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MANAGEMENT OF HYPOGLYCEMIA IN SAUDI ARABIA'S DESERTS

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Abstract:

Background: *The health burden due to diabetes in Saudi Arabia is considerable and expected to rise as the prevalence of diabetes escalates in future years. One of the most common acute causes for diabetics seeking medical attention is the result of inadequate glycemic control, often resulting in hypoglycemia. Hypoglycemia is a serious and potentially life-threatening complication of diabetes and requires prompt intervention. Due to the climate and physical geography of Saudi Arabia, it is likely that many hypoglycemic episodes occur in the desert environment. To effectively manage hypoglycemia in such a setting requires specialized knowledge, flexibility, ingenuity and experience providing care in remote places. The skills and knowledge required to effectively care for ill or injured residents or visitors in remote, isolated and potentially hazardous parts of the world are unique and do not fit into any of the traditional medical specialties. Wilderness Medicine is a relatively new field which encompasses the information, competencies and experience that is required by physicians and other healthcare providers who routinely provide medical care in such environments.*

Aims: *The aim of this paper is to discuss the management of diabetic hypoglycemia, taking into account the unique challenges in Saudi Arabia, as well as identification of knowledge gaps and future research required.*

Method: *The information presented has been drawn from published literature as well as from the authors' practical experience in providing medical care for severely hypoglycemic patients in the pre-hospital setting.*

Discussion: *Potential hazards for the diabetic individual visiting Saudi Arabian deserts and considerations to avert these, have been discussed.*

Conclusion: *To effectively manage hypoglycemia in such a setting requires specialized knowledge and ingenuity. Critical knowledge gaps and research priorities to inform this area have been identified.*

Keywords: *diabetes, desert, wilderness, travel, heat-related illness, hypoglycemia.*

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INTRODUCTION:

The Kingdom of Saudi Arabia (KSA) accounts for approximately 80% of the Arabian Peninsula (New World Encyclopedia, 2018), and has a total population of over 34 million (Country Meters, 2018). In upcoming years, millions of international visitors are also expected to visit KSA for religious pilgrimage, tourism to heritage and historical sites, archaeological explorations, and sporting events. The way for this growth will be made easier as KSA is committed to developing tourism and will commence the issuing of tourist visas in 2018 (Alkhalisi and Quest, 2017). As much of the Kingdom consists of desert (New World Encyclopedia, 2018), it is likely that a considerable proportion of visitors will spend time in these arid areas. However due to the climate, visiting KSA and its desert regions can be hazardous, especially in summer where temperatures often reach 50°C (New World Encyclopedia, 2018).

Consistent with worldwide trends, there is predicted to be a large increase in the prevalence of diabetes among both citizens of the Kingdom as well as among visitors and foreign workers in the next few decades (Shaw et al., 2010). These projections illustrate the importance of a health system that is prepared to manage this challenge, alongside the existing challenges the Saudi healthcare system faces such as a shortage of healthcare professionals and funding, as well as disparities in healthcare accessibility for various parts of the Kingdom (Almalki et al., 2011).

Diabetes is one of the most common non-communicable chronic diseases, resulting in a large worldwide health burden (Shaw et al., 2010). Metabolic and microvascular disturbances associated with diabetes increase the risk of developing complications such as cardiac dysfunction, retinopathy and peripheral neuropathy (Martin et al., 2014). A common cause for diabetics seeking acute medical attention is as a result of inadequate glycemic control resulting in hypoglycemia. Hypoglycemia is defined as serum glucose levels less than 70 mg/dl (3.9 mmol/l) and may initially present with behavioral symptoms such as confusion. However, severe hypoglycemic states may result in seizures, loss of consciousness, and death (Seaquist et al., 2013). To appropriately manage hypoglycemia in the isolated and hazardous desert environments that comprise most of KSA may require flexibility, ingenuity, improvisation and experience providing care in remote places.

AIM AND METHODS:

This review will discuss aspects of the management of hypoglycemia in diabetics in the desert regions of Saudi Arabia far from medical support. The information presented will be drawn from the published literature as well as from the authors' practical experience in providing medical care for severely hypoglycemic patients in the pre-hospital setting.

