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EDITORIAL

Future technology-enabled care for diabetes and hyperglycemia in the hospital setting

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Abstract

Patients with diabetes are increasingly common in hospital settings where optimal glycemic control remains challenging. Inpatient technology-enabled support systems are being designed, adapted and evaluated to meet this challenge. Insulin pump use, increasingly common in outpatients, has been shown to be safe among select inpatients. Dedicated pump protocols and provider training are needed to optimize pump use in the hospital. Continuous glucose monitoring (CGM) has been shown to be comparable to usual care for blood glucose surveillance in intensive care unit (ICU) settings but data on cost effectiveness is lacking. CGM use in non-ICU settings remains investigational and patient use of home CGM in inpatient settings is not recommended due to safety concerns. Compared to unstructured insulin prescription, a continuum of effective electronic medical record-based support for insulin prescription exists from passive order sets to clinical decision support to fully automated electronic Glycemic Management Systems. Relative efficacy and cost among these systems remains unanswered. An array of novel platforms are being evaluated to engage patients in technology-enabled diabetes education in the hospital. These hold tremendous promise in affording universal access to hospitalized patients with diabetes to effective self-management education and its attendant short/long term clinical benefits.

Key words: Diabetes; Inpatients; Continuous subcutaneous insulin infusion; Continuous glucose monitoring; Clinical decision support; Patient education; Self-management

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Core tip: Achieving optimal glycemic control in inpatients with diabetes and hyperglycemia remains a challenge for hospital providers. An array of technology-supported systems are evolving to assist providers and patients in meeting this challenge. Next generation, robust clinical decision support systems embedded in the electronic medical record are well positioned to replace structured order sets in the near term. If demonstrated to be cost effective, fully automated electronic glycemic management systems may become commonplace, in particular in intensive care unit settings. Novel media platforms hold tremendous potential for expanding access to crucial, effective self-management education for all patients with diabetes in hospital settings.

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INTRODUCTION

Adults with diabetes mellitus in the United States account for 7.2 million hospital discharges and 40.3 million hospital days annually[1,2]. Inpatient glycemic control remains suboptimal both in the United States[3] and abroad[4]. Numerous variables impact inpatient glycemic control, including: the pre-admission level of glycemic control[5]; medications prescribed for acute conditions (*e.g.*, steroids)[6]; comorbidities such as acute or worsened renal failure; and nutritional status[7]. Throughout the stay, providers need to identify glycemic trends in the context of multiple dynamic factors to safely and effectively optimize the insulin regimen.

In response to these challenges, technology-enabled systems are being evaluated and adapted for inpatient use. There is significant outpatient experience with diabetes technologies such as continuous subcutaneous insulin infusion (CSII) and continuous glucose monitoring (CGM) systems. Experience with emerging technology systems such as electronic medical record (EMR) based clinical decision support (CDS) for insulin prescription remains limited. Finally, inpatient engagement technology for diabetes education holds the potential to allow access to survival skills education for all inpatients with diabetes.

This editorial will focus on future directions evolving as technology-enabled supports for inpatient diabetes care delivery. For purposes of this discussion, we have grouped these endeavors into three broad categories shown on Table 1.

OUTPATIENT TECHNOLOGIES ADAPTED FOR INPATIENT USE CSII

In 2016 five million persons with diabetes were utilizing CSII pumps[8-10]. Inpatient CSII use is not well characterized, but is likely to grow. CSII for hospital diabetes self-management is considered by the American Diabetes Association (ADA) to be appropriate for select patients[11].

CSII pumps deliver basal insulin (units per hour) to meet insulin requirements in the fasting state and between meals. The pump delivers bolus insulin doses (units) to match nutritional intake and as correction doses when blood glucose (BG) levels are high. Hospital providers need to be cognizant of these basics to safely supervise glycemic management when these patients are under their care. Patient ability to continue pump use in the hospital can be assessed by asking patients to describe essential pump skills such as how to adjust the basal rate, administer a bolus dose, and problem solve correction of an out of target BG[12]. A dedicated insulin pump protocol should address hospital use of CSII, including its use during procedures and in the operating room[13]. Training in pump basics should be provided to nurses and non- endocrinologist inpatient providers, including hospitalists and anesthesiologists, who may be called upon to write CSII orders and oversee glycemic management[14].

