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Case Report

A Rare Case of Polyarthralgias on Insulin Glargine Therapy

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Abstract

Insulin replacement therapy is one of many treatment options that can help to bring about near normoglycemia in patients with type 2 diabetes mellitus (T2DM).Adverse effects of human insulin and its analogs are common and are a significant issue in current diabetes care. However, polyarthralgias on long acting insulin, especially Insulin Glargine is a side effect that has previously never been reported. Here, we present an interesting case of a 61-year-old male patient, who was diagnosed with type two diabetes at the age of 41. The patient was compliant with basal-bolus insulin therapy and his basal insulin was recently changed to Insulin Glargine. In the immediate follow up after this change, the patient reported progressively worsening polyarthralgias necessitating Insulin Glargine to be discontinued. It was assumed that the new Insulin was the cause since the patient returned to his normal state of health upon its discontinuation. This is the first documented case of polyarthralgias on Insulin Glargine therapy in an adult patient. The literature does not have much to offer regarding this paradox and so the exact pathophysiology remains unknown.

ABBREVIATIONS

DM: Diabetes Mellitus; OAD: Oral Ant Diabetic Agents, T2DM: Type 2 Diabetes Mellitus

INTRODUCTION

Type 2 diabetes mellitus is a progressive multi-system disease in which individuals exhibit varying degrees of declining beta cell function, insulin resistance and a failure to suppress postprandial glucagon secretion. It is associated with an array of co-morbidities and potentially devastating complications [1]. Glycemic control as close to normoglycemia as possible can help to reduce the risk of microvascular and macrovascular complications, yet less than one-half of patients with T2DM achieve glycemic targets as recommended by practice guidelines. For many patients with type 2 diabetes, oral antidiabetic agents (OADs) do not provide optimal glycaemic control, necessitating insulin therapy.

Insulin glargine injection (rDNA origin) is a novel recombinant human insulin analog indicated for once-daily subcutaneous administration in the treatment of patients over 17 years of age with Type 1 or Type 2 diabetes mellitus who require basal (long acting) insulin for the control of hyperglycemia. The longer duration of action (up to 24 h) of insulin glargine is directly related to its slower rate of absorption and supports subcutaneous administration of once-daily. The time course of action of insulin subtypes including insulin glargine may vary between individuals and/or within the same individual [2]. Hypoglycemia is the most common adverse effect of insulin therapy, including insulin glargine and the timing of hypoglycemia may differ among various insulin formulations. Other commonly reported adverse effects of Insulin therapy include lipoatrophy, lipohypertrophy, injection site complications, hypersensitivity and weight gain. We document a diabetic male from Pakistan who presented with arthralgias as a complication of Insulin glargine therapy.

CASE PRESENTATION

A 61-year-old male was diagnosed with type 2 diabetes at the age of 41. His initial symptoms included polyuria, polydipsia and unintentional weight loss. The patient was started on oral antidiabetic agents upon diagnosis and was well managed. Approximately 20 years after being diagnosed with diabetes, the patient was started on basal-bolus insulin regimen due to inadequate glycemic control and raised HbA1c. Patient was compliant with Insulin Detemir 25 units once daily in addition to Insulin Aspart 8 units pre-prandial twice daily. The insulin dosing units were gradually increased over the months to Insulin Detemir

35 units and Insulin Aspart 10 units, with no change in the dosing schedule. The patient's recent most HbA1c was 7.5. However, in the recent months the patient experienced hypoglycemic episodes which resulted in an early visit to the primary care physician. Considering this, the long acting Insulin Detemir was changed to Insulin Glargine, keep the dosing schedule and the dosing units the same as Insulin Detemir. Patient returned two weeks later with complaints of gradual onset and progressively worsening polyarthralgias, described as joint pains accompanied by joint stiffness present throughout the day, and mostly in the morning. The knee joints were described to be predominantly affected, followed by the shoulder, and the ankle joints. Careful history taking revealed no precipitating factor for the symptoms in the recent two weeks, including any other medication changes. Physical examination showed normal range of motion in all limb joints, without any erythema or swelling. Laboratory investigations including inflammatory markers, serum ANA, and serum electrolytes were unremarkable. The patient had no family history of arthritis or any autoimmune conditions. There were no reported systemic findings with the arthralgias including any morning or evening stiffness. The symptoms worsened with activity and were relieved with rest. Considering this, Insulin Glargine was discontinued, one week after which the patient reported significant improvement in his symptoms.