DISCUSSION:

Diabetes in Saudi Arabia: a silent epidemic

Over the past three decades, the incidence of impaired glucose tolerance has increased dramatically in Saudi Arabia especially in larger cities such as Riyadh, Dammam and Jeddah where most of the population now reside (Habibzadeh, 2009). A study of 9,149 adult Saudis (7 – 80 years of age) demonstrated the age-adjusted prevalence of Type 2 diabetes mellitus (T2DM) to be 31.6% (Al-Daghri et al., 2011). This figure compares unfavorably to the world-wide prevalence which was predicted to be 6.4% in 2010, increasing to 7.7% by 2030 (Shaw et al., 2010), with the gulf region of the Middle East being referred to as a "hotspot" for diabetes mellitus (Chen et al., 2012). Obesity, which has a marked association with diabetes, also occurs at considerable levels within the KSA population, with a prevalence rate of 28.7% (Memish et al., 2014).

Diabetics are less physiologically tolerant of hot environments (Jacklitsch et al., 2016). T2DM, whether requiring insulin or controlled by oral hypoglycemic medication, is not necessarily a contraindication to desert activities; however, other problems related to diabetes may increase the risk for medical emergencies. Cardiovascular disorders, coronary artery disease, cerebrovascular disorders, peripheral and autonomic neuropathies, poor wound healing especially from animal bites, secondary infections from the saliva of animal bites, insect bites or stings, serious immune sensitivity to the venom of snakes and other poisonous creatures and vulnerability to developing illness associated with exposure to high temperatures such as heat cramps, heat exhaustion and heat stroke all may be associated with this metabolic disorder (Briscoe and Davis, 2006). In contrast, individuals with Type 1 diabetes mellitus (T1DM) have a higher risk of developing hypoglycemia (Briscoe and Davis, 2006), thus it may be prudent to discourage solo travel in the desert or other wilderness areas in Saudi Arabia for the insulin-dependent diabetic.

Hypoglycemia unawareness syndrome

Physiologic responses to hypoglycemia in diabetic patients can be categorized into sympathoadrenergic and neuroglycopenic phases. Initially the sympathoadrenergic phase involves the release of hormones such as epinephrine and glucagon, which manifests with feelings of hunger, dizziness, weakness and anxiety, as well as palpations, sweating and tremors, and is when the individual often becomes subjectively aware of their hypoglycemic state (American Diabetes Association, 2005). The individual may also show evidence of abnormalities in temperature regulation, as well as fluid loss, electrolyte abnormalities and peripheral vasodilation if environmental temperatures are high (Jacklitsch et al., 2016). This phase is considered to be both warning and counter-regulatory mechanism in order to prevent further decline in plasma glucose levels. Diabetic patients often recognize and take action to relieve these symptoms. If further a decline in plasma glucose level occurs, it may progress into the neuroglycopenic phase which clinically manifests with weakness, confusion, and an altered level of consciousness. This phase may further progress into seizures, coma and ultimately death. (American Diabetes Association, 2005).

However some diabetics, often with a history of recurrent hypoglycemic episodes, are unable to recognize when their serum glucose level decreases, even to dangerously low concentrations. This "Hypoglycemia Unawareness" (HU) (Bakatselos, 2011) may present a major decision-making challenge to care-providers during wilderness desert trips due to the difficulty in determining whether the patient requires urgent medical intervention or evacuation, especially those individuals presenting with confusion or concentration difficulties. Furthermore, individuals with HU have 3 times the incidence of severe hypoglycaemia compared with individuals with normal hypoglycemic awareness (Choudhary et al., 2010). As diabetics are predisposed to develop heat related illnesses which may become fatal, careful consideration and planning needs to be undertaken when venturing into a desert environment.

Causes of death

Increased mortality of the elderly due to heat stress may be multifactorial in origin and related to an increased likelihood of multiple co-existing chronic conditions, increased blood coagulability, increased cardiovascular demands from water and electrolyte imbalances, and lowered blood pressure from surface vasodilation (Kim et al., 2012). Furthermore, fitness levels in diabetic individuals which are likely to be decreased in the elderly, are inversely associated to mortality (Church et al., 2004). These negative consequences are apparent in the elderly diabetic with increases in mortality reported for every 1 degree Celsius increase in temperature (Bunker et al., 2016). Heat-related illness can also be associated with medications that an individual has been prescribed. These include anticholinergic medications, beta-blockers, calcium channel blockers, benzodiazepines, diuretics and neuroleptics (Becker and Stewart, 2011). For example, a potentially life-threatening side effect of anticholinergic medication is a decrease or complete cessation of sweating (Chia and Tey, 2013), making it even potentially more difficult for individuals to adapt to high desert temperatures. Increased severity of hypoglycemic episodes has also been associated with the use of widely prescribed antidepressants in the class of selective serotonin reuptake inhibitors (SSRIs) (Sawka et al., 2001). In some diabetic patients on insulin, treatment with SSRIs may actually decrease their self-awareness that their own serum glucose levels are at dangerously low levels (Sawka et al., 2001).