Potential CSII safety issues in the hospital include insertion site infections; mechanical pump failure; the need for frequent pump interruptions (*e.g.*, radiology

Table 1 Technology-enabled strategies for inpatient glycemic management and diabetes care

Technology category	Purpose	Technologies
Outpatient technologies adapted for inpatient use	Support insulin management	Personal continuous subcutaneous insulin infusion pumps
		Continuous glucose monitoring sensor systems
Technologies developed for inpatient use	Diabetes and glycemic care management, including care transitions	Electronic medical record based clinical decision support
		Electronic glycemic management systems
Technology-enabled diabetes education	Engagement in diabetes survival skills education	Electronic medical record-generated, printed education content
		"SMART" TVs Web-based education platform

tests involving ionizing radiation); and handoffs for procedures and diagnostic testing. Expert consensus recommends that appropriate patient selection is essential to safe hospital CSII use. Limited retrospective case series suggest a good safety record. The largest series (n = 164 admissions) found no surgical site infections, mechanical failures, or hospital-acquired diabetic ketoacidosis[15,16]. Both retrospective studies and a single, small randomized trial suggest that when compared to usual care, inpatient CSII use is equivalent for hyperglycemia events and possibly superior in hypoglycemia prevention[17,18].

CGM

CGM systems measure and report BG every 5-15 min. CGM technology is estimated to be used by 4%-26% of Americans with type I diabetes[19]. CGM systems use subcutaneously placed sensors that measure BG in interstitial fluids and typically require changing every 10-14 d. Intensive care unit (ICU) CGM use has been studied for over ten years in both observational and prospective randomized studies of varying size. CGM systems accuracy compared to venous/arterial BG performed in the hospital laboratory and efficacy compared to usual care glycemic outcomes have been examined. The accuracy studies have found data generated by CGM systems to be acceptable. With regards to efficacy, a recent systematic review identified five randomized clinical trials. Most reported no significant difference in glycemic control (*i.e.*, mean glucose or time in range) while two found significant reduction in severe hypoglycemia favoring CGM[20,21]. Concerns regarding appropriateness of CGM use when factors which may impact subcutaneous circulation such as hypotension have been raised[22]. Larger randomized studies are needed to confirm benefits in hypoglycemia prevention for CGM in ICU settings and its cost effectiveness when compared to usual care.

Studies assessing routine CGM use in non-ICU settings are limited to small, uncontrolled prospective studies[23-26]. These studies report no difference in mean daily glucose, and CGM identified more hypoglycemic events compared to traditional point of care testing. However, for patients wishing to use their home CGM devices in the hospital, expert consensus has articulated several important potential safety concerns including the accuracy of CGM data when acute physiologic disturbances are present (*i.e.*, hypoxemia, vasoconstriction, and rapidly changing glucose levels in diabetic ketoacidosis) as well as concerns over correct CGM data interpretation by non- Endocrine inpatient care providers[18], and as a result, routine use of patient-generated CGM readings to guide inpatient insulin prescribing is not currently recommended.

Several insulin pumps now utilize CGM data to auto-modify insulin dosing via computerized algorithms. While there have been studies looking at use of "closed loop" insulin delivery systems for inpatients[27-29], to our knowledge, none have used the commercially available pump devices to date.

INPATIENT SPECIFIC TECHNOLOGIES CDS SYSTEMS

Structured insulin order sets are now widely used in hospitals for subcutaneous insulin ordering and have been shown to improve daily average glucose, reduce glycemic extremes, and reduce prevalence of sliding scale only regimens[30-32]. Based on this evidence, current guidelines recommend the use of structured, electronic order sets that include advice for optimal insulin prescription[8].

CDS refers to electronic systems which assist in clinical decision making via provision of recommendations based on processing and presenting patient specific data at an appropriate time. This contrasts with passive order sets that provide advice that is not patient specific. The ubiquity of inpatient EMRs combined with guidelines for the use of insulin to manage most cases with hyperglycemia make inpatient insulin prescribing ideal for incorporation of CDS into workflow. Controlled evidence of the impact of CDS for inpatient insulin prescribing are lacking. However, the safety and acceptability of the Gluco Tab® mobile insulin prescription CDS system[33] has been reported and recently, the creation and implementation of an inpatient insulin prescription CDS module for the Epic EMR system has been described. This utilizes interactive computerized physician order entry elements which prompt the provider to input relevant factors (*e.g.*, indication for insulin - acute hyperglycemia without prior DM *vs* established DM not on insulin *vs* established DM on insulin) while also extracting other relevant factors (*e.g.*, insulin received in last 24 h) in order to process each element into formulating insulin prescription recommendations; the provider then selects one of the provided options[34]. Studies on the efficacy and safety of this CDS module are in progress.

