, PA: WB Saunders Company, 1992: 457–75.

9) Gulhan Akbaba1, Yusuf Aydın2. 1 Department Endohrinology and Metabolism Diseases, MuglaSitkiKocman University Faculty of Medicine, Mugla, Turkey. 2 Department of Endohrinology and Metabolism Diseases, Düzce University Faculty of Medicine, Düzce, Turkey. ActaMedica Anatolia Volume 2 Issue 2 2014

10) Hirsch IB, McGill JB, Cryer PE, White PF. Perioperative management of surgical patients with diabetes. Anesthesiology 1991;74:346–59.

11) J. J. Sebranek, A. Kopp Lugli and D. B. Coursin. Glycaemic control in the perioperative period. British Journal of Anaesthesia 111 (S1): i18–i34 (2013). Doi:10.1093/bja/aet381

12) J.P.vankuijk, O. Schouten, W. J. Flu, C.A.denUil, J.J.Bax, D. Poldermans. Perioperative blood glucose monitoring and control in major vascular surgery patients. Eur J VascEndovascSurg (2009) 38, 627-634

13) JadelisGiquel; Yiliam F Rodriguez- Blanco; Christina Matadial; Keith Candiotti. Diabetes Mellitus in Anaesthesia. British Journal of Diabetes and Vascular Disease. 2012;12(2):60-64.

14) Jennifer B. Marks, M.D., University of Miami School of Medicine, Miami, Florida. Perioperative Management of Diabetes. Am Fam Physician. 2003 Jan 1;67(1):93-100.

15) John W. Dundee. Effect Of Thiopentone On Blood Sugar And Glucose Tolerance. Department of Anaesthesia, University of Liverpool. Brit. J. Pharmacol. (1956), 11, 458.

16) Jorinde AW Polderman1, Peter L Houweling2, Markus W Hollmann1, J Hans DeVries3, Benedikt Preckel1* and

JeroenHermanides. Study protocol of a randomised controlled trial comparing perioperative intravenous insulin, GIK or GLP-1 treatment in diabetes–PILGRIM trial. BMC Anesthesiology 2014

17) Man Lin Hui,1 Arun Kumar,2 and Gary G Adamscorresponding author3. Protocol-directed insulin infusion sliding scales improve perioperative hyperglycaemia in critical care. Perioper Med (Lond). 2012; 1: 7.. Published online 2012 Oct 6. doi: 10.1186/2047-0525-1-7. PMCID: PMC3964337

18) Meyer EJ, Lorenzi M, Bohannon NV, et al. Diabetes management by insulin infusion during major surgery. Am J Surg 1979;137:323–7.

19) Nadia A Khan, MD, MSc William A Ghali, MD, MPH. Perioperative management of diabetes mellitus. Official reprint from UpToDate® www.uptodate.com. January 11, 2007

20) Peterson L, Caldwell J, Hoffman J. Insulin adsorbance to polyvinylchloride surfaces with implications for constant infusion therapy. Diabetes 1976;25:72–4.

21) SaraM.Alexanian, MarieE.McDonnell, andShamsuddinAkhtar. Creating a Perioperative Glycemic Control Program. Department of Endocrinology, Diabetes and Nutrition, Boston University Medical Center, 88 East Newton Street, Evans 201, Boston, MA 02118,

USA 2Department of Anesthesiology, Yale University School of Medicine, New Haven, CT 06510, USA

22) Tejal A. Raju, M.D., Marc C. Torjman, Ph.D., and Michael E. Goldberg, M.D. Perioperative Blood Glucose Monitoring in the General Surgical Population. J Diabetes Sci Technol. 2009 Nov; 3(6): 1282–1287. Published online 2009 Nov. PMCID: PMC2787027

23) Van Den Berghe G, Wouters P, Weekers S, et al. Intensive insulin therapy in critically ill patients. N Engl J Med 2001;345: 1359–67.

24) Watts NB, Gebhart SP, Clark RV, Philips LS. Perioperative management of diabetes mellitus: steady state glucose control with bedside algorithm for insulin adjustment. Diabetes Care 1986;9:40–5.