Tour group leaders, staff and medics should aware of the potentially fatal combination of hypoglycemia and acute heat stress and need to have a management plan in place if travelling with diabetic individuals.

Preparation for desert travel

Provided that the insulin-treated diabetic has reviewed all the general factors associated with a wilderness trip and the specific hazards presented by the desert environment that may cause complications and has still chosen to undertake the preparation required and accept the risks, a medical treatment plan needs to be generated by the patient's physician. Prior to departure, the frequency and severity of previous hypoglycemic reactions, as well as any previous occurrence of HU should be identified. Individuals with HU have been reported to be less adherent to changes in insulin regimen (Smith et al., 2009), therefore dosage adjustments should take place well before the planned desert visit to allow familiarization with the new schedule.

Insulin dependent individuals should have their treatment optimized prior to departure. To decrease the possibility of experiencing hypoglycemic episodes during desert travel, insulin formulations that are stable with known duration of effect should be prescribed by physicians at least one month prior to departure for the desert to allow testing and adjustment of doses (Table 1). Insulin-dependent diabetics should be taught to administer their medication

subcutaneously prior to exercise in a location away from exercising muscle to decrease the risk of hypoglycemia (Younk et al., 2011). However, absorption of subcutaneous insulin during exercise may depend on the type of insulin used. A study of the long-acting insulin analog glargine injected subcutaneously into the thigh on the evening before an intense 30-minute exercise session in patients with T1DM did not show an increased rate of absorption, but plasma glucose fell during exercise (Chantelau et al., 1989). Intramuscular insulin injection should be avoided as the variable absorption rate may increase the possibility of developing hypoglycemia (Birkebaek et al., 2008).

Table 1. Types, Names, and Uses of Insulin

Insulin	Onset (hours)	Peak (hours)	Duration (hours)	Uses	Notes
Rapid-acting (insulin analogs lispro, aspart, glulicine)	< 0.5	0.5 – 3	3-5	Meal coverage if taken up to 15 min before eating; adjust for elevated blood glucose levels	Insulin of choice for pumps. Rapid action may not be desirable during periods of physical activity because it may lead to more hypoglycemia
Short-acting (human regular)	0.5 – 1	2 - 5	Up to 12	Meal coverage if taken 30-45 min before eating	May last too long, leading to hypoglycemia
Intermediate-acting (human NPH)	1.5 – 4	4 – 12	Up to 24	Meal coverage (lunch) if taken in the morning	More active early in the dosage or can linger longer than anticipated; either can cause hypoglycemia
Long-acting (insulin analogs glargine, detemir)	0.8 – 4	None	Up to 24	Basal	Once-a-day injection; cannot be mixed with other insulins; soluble until injected

Another measure to prevent exercise-associated hypoglycemia is to reduce the dose of insulin that will be in effect during exercise (Streja, 2005). The best strategy for insulin-dependent diabetics is to monitor blood glucose while still at home before, during, and after exercise to predict changes and adjust insulin doses accordingly (Table 2). This means that before travelling to desert environments, insulin dependent diabetics should exercise daily at a level of physical activity such as that anticipated on the wilderness trip, so that adjustments in insulin dosing can be made. Differences in nutritional intake, in addition to increased exercise, during the time spent in the desert should also be anticipated when planning insulin regimens. Patients with diabetes may engage in strenuous physical activity without experiencing problems, but it is important for the patient to focus on the timing of exercise in relation to meals and insulin dosing (Heller et al., 2010).

Table 2. Matching insulin treatment schedules with exercise schedules.

Treatment Type	Advantages	Disadvantages
Standard: two injections, mixed intermediate- and short-acting insulins	Easy to perform	Poor match with exercise, rigid time restraints, least likely to give good metabolic control and health
Intensive: three or more injections a day	Better control, more flexible timing, less hypoglycemia in the evening	More frequent testing, harder to learn
Extended: glargine for basal plus lispro/aspart for meals	Least amount of time rigidity, most protection against hypoglycemia, excellent metabolic control	Much more effort to master and do well
Continuous infusion (pump)	Most flexible (no injections most days), low hypoglycemia risk overnight, best metabolic control Basal insulin infusion rate can be adjusted to accommodate increased insulin sensitivity due to increased activity	Needs expensive device, harder to master, must remove pump for some activities; need to carry syringes in case of mechanical failure Risk for infusion site infections