ELECTRONIC GLYCEMIC MANAGEMENT SYSTEMS

While CDS systems rely on user input and chart extraction of key information, more automated CDS systems require minimal provider input and are termed electronic glycemic management systems (eGMS). Several proprietary eGMS systems have been developed for intravenous insulin infusion and subcutaneous administration. Examples include Glytec's GlucommanderTM system[35], GlucoStabilizer®[36] by Medical Decision Networks, and Monarch's EndoTool®[37]. These software systems use multivariate algorithms to continuously recalculate the appropriate insulin dose, adjusting to patient specific variables. Generally, the initial insulin dose is set by the provider based on a weight-based calculation or custom order and the algorithm makes subsequent insulin dosing adjustments. There are several potential advantages to such a system, including reduction in hypoglycemia and hyperglycemia, reduction in the cost of care, improvements in patient safety and provider satisfaction.

Reduction in hypoglycemia rates has been shown in several eGMS studies. Rabinovich *et al*[38] used the Glucommander eGMS to show reduction in BG < 3.9 mmol/L from 21.5% to 1.3% ($P < 0.0001$) and severe hypoglycemia reduction from 5.4% to 0.01% ($P < 0.0001$) in a retrospective review of critically ill patients on insulin infusions. A comparison between the eGMS and a computerized basal-bolus order set for non-critically ill patients on subcutaneous insulin also found a difference in glucose < 3.9 mmol/L (1.9% *vs* 2.8%, $P = 0.001$)[39]. These results may be magnified when an eGMS is implemented where basal-bolus insulin therapy is not prevalent. Newsom *et al*[40] found the rates of use of sliding scale insulin go from 95% to 4% after eGMS implementation, moderate and severe hypoglycemia rates drop by 21% and 50% respectively, reduced length of stay and fewer point of care tests per patient. Although there is limited data demonstrating potential cost savings[41], convincing hospital leadership to invest in them may present a challenge. It remains to be determined where they will fit in the big picture of technology supported inpatient glycemic management as CDS tools evolve and data to support each model accumulates.

TECHNOLOGY-ENABLED DIABETES EDUCATION IN THE HOSPITAL

Deficits in diabetes knowledge and self-care management skills contribute to hospitalizations among persons with diabetes. Hospitalization presents an opportunity to provide education to this population, many of whom may not otherwise have access to this service. An accumulating body of evidence suggests that inpatient diabetes education, improving communication of discharge instructions and involving patients in medication reconciliation may reduce risk for early readmissions[42] and improve outcomes, including hemoglobin A1C and risk of readmission to the Emergency Department[43-46].

The ADA recommends that education be provided during an admission when a need is identified[8]. Content focused on "survival skills" to enable safe self-management until further outpatient instruction, as needed, is recommended. Inpatient diabetes education should also include a discharge plan for continuity of diabetes care as the transition from hospital to home is especially challenging and is associated with a high risk of negative outcomes, including readmissions[8]. Inpatient diabetes education delivery may be supported by both "low-tech" and increasingly by "high-tech" patient engagement strategies as shown on Table 2.

While patient engagement technologies offer the potential to expand the reach of education, in the hospital setting research in this field is emergent and outcomes data is lacking. It is crucial to patient engagement that technology tools are user friendly from a human factors perspective and that support is available to assure patient access and movement through the education content. Finally, if education is to be individualized, data security and privacy need to be assured[47].

Patient education systems are evolving from basic methods to high-tech-enabled systems. Low-tech methods include generic diabetes education sourced from providers such as KRAMES and Healthwise® and delivered *via* "SMART" TVs. These systems offer the advantage availability at every bed in the hospital and delivery through a familiar platform. Reports assessing the impact this type of education are lacking. In addition, whether hospitalized patients would choose to watch health information videos in large numbers remains in question. The Diabetes To Go study explored the effectiveness of video-based inpatient diabetes education in a large urban teaching hospital. Adults with diabetes participated in survival skills education delivered at the bedside *via* DVD player. Significant improvements in diabetes knowledge and medication adherence, as well as a trend towards reduction in hospital admissions in the 3 mo post- intervention were observed[37].

High-tech support for individualized diabetes education can potentially be delivered from the internet *via* tablet computer or smartphone using a web-interface from an education platform or embedded directly onto a tablet computer. Such platforms have ability to administer surveys and subsequently auto-direct the user to content tailored to responses. Staff must deliver the devices to the bedside, if they are not included with each bed, and staff time is often required to familiarize the patient with the platform.

Education delivery *via* personal-use devices also requires attention to infection control, physical device management and ergonomics. While web-based patient education technologies are being studied in the outpatient setting, inpatient studies are needed.

Finally, there are over 5000 technology applications and a wide variety of telehealth coaching programs available for diabetes education support. Among these technologies, very few have reported data or conducted clinical trials to assess impact on outcomes and none to-date has targeted education for inpatients with diabetes[48].