25) White NH, Skor D, Santiago JV. Practical closed-loop insulin delivery: a system for the maintenance of overnight euglycemia and the calculation of basal insulin requirements in insulin dependent diabetes. Ann Intern Med 1982;97:210–3.

ANNEXURES

PROFORMA

NAME:

AGE:

SEX:

WEIGHT

DIAGNOSIS:

SURGICAL PROCEDURE DONE:

PRE OP ASSESSMENT:

HISTORY: Any Co-morbid illness diabetes mellitus, IHD, Bronchial asthma, COPD, Pulmonary tuberculosis etc.

EXAMINATION:

General examination

Pulse - BP - Respiratory Rate - temperature - SaO2-

Respiratory system

Cardiovascular system

Central nervous system

Gastrointestinal system

Local examination

INVESTIGATIONS

Hb/PCV, CBC, RFT, LFT, RBS, FBS, HbA1c

REGIMEN														
S.NO	NAME	AGE	SEX	GA/RA	FFBS	PPBS	BS0	INS0	BS1	INS1	BS2	INS2	BS3	INS3

ABBRIEVATIONS

GA/RA	General Anaesthesia / Regional Anaesthesia
FBS	Fasting Blood Sugar
PPBS	Post Prandial Blood Sugar
BS0	Blood Sugar at hour 0
INS0	Insulin Dose at hour 0

INFORMATION TO PARTICIPANTS

Investigator: Dr.GLADWIN. J. FERNANDES

Name of the Participant

Title: **"A PROSPECTIVE RANDOMISED STUDY COMPARING DIFFERENT APPROACHES TO INTRAOPERATIVE MANAGEMENTOF DIABETES MELLITUS– THE VELLORE REGIMEN VS INTERMITTENT IV BOLUS REGIMEN"**

You are invited to take part in this research study. We have got approval from the IEC. Your are asked to participate because you satisfy the eligibility criteria.

What is the Purpose of the Research:

We want to compare different intraoperative glucose control regimen for efficacy.

The Study Design:

Patients in the study will be divided into two groups, each group consisting of 35 patients.

Group A – patients for The Vellore Regimen Group B – Patients for the Intermittent IV Bolus Regimen.

Patients will be evaluated clinically and investigated

Blood glucose readings will be taken at every hour intraoperatively and intervention relevant to the group will be administered

Benefits

The study will help to decide on a convenient and effective plan for intraoperative blood glucose control

Discomforts and risks

The study poses hardly any risk as the regimens have been in use for a long time and any shift of blood glucose to the extremes will be appropriately dealt with. Patients who don't want to be part of study may withdraw as per their wish.

Time :

Date :

Place :

Signature / Thumb Impression of Patient

Patient Name:

Signature of the Investigator : _____

Name of the Investigator : _____

PATIENT CONSENT FORM

Study Title: **"A PROSPECTIVE RANDOMISED STUDY COMPARING DIFFERENT APPROACHES TO INTRAOPERATIVE MANAGEMENT OF DIABETES MELLITUS– THE VELLORE REGIMEN VS INTERMITTENT IV BOLUS REGIMEN"**

Study Centre: INSTITUTE OF ANAESTHESIOLOGY AND CRITICAL CARE, RAJIV GANDHI GOVT. GENERAL HOSPITAL, MADRAS MEDICAL COLLEGE, CHENNAI 600003.

Participant Name: Age: Sex: I.P.No:

I confirm that I have understood the purpose of procedure for the above study. I have had the opportunity to ask questions and all my questions and doubts have been answered to my satisfaction.

I understand that my participation in the study is voluntary and that I am free to withdraw at anytime without giving any reason.

I understand that the investigator, regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to current study and any further research that may be conducted in relation to it, even if I withdraw from the study. I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from the study.