Prior to departure for the desert, individuals should be briefed on potential risks to maintaining glycemic control while visiting desert environments. These may include the potential for adverse drug effects in hot environments, irregular meal schedules, and the possibility of an increased level of exercise compared with their usual activities of daily life. Frequent monitoring of serum glucose levels should be encouraged, as should constant access to dextrose or glucose tablets for the treatment of hypoglycemia (Bashir et al., 2012). Individuals participating in similar activities should also undergo instruction on the signs and symptoms of hypoglycemia and basic medical interventions for hypoglycemia. The team leader should be informed immediately if any individual feels different than normal in any manner, as rapid medical intervention may be required. As a precaution, travel into the desert in the warmer periods of late spring or early summer should be discouraged in persons with a history of severe or frequent reactions or a history of HU.

Prevention strategies

Monitoring of blood glucose should occur more frequently early during a trip to desert environments to titrate for the effects of increased exercise and heat on insulin dose, snacks of carbohydrates and meal times. Hypoglycemia associated with exercise is possible not only during exercise, but late-onset post-exercise hypoglycemia can also develop for many hours after exercise (Davey et al., 2013). This delayed hypoglycemia has many causes including an increase in insulin sensitivity as well as a high level of glucose uptake by muscles and the liver to replenish depleted glycogen stores (Davey et al., 2013). Therefore, after exercise, especially if the amount or intensity is higher than which one is accustomed, the monitoring of blood glucose levels should continue for many hours, including overnight if the exercise took place during the afternoon and was of high intensity. Riddell et al (2006) also recommends that insulin which has decreased immediate and long-term actions may need to be used, as well as declaring the value of ingesting slow-acting carbohydrates post exercise (Riddell and Perkins, 2006). For individuals with a history of poorly controlled T1DM, continuous glucose monitoring may be considered. Monitoring blood glucose in this manner has been shown to improve glycemic control over 3 months (Deiss et al., 2006), so instigating this system well before spending time in a desert environment would be advisable.

Specialized training of group tour leaders regarding the nature of diabetes especially the dangers posed by hypoglycemia, possession of effective and ruggedized communication equipment to obtain voice or on-line medical support, and knowledge of how to best to contact the nearest clinical facilities for treatment advice is required. If is known that there will be a diabetic in an upcoming group tour to the desert the tour operators' standard medical kits (Brubaker, 2005) may need to be modified to include bags of Dextrose 50%, IV administration sets and glucose testing kits (Table 3). It is important to be aware that the accuracy of glucose testing equipment can be affected by high altitude and extremes of temperature, with many glucometers not working effectively at temperatures above 40°C (Richards and Hillebrandt, 2013). The use of multiple meters with control glucose solutions can lend some confidence. Similarly, the storage of insulin needs to be considered in high temperature environments. Insulin should be stored at 2-8°C,

however, may be stored <25°C for up to 4 weeks. Storage in temperatures of 32 - 27°C for extended periods may decrease insulin potency (Richards and Hillebrandt, 2013).

Table 3. Listing supplies and requirements for international border crossings.

Insulin Supplies	Requirements for international border crossings
Insulin	Three times the amount anticipated for each type of insulin, stored at non-extreme temperatures
Insulin pens and needles (if applicable)	One extra pen and three times the anticipated number of needles
Pump supplies (if applicable)	Three to five times the amount anticipated
Syringes	Enough to cover the entire trip if on the pen or pump; two to three times the anticipated requirement if using syringes alone
Glucose meter	Two different meters with extra batteries for each
Glucose strips and lance/lancets	Three times anticipated number of strips for each meter, two lances, and three times the anticipated number of lancets; a supply of visually read strips should also be taken as a backup in the event of meter failure
Ketone strips	Two packages
Carbohydrates	One package (50 g) per day
Dried fruit and cookies (slower-acting carbohydrates)	Several individually wrapped packages per day
Glucagon kit (this must be protected from breakage)	Two kits
Intravenous setup	One complete kit
Single-use sterile needles and syringes	Several 18-g and 10-mL syringes, respectively, in the event that medical treatment is required in a hospital or clinic with limited resources
Insulated packs	Enough to carry all supplies