CONCLUSION

Despite the current challenges in achieving optimal glycemic control in the hospitalized patient, there are an array of technology-based systems that have the potential to impact the future of inpatient glycemic management. Of the systems reviewed to-date, EMR-based CDS systems which facilitate insulin management and technology-enabled education would appear to hold the greatest potential for widespread dissemination and impact in a cost-effective fashion. Inpatient use of personal CSII pumps and CGM systems will likely continue to grow making it necessary for hospitals to develop policies and familiarize providers with their use. Electronic Glucose Management systems, whether EMR-based or provided by third parties, will also likely play a role in inpatient glycemic management, particularly in intensive care units. Long after an admission, it is reasonable to believe that technology-enabled diabetes education delivered in the hospital could afford the patient clinical benefit, such as has been documented with traditional outpatient diabetes education approaches. Ongoing research to compare and contrast the potential for impact of each of these technologies in hospital diabetes care management and to develop the business case for their use is needed to help enlighten future use strategies.

Table 2 Inpatient diabetes education delivery - current and future states

Modality	Current state	Future state
1:1 at the bedside	Unit nurse/Physician/educator provides basic education- often skills based, *e.g.*, insulin instruction, and/or printed generic content	Supplemented by printed individualized electronic medical record clinical decision support generated content based on diagnoses, procedures, medications
Low-tech	Generic education content delivered *via* SMART TV or video	Video-based survival skills education content individualized for diabetes medications prescribed at discharge Provider and/or electronic medical record clinical decision support prescribes targeted generic education content
High-Tech	Generic education content prescribed for delivery at bedside on TV or tablet computer from web-based platform	Individualized education delivered via an interactive patient engagement platform Content auto-directed to learner based on embedded survey responses "App" for telehealth coaching prescribed, *e.g.*, BlueStar[49]

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GUIDELINES

Another simple regimen for perioperative management of diabetes mellitus

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Abstract

Persons with diabetes who require surgical procedures are increasing day by day. Many of the regimens available to manage patients with diabetes perioperatively are complex. Hence, the junior doctors and the paramedics (Primary care providers on a 24/7 basis) find it difficult to execute them. We need a simple regimen that can be executed in a primary care setting/general floor as it is becoming difficult to accommodate the patients in a sophisticated setting because of the increasing burden of the disease. We suggest a simple regimen in this article (Ram's regimen) which we believe safer, economical and more effective than few simple regimens available to date. Moreover, this regimen does not require any additional equipment such as syringe pumps, measured-volume set, *etc*. Hence, this regimen can be implemented in a primary care setting/general floor easily and we hope that it will be useful for doctors of various specialties and their patients.

Key words: Diabetes mellitus; Insulin therapy; Perioperative management; Simple regimen

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Core tip: Peri-operative management of diabetes is like walking a tightrope. Complexity of the regimens adds fuel to the fire. We propose a simple regimen, which we believe safer, economical and more effective. "User-friendly" for the primary care providers on 24/7. Executable in a primary care set-up/general floor too, which is becoming inevitable because of the increasing burden of the disease.

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INTRODUCTION

Patients with diabetes who require surgical procedures are increasing day by day. The frequency of surgical procedures as well as the duration of stay in the hospital is more in them when compared to those who do not have diabetes[1]. The two major types of regimens[2] available for managing patients with diabetes peri-operatively are (1) subcutaneous insulin; and (2) variable-rate intravenous insulin infusion (VRIII) administered continuously. In our opinion, the latter one, which is commonly followed currently in many parts of the world, is cumbersome for the patients as well as the junior doctors/paramedics (Primary care providers on 24/7) as they require hourly checking of glucose. Also, there is a potential possibility of equipment failure resulting in unintended dose or total stopping of insulin being delivered to the patient in this method, leading to extremes of blood glucose levels. Concerning the subcutaneous regimens, there is a possibility of "peaks and valleys" in the blood glucose levels because of mismatching between the duration of action of insulin and intravenous dextrose/uncertainty of oral intake (as the case may be). Also, the absorption of subcutaneous insulin is unpredictable particularly in the perioperative period[3].

"No Glucose-No Insulin" method adopted by some anesthesiologists (probably due to the complexity of the regimens and/or fear of hypoglycemia) is not acceptable on many occasions or dangerous sometimes as there is a potential chance of starvation ketosis and electrolyte imbalances[4].Although the peri-operative team (anesthesiologists, surgeons, and paramedics) is overburdened with many tasks, the management of diabetes cannot be put on the backburner. Nevertheless, it is unfortunate that it (ignoring the management of diabetes) happens commonly. One of the important causes for this could be the complexity of the regimens, which cannot be brushed aside as a "lame excuse".