Time:

Date:

Place:

Signature of the investigator: Signature/thumb impression of patient

Name of the investigator: Patient name

ஆராய்ச்சி ஒப்புதல் படிவம்

ஆராயச்சியின் தலைப்பு

நீரிழிவு நோயாளிகளின் அறுவை சிகிச்சையின்போது அவர்களின் இரத்தத்தின் சர்க்கரை அளவை கட்டுப்படுத்தும் பல்வேறு சிகிச்சை முறைகளை ஒப்பிட்டு பார்த்தல்

ஆய்வு நிலையம் : மயக்கவியல் துறை, சென்னை மருத்துவக் கல்லூரி சென்னை - 3.

பங்கு பெறுவரின் பெயர் :

பங்குபெறுபவரின் எண் :

பங்குபெறுபவர் இதனை (✓) குறிக்கவும்

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டது. ☐

நான் இவ்வாய்வில் தன்னிச்சையாகதான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்றும் அறிந்து கொண்டேன். ☐

இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்த மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ☐

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக்கொள்ளவும் அதை பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கின்றேன். ☐

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்து கொள்வதுடன் 'இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்று உறுதியளிகிறேன். ☐

அறுவை சிகிச்சையின்போது மணிக்கு ஒருமுறை இரத்தத்தின் சர்க்கரை அளவு பரிசோதிக்கப்பட்டு அதற்கு தக்கவாறு இன்சுலின் மருந்து அளிக்கப்படும். இதனால் தீமைகள் எதுவும் இல்லை என்பதை தெளிவாக புரிந்துகொண்டேன். ☐

பங்கேற்பவரின் கையொப்பம் ..... இடம்..... தேதி.....

கட்டைவிரல் ரேகை

பங்கேற்பவரின் பெயர் மற்றும் விலாசம் .....

ஆய்வாளரின் கையொப்பம் ..... இடம்..... தேதி.....

ஆய்வாளரின் பெயர் .....

ஆராய்ச்சி தகவல் தாள்

ஆராய்ச்சி தலைப்பு

நீரிழிவு நோயாளிகளின் அறுவை சிகிச்சையின்போது அவர்களின் இரத்தத்தின் சர்க்கரை அளவை கட்டுப்படுத்தும் பல்வேறு சிகிச்சை முறைகளை ஒப்பிட்டு பார்த்தல்

ஆராய்ச்சியாளர் பெயர் : மருத்துவர்.கிளாட்வின் ஜோசப் பெர்ணாண்டஸ்

பங்கேற்பாளர் பெயர் :

ஆராய்ச்சியின் நோக்கம்

அறுவை சிகிச்சையின்போது சர்க்கரை நோயாளிகளை இரண்டு குழுக்களாக பிரித்து அனைவருக்கும் மணிக்கு ஒருமுறை இரத்தத்தின் சர்க்கரை அளவை சோதித்து பார்த்தல்.

இரண்டு வகையான சர்க்கரையின் அளவை கட்டுப்படுத்தும் சிகிச்சை முறைகளை கையாண்டு அவற்றின் பலனை ஒப்பிட்டுப்பார்த்தல்.

ஆய்வு முறை

ஆய்வில் பங்குபெறும் சர்க்கரை நோயாளிகள் இரண்டு குழுக்களாக பிரிக்கப்படுவர் (அறுவை சிகிச்சையின்போது) அனைவவருக்கும் மணிக்கு ஒருமுறை இரத்தத்தின் சர்க்கரை அளவு பரிசோதிக்கப்படும்.

குழு-1 வேலூர் மருத்துவக்கல்லூரி தொடர் இன்சுலின் சிகிச்சை முறை

குழு-2 இடைவிட்டு இன்சுலின் அளிக்கும் சிகிச்சை முறை

நன்மைகள்

நீரிழிவு நோயாளிகளுக்கு அறுவை சிகிச்சையின்போது இரத்தத்தில் சர்க்கரை அளவை கட்டுப்படுத்த எளிமையான மற்றும் சிறந்த சிகிச்சை முறையை அறியமுடியும்.

பக்கவிளைவுகள்

மணிக்கு ஒருமுறை சர்க்கரையின் அளவு கண்காணிக்கப்படும். அதன் பிறகே தேவையான அளவு இன்சுலின் மருந்து செலுத்தப்படுவதால் பக்கவிளைவுகள் ஏதுமில்லை.