DISCUSSION

Diabetes is a chronic metabolic disease that threatens human health worldwide. With the advancements of health care, many different treatment options are available for patients with diabetes; however, development of semi-synthetic Insulin and its different analogues was revolutionary in the management of diabetes. Synthetic human insulin was the first promising molecule of the biotech industry with the use of recombinant DNA technology. With the passage of time, insulin has been refined and modified based on the requirements and needs of the people. These different configurations of insulin help to maintain adequate glycemic control and minimize complications.

Glargine is unique amongst the insulin analogues in that it provides a steady basal amount of insulin owing to its slow-release properties. Furthermore, this basal level of active glargine is also void of peaks in activity that can result in harmful hypoglycemic events. Because of this profile Glargine has experienced widespread use for both its effectiveness in glycemic control and because of its safety. Insulin glargine is completely soluble at pH 4, which is also the pH of the administered solution, and has low solubility at physiological pH 7.4. Upon subcuteous injection, the solution is neutralized resulting in the formation of micro precipitates. Small amounts of insulin glargine are released from micro precipitates giving the drug a relatively constant concentration over time profile over 24 hours with no pronounced peak

The literature on polyarthralgias as a result of type 2 diabetes treatment with Insulin Glargine is very limited. Found only in a few review articles as a possible side effect, there is virtually no documented clinical case of joint pain being experienced as a side effect of Insulin Glargine administration for diabetic control [3,4]. In the sparse mention of this possible side effect, it is usually attributed to a coexisting condition not related to Glargine use [5]. It is possible that this side effect has gone underreported or that it could be present in a subpopulation previously not studied. We propose a possible mechanism for polyarthralgias with Insulin Glargine. Given that at physiological pH this protein can precipitate as a function of its slow-release property, perhaps this has an adverse effect if it occurs in joint spaces with sustained use [6,7]. It is also possible that this side effect is more pronounced in a subset of people that may have an increased predisposition to the formation of micro precipitates due to an altered immunological mechanism. The micro deposits may result in pain and inflammation akin to uric acid crystals in gouty arthritis.

Although the common side effects of exogenous Insulin are well documented, minor side effect can potentially go unreported or mistaken for other etiologies. Regular follow ups with the patients are essential to document these underreported side effects. We find this case report to be a valuable contribution to the limited data available on the less common side effects of Insulin therapy. More research on the mechanism behind this reported side effect would be of great contribution to the therapeutic world.

REFERENCES

1. Russell-Jones D, Vaag A, Schmitz O, Sethi B, Lalic N, Antic S, et al. Liraglutide vs insulin glargine and placebo in combination with metformin and sulfonylurea therapy in type 2 diabetes mellitus (LEAD-5 met+SU): a randomised controlled trial. Diabetologia. 2009; 52: 2046-2055.

2. Lantus® Product Monograph, Data on File Antidiabetic Agent Long-acting Recombinant Human Insulin Analogue. Sanofi Aventis Inc Canada. Date of Revision. 2010.

3. Fei Wang, Jana M. Carabino, Cunegundo M. Vergara. Insulin glargine: A systematic review of a long-acting insulin analogue. Clin Ther. 2003; 25: 1541-1577.

4. Warren E, Weatherley-Jones E, Chilcott J, Beverley C. Systematic review and economic evaluation of a long-acting insulin analogue, insulin glargine. Health Technol Assess. 2004. In: NIHR Health Technology Assessment programme: Executive Summaries. Southampton (UK): NIHR Journals Library. 2003.

5. Darby EG, Jenifer CW, Julienne KK. The Use of Insulin Glargine with Gestational Diabetes Mellitus. Diabetes Care Feb. 2006; 29: 471-472.

6. Owens DR, Bolli GB. Beyond the era of NPH insulin--long-acting insulin analogs: chemistry, comparative pharmacology, and clinical application. Diabetes Technol Ther. 2008; 10: 333-349.

7. Blundell T, Dodson G, Hodgkin D, Mercola D. Insulin: the structure in the crystal and it reflection in chemistry and biology. Adv Protein Chem. 1972; 26: 279-402.

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