WHAT SHOULD BE THE OBJECTIVES OF THE REGIMEN?

It is disheartening to note that the level of confidence in managing patients with diabetes among junior doctors in the United Kingdom was poor, according to an article published in 2011[5]. We are afraid that the scenario would be "no different" anywhere, even now. As we are aware of the fact that the peri-operative period consists of inherent problems such as starvation, anxiety, pain, unstable hemodynamics, *etc*. which would have a major impact on patients with diabetes, the complexity of the regimens of perioperative management would add only fuel to the fire. Furthermore, a recent review article about the update of peri-operative hyperglycemia has stated that many studies have established the fact that hyperglycemia is an important cause for increased mortality and morbidity in general surgery patients[2]. On the other hand, it is mentioned in the same review article that there is a potential chance of hypoglycemia causing death in intensive insulin regimen compared to the moderate one[2].Hence, a simple regimen having features such as a moderate target, which can be followed by the trainee doctors and the paramedics round the clock easily thereby improving their confidence, which would also provide a stable blood glucose level, is the need of the hour. Besides, it should be executable in any variety of the places of a hospital (operating room, recovery area and general floors)[3].

Mode of the regimen

Ram's regimen (Table 1) suggested in this article is based on an old concept concerning the dose of insulin only (Incidentally, we found that it was originally suggested for continuous insulin infusion)[6] and modified in all other aspects by the first author who has been adopting this regimen for over two decades. Indeed, the dose of insulin is also modified slightly to remember it easily in the increments of numerical five (5, 10, 15, 20 Units at the rate of 25 drops per minute). After preparing the solution with calculated insulin (Table 1), it can be administered through a separate small-bore intravenous line (Metabolic line) in addition to a large-bore intravenous line (Hemodynamic line) or as a piggyback through a three-way connector to only one line according to individual preference at the rate of 100 mL per hour (*i.e.*, 25 drops per minute or by drop-infusion pump if available). In emergencies where we might encounter a case with very high levels of glucose too, it can be initially stabilized with short-acting insulin (one unit of insulin for every 30 mg/dL rise above 180 mg/dL) administered in 100 mL of isotonic saline over 30 min to one hour. Once the target glucose level (140-180 mg/dL) is achieved, we can switch over to the regimen. Similarly, if a slightly more strict control (120-150 mg/dL) is needed (for instance, joint replacement surgeries) 2.5 U of insulin (0.5 U/h) can be added in the 500 mL solution in addition to the calculated insulin.

WHY ANOTHER SIMPLE REGIMEN?

To our knowledge, there are only a few simple regimens available to date. The Alberti and Thomas regimen[7], a simple algorithm for the VRIII[3], and the Vellore regimen[8] to name a few. We believe that our regimen is simpler, safer and economical than those few simple regimens, on the following grounds:

(1) Despite its great features such as safety, simplicity and classical concepts, there is a chance of hyponatremia in Alberti regimen[4] (we believe that it is quite possible in Vellore regimen too), which is unlikely in our regimen as we recommend dextrose in isotonic saline instead of plain dextrose. Moreover, a majority of the VRIII regimens do not recommend routine administration of the required dextrose on an hourly basis (which is mandatory), yet Marks JB recommends 5 g of dextrose per hour as a separate infusion which would prevent protein breakdown, ketosis or hypoglycemia[3]. Nonetheless, hyponatremia is more likely to happen in any regimen that advocates plain dextrose for prolonged duration[9].We recommend 10% dextrose for patients who are susceptible to water load. The dose of insulin needs to be doubled and the rate of administration has to be halved in that case. Despite this, if any patient develops hyponatremia, it should be corrected judiciously by adminis-tering hypertonic saline through a central line and/or diuretics according to the case.

(2) Vellore regimen suggests potassium supplementation only when the level reaches 3.5 mEq/L or below, whereas Alberti regimen recommends 10 mmol for every bottle. We suggest it for selected patients (Table 1).

(3) This regimen doesn't require even the 100 mL measured-volume-set as well as hourly checking of glucose, unlike the Vellore regimen. Hence, it is simpler and economical.

(4) We suggest the target glucose of 140-180 mg/dL, which is moderate, aimed to prevent both extremes of glucose levels.