இந்த முறையான ஆய்வு ஏற்கனவே பல இடங்களில் நடத்தப்பட்டுள்ளது. மேலும் இதன் பாதுகாப்பு உறுதிசெய்யப்பட்டுள்ளது. நீங்கள் இந்த ஆய்வில் பங்குகொள்ள விரும்பவில்லை என்றால் எப்போதும் உபயோகிக்கப்படும் மருந்தே கொடுக்கப்படும். உங்கள் பாதுகாப்பே எங்களின் முக்கிய நோக்கம்.

இந்த ஆய்வு சம்பந்தமான எல்லா புள்ளி விவரங்கள் மற்றும் நோயாளிகளின் விவரங்கள் ரகசியமாக வைக்கப்படும். இந்த ஆய்வு சம்பந்தப்பட்ட எல்லா பரிசோதனைகள், மருந்துகள் மற்றும் மருத்துவ சேவைகள் அனைத்தும் நோயாளிகளுக்கு இலவசமாக வழங்கப்படும்.

ஆய்வாளரின் பெயர் **பங்குபெறுபவரின் பெயர்**

ஆய்வாளரின் கையொப்பம் **பங்குபெறுபவரின் கையொப்பம்**

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

EC Reg No.ECR/270/Inst./TN/2013
Telephone No. 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr.Gladwin Joseph Fernandes
Postgraduate M.D.(Anaesthesiology)
Madras Medical College
Chennai 600 003

Dear Dr.Gladwin Joseph Fernandes,

The Institutional Ethics Committee has considered your request and approved your study titled **"A prospective randomized study comparing different approaches to intraoperative blood glucose control – the Vellore regimen vs Intermittent intravenous bolus regimen" No.22042015.**

The following members of Ethics Committee were present in the meeting held on 07.04.2015 conducted at Madras Medical College, Chennai-3.

1. Prof.C.Rajendran, M.D.,	: Chairperson
2. Prof.R.Vimala, M.D., Dean, MMC, Ch-3	: Deputy Chairperson
3. Prof.B.Kalaiselvi, M.D., Vice-Principal, MMC, Ch-3	: Member Secretary
4. Prof.B.Vasanthi, M.D., Prof. of Pharmacology, MMC	: Member
5. Prof.P.Ragumani, M.S., Professor of Surgery, MMC	: Member
6. Prof.S.Baby Vasumathi, Director, Inst. Of O&G, MMC	: Member
7. Prof.K.Ramadevi, Director, Inst.of Biochemistry, MMC	: Member
8. Prof.Saraswathy, M.D., Director, Pathology, MMC, Ch-3	: Member
9. Prof.K.Srinivasagalu, M.D.,Director, I.I.M. MMC, Ch-3	: Member
10.Thiru S.Rameshkumar, B.Com., MBA	: Lay Person
11.Thiru S.Govindasamy, B.A., B.L.,	: Lawyer
12.Tmt.Arnold Saulina, M.A., MSW.,	: Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