Preventive measures include ingesting extra food in the form of 15 to 30 g (0.5 to 1 oz) of quickly absorbed carbohydrate (e.g., juice, hard candies, glucose tablets or whole milk), taken at least a half hour prior to, and approximately every 30 minutes during strenuous activity. If monitoring shows consistently low blood glucose levels, it is probably wise to postpone or at least plan a decreased daily exercise regimen as hypoglycemic diabetics not yet acclimatized to the desert climate are at particular risk of adverse health outcomes. Fluid intake should also be increased for diabetic visitors to the desert to avoid hypovolemia due to increased exercise, fluid losses, and serum electrolyte and glucose serum abnormalities in those unaccustomed to high desert temperatures (Brubaker, 2005). In addition to increased fluid intake, diabetic patients with a history of recurring hypoglycemic episodes should supplement increased fluid intake with some more salt than usual at mealtime unless contraindicated (e.g., history of cardiovascular disease, recent heart attacks or strokes, high blood pressure) (Graveling and Frier, 2010). While in the harsh desert environment such individuals always need to carefully balance efforts to maintain adequate fluid volume, serum electrolyte concentrations and sufficient glucose to support increased metabolic demands.

MANAGEMENT:

If a diabetic member of the group presents with life-threatening symptoms, immediate action is imperative. If there is a medic or someone trained as a "first responder" employed by the tourism company or the team leader in charge of groups visiting desert regions, this person should immediately obtain a tube of blood from any tour group member with abnormal mentation or who has lost consciousness via venipuncture for later determination of serum glucose just before giving a bolus of intravenous dextrose. If there are no facilities or personnel to perform

venipuncture, glucose levels can be checked with a drop of blood with a portable blood glucose monitor. Diabetic travelers to remote areas should be advised to carry a blood glucose monitor at all times. If no testing for blood glucose level is available at all, a bolus of glucose should still be administered to any unconscious patient or someone with altered mental status and a history of diabetes. Giving a bolus of concentrated glucose solution is both diagnostic and therapeutic. If the patient is hypoglycemic, their conscious level or mental status often improves very quickly. Even if the altered mental status was caused by hyperglycemia, a single bolus of glucose will usually not worsen the patient's condition. However, if the patient's altered mental status was caused by hypoglycemia, not administering any glucose solution may be fatal or cause permanent neurological injury.

If the patient recovers after the infusion of glucose, potential causes of the episode of hypoglycemia should be considered including; recent infections illnesses, alterations in drug regimen, changes type of food consumed or time of meals, and previously unrecognized electrolyte imbalances. Head trauma from a fall with expanding subdural hematoma may also need to be considered in the differential diagnosis. All individuals who exhibit a sudden loss of consciousness in this setting should be evacuated as soon as possible to the nearest emergency department for a more thorough evaluation.

Critical Knowledge Gaps

- Knowledge of risk factors contributing to episodes of hypoglycemia is essential to accurate recognition, treatment and disposition of diabetic patients in wilderness desert environments.
- A more thorough understanding of long-term health outcomes of recurrent hypoglycemic episodes
- The underlying causes of both recurring hypoglycemia and HU syndrome have not been well established. Such information will assist caregivers to effectively evaluate diabetics with HU.
- The quality of care currently provided by tour group staff, medics and guides to individuals who suffer some acute complication of their diabetes in desert regions.

Research Priorities

- Clinical, laboratory and epidemiologic studies examining the relationship between hypoglycemia occurring in a desert environment and the contribution of such issues as; participating in unusually rigorous physical activity, sleep loss, circadian desynchronization, heat-related illnesses, changes in therapeutic regimens, and adverse drug reactions.
- Population-based epidemiologic studies of variation in susceptibility of diabetics to suffer hypoglycemic episodes depending on Arabian Peninsula location.
- Examination of the quality of pre-hospital emergency medical or ambulance care of diabetics experiencing life-threatening hypoglycemia in Saudi Arabia, comparing different geographical areas.

CONCLUSION:

Effective management of hypoglycemia in diabetic individuals situated in isolated desert environments requires knowledge, flexibility, ingenuity and experience providing care in remote places. The need for expertise in providing appropriate and potentially life-saving care to diabetic residents and visitors in KSA is expected to intensify as tourism to this region and the prevalence of diabetes increases. This paper summarizes steps that can be taken to minimize the likelihood of adverse events in the diabetic individual in the remote desert settings that comprise much of KSA.

Abbreviations

HU – hypoglycemia unawareness
KSA – Kingdom of Saudi Arabia
T1DM – Type 1 diabetes mellitus
T2DM – Type 2 diabetes mellitus

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Ethical approval

For this type of study formal consent was not required

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