(5) Technically analyzing, Vellore regimen is similar to VRIII regimens with only a change of administering the calculated insulin in 100 mL of 5 % dextrose together instead of insulin as a separate infusion. All the VRIII regimens, as well as the Vellore regimen, require hourly checking of glucose level. In addition to being cumbersome to patients as well as care providers, we believe that there is a possibility of fluctuations in the blood glucose values in these regimens which could be due to the fact that the controlling of diabetes happens retrospectively *i.e.*, the dose of insulin is calculated on the glucose level which probably reflects the metabolic trend of the previous hour, but administered for the subsequent hour. In this context, it is worth to note that it is a usual practice to adjust the night dose of insulin for any deviations of fasting blood glucose and the morning dose of insulin concerning post-lunch values, hence considered a prospective approach. Although the scenario is different (longer-acting subcutaneous versus short-acting intravenous insulin, oral feeds versus intravenous glucose *etc.*) concerning the perioperative period, we believe that the retrospective element would probably play a lesser role in our regimen when compared to VRIII or Vellore regimen. This is because we recommend administration of required dextrose (5 g/h) and the calculated insulin (based on clinical conditions and other factors) together from the beginning to achieve a moderate glucose level (140-180 mg/dL). Hence, our regimen requires only two-hourly checking of glucose until four hours and fourth hourly once stabilized, as it is expected to provide a reasonably stable glucose level. Furthermore, it is easier for the junior doctors/paramedics to follow-up, as the crucial period of control would be usually over within the first few hours under the supervision of a senior physician. Once stabilized, the patient can be managed on the general floor also.

(6) Marks JB mentions that glucose-insulin-potassium (GIK) regimen has easier maintenance following initial stabilization despite its drawback of inability to adjust the dose of insulin and the dextrose administration independently, warranting preparation of new solution[3]. Nonetheless, our regimen (having a similar concept) requires preparation of a new solution only for a rare occasion (glucose value of less than 100 mg/dL). We can add the extra units of insulin in the remaining solution taking sterile precautions, for any value of above 180 mg/dL.

And (7) Alberti regimen is safe because of its salient feature of administering the combination of insulin with dextrose[4]. Although our regimen is based on a similar concept, the following variations are worth noting: (1) 5% dextrose with isotonic saline versus plain 10 % dextrose; (2) The dose of insulin is based on clinical conditions and other factors thus tailoring to individual needs. Alberti *et al* had stated this point in 1979 itself, that the starting therapy of their GIK regimen should not be

Table 1 Ram's regimen (dose of insulin)* Target glucose level 140-180 mg/dL.

Condition of the patient	Dose of insulin, *i.e.*, units of insulin per gram of dextrose per hour (U/g per hour)[6]	Total insulin in 500 mL of 5% dextrose isotonic saline solution
General guideline	0.2-0.4	5 to 10 U
Obese/hepatic dysfunction	0.6	15 U
Severe infections/sepsis/steroid therapy	0.6-0.8	15 to 20 U

* The dose of insulin can be chosen based on the clinical condition mentioned above as well as other factors such as preoperative requirement of insulin/other anti-diabetic drugs, the preoperative blood glucose level. The solution can be administered at 100 mL/hour. Check capillary glucose two hourly for the first four hours. Add 1 U of insulin per hour for every 50 mg of rising of glucose level above 180 mg (*e.g.*, If it is 280 mg after two hours, it would become 2 U/h, *i.e.*, 6 U for the remaining 300 mL of solution). If the glucose level is between 100 and 140 mg, start 10% dextrose at 50 mL per hour simultaneously, and reduce the insulin dose by 0.5 U per hour in the subsequent preparations. If <100mg, give only 10% dextrose until it reaches 140mg, and reduce the insulin dose by 1 U per hour (minus five of total dose calculated previously) in the subsequent preparations. Once stabilized, the capillary glucose can be checked every four hours. Potassium can be added if required as in cases of (1)hypokalemia; (2)gastrointestinal procedures; and (3)requirement of infusion for more than five hours.

adhered blindly to each and everybody ("Patients will always vary") rather it must be flexible with an application of common sense too[7]; and (3) Addition of potassium in selected patients.

CONCLUSION

As the perioperative management of diabetes is inherently complex, simpler and safer the regimen better for all persons involved in the care. We hope that the regimen suggested here will be useful for all care providers, educators as well as the patients regardless of the care setting. We certainly agree that our regimen needs to be studied in the future to prove the advantages we have claimed here.

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MINIREVIEWS

Oral manifestations in patients with diabetes mellitus

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Abstract

The purpose of this article was to increase the knowledge about oral manifestations and complications associated with diabetes mellitus. An overview was performed on Google, especially in recent reliable papers in relation to diabetes mellitus and its oral manifestations (keywords were "diabetes mellitus", "oral manifestations", and "oral complications"). Data were collected and the results were declared. Diabetes mellitus is one of the most common chronic disorders characterized by hyperglycemia. This disease can have many complications in various regions of the body, including the oral cavity. The important oral manifestations and complications related to diabetes include xerostomia, dental caries, gingivitis, periodontal disease, increased tendency to oral infections, burning mouth, taste disturbance, and poor wound healing. Oral complications in diabetic patients are considered major complications and can affect patients' quality of life. There is evidence that chronic oral complications in these patients have negative effects on blood glucose control, so prevention and management of the oral complications are important.