MASTER CHART

INSULIN BOLUS REGIMEN

S.NO	NAME	AGE	SEX	GA/RA	FBS	PPBS	BS0	INS0	BS1	INS1	BS2	INS2	BS3	INS3
1	JAYACHANDRAN	52	M	GA	110	144	122	0 IU	130	0 IU	110	0 IU	130	0 IU
2	ABHISHEK	56	M	RA	108	133	127	0 IU	133	0 IU	138	0 IU	154	2 IU
3	ABDUL	42	M	RA	126	200	200	5 IU	183	4 IU	174	3 IU	156	2 IU
4	NARAYANAN	60	M	GA	106	148	108	0 IU	152	2 U	163	5 IU	124	0 IU
5	GOPAL	55	M	RA	110	150	112	0 IU	128	0 IU	188	8 U	167	5 IU
6	GOPINATH	57	M	RA	112	149	156	2 IU	118	0 IU	120	0 IU	157	2 IU
7	SHIVASHANKAR	59	M	GA	128	189	210	5 IU	229	12 IU	226	12 IU	130	0 IU
8	ASMIT	46	M	RA	116	155	188	4 IU	167	3 IU	134	0 IU	176	5 IU
9	POOJA	50	F	RA	100	132	110	0 IU	170	5 IU	157	2 IU	156	4 IU
10	RUDRAKSHA	43	M	RA	102	130	173	3 IU	156	2 IU	166	5 IU	124	0 IU
11	SENTHIL	51	M	RA	113	128	160	2 IU	112	0 IU	170	5 IU	112	0 IU
12	AKASH	40	M	RA	110	133	146	2 IU	200	9 IU	150	4 IU	158	6 IU
13	TEJAS	55	M	RA	122	190	200	5 IU	190	4 IU	122	0 IU	140	0 IU
14	VINITA	56	F	RA	114	135	166	3 IU	130	0 IU	110	0 IU	112	0 IU
15	PUNEET	56	M	GA	117	139	157	2 IU	150	2 IU	174	5 IU	156	6 IU
16	DHYANESHWARAN	59	M	RA	120	140	145	2 IU	103	0 IU	159	4 IU	188	12 IU
17	DHANAM	53	F	RA	130	210	222	6 IU	228	12 IU	230	18 IU	227	18 IU
18	ADITI	48	M	GA	118	150	168	3 IU	140	0 IU	188	8 IU	240	19 IU
19	RAMGOPAL	54	M	RA	119	172	134	0 IU	157	4 IU	122	0 IU	117	0 IU
20	ANAND	54	M	GA	127	178	220	6 IU	159	2 IU	100	0 IU	124	0 IU
21	BHARATH	42	M	RA	125	157	180	4 IU	99	0 IU	160	4 IU	154	4 IU
22	YUVARAJAN	53	M	GA	110	120	150	2 IU	129	0 IU	172	5 IU	166	5 IU
23	SHAKTIVEL	44	M	RA	111	133	103	0 IU	160	4 IU	155	4 IU	170	7 IU
24	POOVARASAN	58	M	GA	114	134	155	2 IU	185	8 IU	140	0 IU	128	0 IU
25	SEKAR	59	M	RA	109	123	112	0 IU	130	0 IU	120	0 IU	133	0 IU
26	KATHIR	53	M	RA	106	118	129	0 IU	144	4 IU	58	0 IU	151	4 IU
27	SALIM	47	M	RA	117	160	188	4 IU	240	13 IU	166	5 IU	174	IU
28	SHIVAKARTHIK	56	M	GA	127	206	203	5 IU	180	4 IU	154	4 IU	166	7 IU
29	VINOD	58	M	GA	109	128	151	2 IU	198	9 IU	158	4 IU	168	7 IU
30	JAGADISHWARAN	49	M	GA	108	130	130	0 IU	144	4 IU	127	0 IU	118	0 IU
31	ANBARASAN	52	M	RA	107	136	135	0 IU	148	4 IU	130	0 IU	126	0 IU
32	SUNIL	50	M	RA	104	128	111	0 IU	155	4 IU	160	6 IU	117	0 IU
33	SURESH	51	M	RA	113	140	158	2 IU	226	12 IU	162	5 IU	159	4 IU
34	DEEPAK	51	M	RA	119	142	190	4 IU	160	4 IU	150	2 IU	190	8 IU
35	ANKIT	47	M	RA	112	138	154	2 IU	100	0 IU	120	0 IU	144	6 IU

