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Feature Article

Optimizing insulin delivery for patients with diabetes

Naushira Pandya, MD, CMD, FACP [a,*], Nancy Losben, RPh, CCP, FASCP, CG [b], Jane Moore, RN, BSN, MS, MSN [c,d]

[a] Department of Geriatrics, Kiran. C. Patel College of Osteopathic Medicine, Nova Southeastern University, 3200 S. University Drive, Fort Lauderdale, FL 33328
[b] Quality: Omnicare, A CVS Health Company, Moorestown, New Jersey
[c] Tischer Moore Consulting Group, Bridgeport, New York
[d] National Association of Nursing Administrators in Long Term Care, Springdale, Ohio

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ABSTRACT

Management of diabetes for residents in long-term care settings is particularly challenging, due to the wide range of physical and mental limitations that bear on efficacy of their medications, as well as practical issues associated with the optimal administration of these medications. Foremost among the practical issues for residents requiring insulin injections, is the need to ensure that it is consistently delivered to the circulation at the target rate and dosage, thereby avoiding life-threatening episodes of hypoglycemia. Recent evidence from a multinational survey has elucidated principles of insulin injection technique, including optimal needle length and site rotation that can greatly improve consistency in delivering insulin to the subcutaneous compartment, while reducing pain, improving patient compliance, and limiting the total daily dosage. The present review consolidates these findings and highlights the most critical take-home messages for healthcare professionals working in this area.

Introduction

Diabetes is a common condition among the elderly (≥65 years of age), that affects 25–40% of long-term care residents[1] and overall accounts for nearly 25% of hospitalizations and 21% of hospital re-admissions in the U.S. each year.[2] Moreover, according to the Minimum Data Set (MDS)[a] Frequency Report, 66.7% of Medicaid and Medicare long-term care residents surveyed reported receiving insulin injections from one to seven times in the prior week.[3] Wide variations in functional and cognitive impairments and co-morbidities in this population suggest that an inter-professional collaborative approach utilizing practitioners, nurses, pharmacists, therapists, first line and family caregivers to develop and implement an individualized treatment regimen for glycemic control would be beneficial. An essential component of this regimen is the manner and timing of insulin injections. The current consensus is that treatment regimens including insulin should be simplified when possible with a reduction of the number of insulin injections and glucose checks.[1]

Their effectiveness also depends on each injection delivering the prescribed dosage of insulin to the bloodstream over a predictable period of time. Otherwise, blood glucose levels can fluctuate widely, with potentially serious short- and long-term consequences.

While aggressive glycemic targets have been widely advocated to slow long term progression of diabetes, in the elderly, the consequences of hypoglycemia are of paramount concern, favoring more moderate glycemic targets and measures which minimize risk of overly tight control. Hypoglycemia related to insulin use is

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* Corresponding author. Department of Geriatrics, Kiran. C. Patel College of Osteopathic Medicine, Nova Southeastern University, 3200 S. University Drive, Fort Lauderdale, FL 33328.
E-mail address: pandya@nova.edu (N. Pandya).

[a] Minimum Data Set: The federally-mandated data assessed for each resident of a Medicare or Medicaid-certified nursing home and which provides the foundation for the patient's care.

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the cause for approximately 100,000 emergency room visits per year in the US.[4]

In post-acute and long-term residents, the presentation may be atypical, with blunting of adrenergic symptoms (e.g., sweating, palpitations), and there is evidence that more neuroglycopenic symptoms such as altered behavior, lethargy, falls, weakness, focal neurological symptoms, and seizures are prevalent.[5] Intensive glucose lowering treatment in Type 2 DM increases (doubles) risk of severe hypoglycemia,[6] with potentially catastrophic consequences. Because residents on intensive insulin regimens may progressively lose awareness of impending hypoglycemia, glycemic targets in such individuals should be liberalized.[7] Avoidance of prolonged or repeated episodes is important since these are known to be associated with worsening of cognition.[8]

Insulin injection techniques must be individualized according to each patient's body type (e.g. thin versus obese), suitable injection sites, pain threshold, competence and preferences, under guidance of facility staff and caregivers following safe and consistent practices.[9] Engineered injection devices, particularly safety pens, are increasingly utilized to enhance treatment satisfaction and reduce insulin dosing errors and needle stick injuries, while also constraining overall costs of treatment.