Key words: Diabetes mellitus; Oral complications; Oral manifestations; Periodontal disease; Xerostomia

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Core tip: Since diabetes mellitus is a common disease and can have some annoying manifestations in the patient's mouth, it is important for physicians to be aware of these manifestations and to treat them properly.

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INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disease characterized by hyperglycemia due to either a deficiency of insulin secretion or resistance to the action of insulin or both[1-3]. Chronic hyperglycemia leads to different complications in various regions of the body including the oral cavity, so blood glucose control is very critical[4]. Possible mechanisms that may be related to oral complications of diabetes include impaired neutrophil function, increased collagenase activity, and a reduction in collagen synthesis, microangiopathy, and neuropathy[4].

The oral manifestations and complications related to DM include dry mouth (xerostomia), tooth decay (including root caries), periapical lesions, gingivitis, periodontal disease, oral candidiasis, burning mouth (especially glossodynia), altered taste, geographic tongue, coated and fissured tongue, oral lichen planus (OLP), recurrent aphthous stomatitis, increased tendency to infections, and defective wound healing[1-8]. The intensity of diabetic complications is usually proportional to the degree and duration of hyperglycemia[5]. In this study, we briefly reviewed DM and its oral manifestations and complications in recent reliable scientific papers.

XEROSTOMIA

People with diabetes experience salivary dysfunction, which can lead to decreased salivary flow and change in saliva composition. The estimated universal prevalence of xerostomia among diabetic patients ranges between 34% and 51%[1,2]. Xerostomia can lead to numerous problems such as difficulty in eating, swallowing, and speaking. It can actually have a negative effect on patients' quality of life. Many studies have detected impaired salivary function in adults with diabetes. The etiology is unknown, but may be related to polyuria, autonomic neuropathies, and microvascular changes and alterations in the basement membranes of salivary glands[2,4,5,7,8]. There is a significant relationship between the degree of xerostomia and glucose levels in saliva. Notably, the highest level of salivary dysfunction is observed in diabetics with poor glycemic control[4,5].

DENTAL CARIES

Diabetic patients are susceptible to the development of new and recurrent dental caries. Reduced cleansing and buffering capacity of the saliva, increase of carbohydrate in the saliva, and increased level of oral yeasts, mutans streptococci and lactobacilli can lead to an increase in the incidence of tooth decay. In addition, chronic hyperglycemia may cause irreversible pulpitis leading to pulp necrosis[1,2,5,7,8]. Some studies have shown that apical periodon-titis and radiolucent periapical lesions are more common in diabetic compared to nondiabetic individuals[1,5,9].

PERIODONTAL DISEASE

Poor glycemic control can be associated with the outbreak and progression of gingivitis, periodontitis, and alveolar bone loss. Periodontal disease has been reported with increased incidence and prevalence in patients with type 1 and 2 diabetes. Prevalence of severe periodontitis in diabetic patients compared to nondiabetics has been found to be 59.6%:39%[3,7,8,10].

Possible mechanisms for explanation of increased susceptibility to periodontal diseases include alterations in host defense response (such as neutrophil dysfunction), subgingival microflora, structure and metabolism of collagen, vascularity, and gingival crevicular fluid and also, inheritance patterns. Furthermore, several risk factors have been reported, which make these patients more susceptible to the development of periodontal disease including poor oral hygiene, poor metabolic control, longer duration of diabetes, and smoking[3,6-8].

It is noteworthy that numerous studies have shown that periodontal disease has a negative impact on diabetes, and the treatment of periodontal disease has a desirable effect on blood glucose control. The elimination of pathogens by treatment leads to a decrease of inflammation, which in turn reduces insulin resistance; this in turn decreases glucose levels. Therefore, there is a two-way relationship between periodontal disease and diabetes[1,3,5,10]. In adults, periodontal disease is the main reason for tooth mobility and consequently, loss of it. Therefore, treatment of periodontitis, in addition to lowering blood glucose levels, can prevent tooth loss[11].

ORAL INFECTIONS

Patients with diabetes are more susceptible to the development of various oral infections including fungal and bacterial infections. Decreased salivary flow rate and the absence of its antimicrobial effects can cause these infections. In addition, an impaired defense mechanism and poor metabolic control may play an important role in developing infection[2,7,8].