VELLORE REGIMEN														
S.NO	**Name**	**Age**	**Sex**	**GA/RA**	**FBS**	**PPBS**	**BS0**	**INS0**	**BS1**	**INS1**	**BS2**	**INS2**	**BS3**	**INS3**
1	PALANI	50	M	RA	109	146	108	1 IU	110	1 U	128	1 IU	124	1 IU
2	RAGHU	50	M	GA	128	205	220	3 IU	200	2 IU	146	1 IU	130	1 IU
3	BRAHADISHWARAN	55	M	RA	110	150	126	1 IU	124	1 IU	159	2 IU	142	1 IU
4	SARAVANAN	44	M	RA	116	155	156	2 IU	160	2 IU	155	2 IU	155	2 IU
5	ELMALAI	58	M	GA	100	138	134	1 IU	128	1 IU	137	1 IU	161	2 IU
6	RAJENDRAN	59	M	RA	112	148	157	2 IU	119	1 IU	146	1 IU	122	1 IU
7	KARTHIKEYAN	59	M	RA	115	142	180	2 IU	156	2 U	162	2 IU	118	1 IU
8	JAGADISH	44	M	RA	124	170	200	2 IU	172	2 IU	161	2 IU	146	1 IU
9	VANAJA	42	F	RA	122	160	209	3 IU	110	1 IU	149	1 IU	139	1 IU
10	PRABHAKARAN	44	M	GA	105	138	112	1 IU	118	1 IU	138	1 IU	170	2 IU
11	PRADEEP	38	M	RA	118	190	144	1 IU	168	2 IU	186	2 IU	163	2 IU
12	SATHISH	56	M	RA	130	210	202	3 IU	228	3 IU	232	3 IU	154	2 IU
13	RAJANANDAN	55	M	GA	102	130	112	1 IU	154	2 U	150	1 IU	129	1 IU
14	RAM	40	M	RA	120	196	133	1 IU	140	1 IU	149	1 IU	144	1 U
15	RAMANIKANT	41	M	RA	109	145	114	1 IU	122	1 IU	130	1 IU	138	1 IU
16	SAKIR AHAMAD	52	M	RA	125	189	167	2 IU	135	1 U	160	2 IU	177	2 IU
17	MANI	47	M	GA	110	150	118	1 IU	186	2 IU	158	2 IU	152	2 U
18	KULANTHAIVELU	51	M	GA	113	155	170	2 IU	159	2 IU	120	1 IU	126	1 IU
19	GEETA	54	F	RA	125	170	210	3 IU	120	1 U	140	1 IU	133	1 IU
20	LAXMAN	45	M	GA	117	160	136	1 IU	112	1 IU	151	2 IU	122	1 IU
21	JOHN	54	M	RA	102	130	152	2 IU	160	2 U	175	2 IU	158	2 IU
22	PRAKASH	58	M	GA	109	140	150	1 IU	159	2 IU	110	1 IU	110	1 IU
23	MOHAMMAD	44	M	RA	110	142	190	2 IU	110	1 IU	133	1 IU	108	1 IU
24	SURENDRA	59	M	RA	113	149	140	1 IU	102	1 IU	154	2 IU	140	1 IU
25	VIPIN	53	M	RA	112	150	183	2 IU	160	2 IU	164	2 IU	166	2 IU
26	BHASKAR	53	M	GA	127	190	216	3 IU	230	3 IU	180	2 IU	122	1 IU
27	VIJAY	52	M	RA	118	180	190	2 U	200	2 IU	176	2 IU	138	1 IU
28	JAYAM	59	M	RA	124	186	207	3 IU	166	2 IU	130	1 IU	110	1 IU
29	RAVI	57	M	RA	117	159	154	2 IU	104	1 IU	122	1 IU	159	2 IU
30	RAMANATHAN	48	M	RA	118	160	132	1 IU	112	1 U	126	1 IU	122	1 IU
31	BALASUBRAMANYAM	55	M	GA	104	144	107	1 IU	170	2 IU	128	1 IU	136	1 IU
32	RAGUDEEPAN	55	M	RA	123	188	175	2 IU	180	2 IU	154	2 IU	136	1 IU
33	AMIT	58	M	RA	129	190	205	3 U	150	1 IU	160	2 IU	165	2 IU
34	ZAKHIR	49	M	RA	120	150	150	1 IU	108	1 IU	136	1 IU	144	1 IU
35	AHMED	52	M	RA	117	155	140	1 IU	109	1 IU	129	1 IU	140	1 IU