Improving glucose management in elderly residents of long-term care facilities remains challenging, and requires a multifaceted approach which takes into account the unique clinical history, existing complications, prognosis, and preferences of each patient. However, recent evidence from a multinational survey of injection techniques has elucidated the opportunity for broad application of basic principles to greatly minimize insulin injection errors. Here, we review details of this survey.[10] the best practice recommendations it triggered.[11] and the implications these have for management of potential injection complications.[12]

Principles of insulin injection

Effectiveness of an insulin injection depends on several key factors, including the type of insulin, caloric intake, physical activity, renal or hepatic insufficiency, cardiac failure, and the tissue level into which it is injected. For example, the pharmacokinetics of long-acting, NPH, regular, and rapid acting insulin analogs, as well as continuous subcutaneous insulin (CSII) infusion vary considerably. In one study, the onset of action is earlier with NPH (0.8 ± 0.2 h) and CSII (0.5 ± 0.1 h), versus glargine (1.5 ± 0.3 h) ($P < 0.05$) (mean ± SE).[13] Loss of renal and hepatic function can alter the half-life of injected insulin in the circulation, and physical activity can increase sensitivity of skeletal muscle to insulin.[14] While all of these potential factors are normally considered in determining a patient's insulin regimen, this is predicated on the assumption that the prescribed dosage is delivered accurately, and into a tissue environment where its absorption rate into the circulation is predictable.

However, insulin is absorbed at a more rapid and variable rate when injected into an active muscle, compared to insulin administered into the subcutaneous space. This was demonstrated in a study measuring the kinetics of ^{125}I-labelled NPH insulin. Injection of insulin by the intramuscular route versus the subcutaneous route resulted in more rapid absorption (T50%[b]: 5.3 h versus 10.3 h), higher peak rate of absorption (11%/h versus 6%/h) and greater intra-patient variation in absorption.[15] The decrease in plasma glucose has also been shown to be greater up to 80 minutes after IM injection, versus SC injection.[16] Thus, it is critical that the injections be administered in a manner that ensures delivery to the SC space

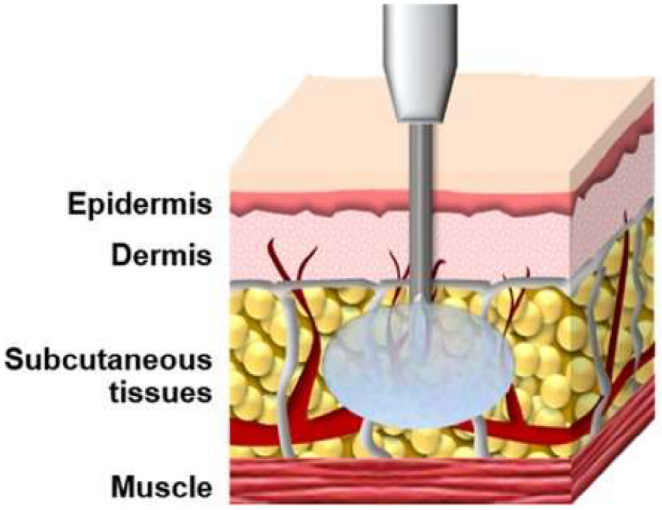

Fig. 1. Idealized subcutaneous injection. This figure demonstrates an idealized injection of medication into the subcutaneous layer, needle placement at 90 degrees, and the needle tip remaining well above the muscle layer.[17]

(Fig. 1), thereby avoiding inadvertent injection into the underlying muscle tissue, which increases risk of insulin overdose and hypoglycemia.

Since skin thickness does not vary greatly according to body type, the shortest needle that can penetrate this layer, perpendicular to the skin surface, can be utilized for a wide range of patients. An exception to this would be the case of patients with a very thin body habitus (e.g. cachectic or sarcopenic individuals), particularly with injections into the limbs, where lifting a skinfold is necessary to avoid IM injection. IM injections primarily occur with the use of longer needles and may result in a higher risk of bleeding, bruising, and stinging pain. In particular, use of needles ≥8 mm, which is common in LTC settings, has been associated with a significantly increased risk of IM injection.[18]

Another source of variability in delivery/absorption of injected insulin is the presence of insulin lipohypertrophy, defined as a localized hypertrophy of subcutaneous fat at insulin injection sites caused by the lipogenic effect of insulin. In contrast to the effects of intramuscular injections, injections of insulin into sites of lipohypertrophy tend to delay its absorption.[19] necessitating higher total daily dosage (TDD), while increasing risk of both hyperglycemia and hypoglycemia, and worsening the lipohypertrophy itself. Some evidence suggests that lipohypertrophy may be a reaction to the TDD of insulin, the failure to rotate insulin injection sites as recommended, or both.[10] Since many patients favor injecting into sites of lipohypertrophy because they are less painful, they need to be instructed on the identification and avoidance of those sites. A recent study found that with appropriate injection site rotation, A1C was 0.57% lower, and associated with a reduction of TDD by 4.7 units of insulin.[12] While A1C targets may be less stringent for residents with limited life expectancy, advanced diabetes complications, or extensive comorbidities,[10,20] improper insulin injection technique should be considered as a causal factor when there is a change in glucose control and in the target A1C. Ideal sites of injection are in the abdomen, buttocks and thighs, and upper arms,[11] with continuous rotation, including spacing of injections at least 1 cm from each other, and avoiding reuse of a single injection site more often than every 4 weeks.[10]

However, for best results it is important to stick with a consistent body part and "rotate" among several sites within that body

[b]T50%: The time required for 50% absorption of insulin following an injection.