Oral candidiasis is an opportunistic fungal infection. The prevalence of that is increasing, as it is one of the most common fungal infections. Higher candida colonization rates were reported in patients with diabetes type 1 when compared to type 2 (84% *vs* 68%, respectively), while the percentage in nondiabetic subjects was about 27%[2,12].

Oral candidiasis can be developed by numerous predisposing factors including xerostomia. Salivary dysfunction in these patients can contribute to higher carriage of fungi. Candida-related lesions include denture stomatitis, angular chelitis, and median rhomboid glossitis[2] (Figure 1). Candida infection is more prevalent in diabetic patients who smoke, wear dentures, have poor glycemic control, and use steroids and broad spectrum antibiotics[2,7,8].

BURNING MOUTH

Burning sensation or dysesthesia in the oral cavity of diabetic patients is attributed to poor glycemic control, metabolic alterations in oral mucosa, angiopathy, candida infection, and neuropathy[1]. Neuropathic pain in these patients can be manifested as burning, tingling, or even as electric shock or stabbing sensation that these symptoms may be very debilitating. These pain sensations have a considerable effect on the physical and psychological functions, and are associated with the level of sleep disturbance, anxiety, and depression[1,4].

TASTE DYSFUNCTION

Taste dysfunction can occur in patients with poorly controlled diabetes. In a cross-sectional study, among diabetic or prediabetic patients, 5.7% had a sweet taste disorder and 8.6% had a salt taste disorder[8,13]. Salivary dysfunction can cause altered taste sensation or raise of detection thresholds. Neuropathy also increases the threshold of taste. This sensory dysfunction can inhibit the ability to maintain a good diet and can lead to poor glucose regulation[1,2,4,7,8].

ORAL MUCOSA ALTERATIONS

Some oral mucosa alterations such as coated and fissured tongue, geographic tongue, recurrent aphthous stomatitis, and some premalignant lesions including lichen planus can be associated with diabetes[1,2,5,7,8] (Figure 2). Susceptibility of these patients to oral cavity changes is still controversial, but insufficient control of diabetes, immunological alteration, microcirculatory changes with decline of blood supply, xerostomia and alteration in salivary flow and composition, and smoking have been mentioned[1]. OLP occurs more frequently in patients with type 1 diabetes compared to type 2, because type 1 diabetes is considered an autoimmune disease, and OLP has an underlying autoimmune mechanism[2,8]. Acute hyperglycemia causes changes in the immune responsiveness in diabetic patients[2].

POOR ORAL WOUND HEALING

Delayed healing of soft and hard tissues in diabetic patients is a well-known complication during oral surgeries[2,8]. Based on some studies, effective factors in the prolonged wound healing of these patients include delayed vascularization, diminished blood flow and hypoxia, a reduction in innate immunity, decreased growth factor production, and psychological stress[2,14].

CONCLUSION

Figure 1 Candida-related lesions. A: Denture stomatitis; B: Angular chelitis; C: Median rhomboid glossitis.

Oral complications in patients with DM are considered major complications of the disease and can impress the patients' quality of life. There is evidence that chronic and persistent oral complications in these patients adversely affect blood glucose control. Thus, prevention and management of oral complications due to diabetes are considerable.

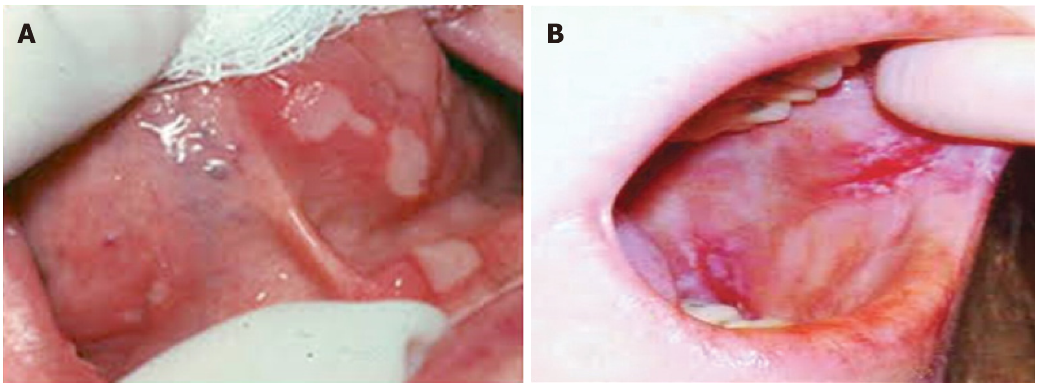

Figure 2 Oral mucosa alterations. A: Recurrent aphthous stomatitis; B: Oral lichen planus.

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