

SAFETY & EFFICACY OF MICRO NEEDLE ARRAY INSULIN PATCHES AND SUBCUTANEOUS ADMINISTRATION OF INSULIN: A COMPARATIVE ANALYSIS

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Abstract

Type I Diabetes mellitus (DM) patient's pancreas is not able to release sufficient amount of insulin. Insulin plays a key role in controlling blood glucose level. Generally, the primary outcome of Type I DM are to maintain the blood glucose levels in normal levels and prevention of Diabetic ketoacidosis (DKA) and the secondary outcome is to prevent organ damage like Diabetic retinopathy, Diabetic neuropathy, Diabetic nephropathy, etc. Currently, there are distinct forms of insulin's are available for subcutaneous (SC) administration. This includes Rapid-acting, Intermediate-acting, Long-acting, and Short-acting. For SC administration of insulin, there are different devices are available for administration of insulin, which includes insulin syringes, insulin infusion pumps, jet injectors, pens and insulin patches. The main objective of this study is to assess the safety and efficacy of SC administration insulin and Microneedle-array insulin patches (MNAIPs). In this study, we have conducted a systematic literature review of original articles and review articles. After reviewing we were found the several advantages of MNAIPs. Comparing the SC injections with MNAIPs having several advantages which include Good Safety and Efficacy, Good Bioavailability, Pain-free delivery, Minimal skin trauma and lack of bleeding. These advantages may enhance patient quality of life.

Keywords:

Diabetic ketoacidosis, Bioavailability, Pain-free drug delivery, Insulin syringes, Insulin infusion pumps..

Introduction

External administration of Insulin plays a key role in controlling blood glucose levels in Type I DM patients and selective individuals of Type II DM patients (1). Currently, different insulin delivery systems are available for insulin administration in diabetic patients with different costs and efficacy, Which Includes insulin syringes, insulin infusion pumps, jet injectors, pens and insulin patches (2). Insulin cannot be administered orally as it is severely degraded in the Gastrointestinal tract (GIT) by the process of digestion (3).

Currently, the choice of insulin drug delivery system relies on the patient's economic status and health circumstances are a higher challenge in healthcare practice. There are different barriers involved during the insulin prescribing, administration like the discreteness of delivery, fear of injection, dosing of insulin and cost of insulin.

There are distinct forms of insulin's are available for SC administration. This includes Rapid-acting, Intermediate-acting, Long-acting, and Short-acting. Nowadays, several patients are experienced with adverse drugreactions (ADRs) and side effects after SC administration of insulin, such as hypoglycemia, and Diabetic ketoacidosis (DKA) (4).

Microneedle-array Insulin patches [MNAIPs] are presently an experimental type of insulin delivery at an early point of studies. MNAIPs are releasing insulin automatically into systemic circulation depending on blood glucose concentrations through the SC path. According to prior studies, SC administration may trigger several ADRs compared with MNAIPs (5).

The main objective of this study is to assess the safety and efficacy and ADRs of SC administration insulin and MNAIPs. In generally the safety and efficacy may affect the quality of life of diabetic patients.

Materials and methodology

In this study, we have conducted a systematic literature review of original articles and review articles. This study mainly focused on the advantages and disadvantages of the SC administration of insulin and MNAIPs. These advantages and disadvantages show the impact on safety and efficacy.

Results and discussion

After reviewing the previously published articles and databases, we found that various advantages and disadvantages of insulin SC administration and MNAIPs. Generally, the primary outcome of type I DM is to maintain the blood glucose levels in normal levels and prevention of DKA and the secondary outcome is to prevent organ damage like diabetic retinopathy and diabetic neuropathy, etc.

Cons of Subcutaneous Insulin Injections: -

- **Smooth muscle cell proliferation:** Frequent SC injection administrations may cause blood vessel endothelial injury may occur. It leads to irregular smooth muscle cell proliferation may occur (6).
- **Transmits the pathogens:** -Repeated usage of insulin pens may have the probability of viral and bacterial infections (7).
- **The Burden of daily injections:** - Daily SC administration can cause a heavy economic strain on the patient. It is one of the causes of patient noncompliance (8).
- **Physiological and psychological stress:** - Daily subcutaneous insulin administration may trigger physiological and psychological disturbance. It causes psychological modifications such as anxiety, depression, mania, and schizophrenia. (9)
- **Medication administration errors:** -The patient should be aware of SC administration. Irrational drug administration may cause drug deposition that may occur in the SC tissue of the skin. It leads to local hypertrophy and lipid depositions may occur (10).

Pros of Subcutaneous Insulin Injections:-

Nowadays, SC insulin injections are easily available in all areas in different forms, at a reasonable cost.

Cons of Microneedle array insulin patches:-

- Currently, this is not easily available and expensive.
- Patients need minimal training in their usage guidelines.
- MNAIPs are contraindicated in patients with psoriasis and dermatitis. These patients are extremely susceptible to skin-hypersensitive responses.

Pros of Microneedle array insulin patches:-

Microneedle-array insulin patches automatically release insulin depending on blood glucose levels. The MNAIPs may have fast response, ease of administration, excellent biocompatibility. The MNAIPs are having the Good bioavailability, pain-free delivery, and minimal skin trauma, lack of bleeding, less introduction of pathogens.

Smooth muscle cell proliferation and muscular damage may occur.	No cellular level and muscular level damage.
Economical Burden of daily injections.	There is no economic burden on patients.
It is a painful administration.	It is Painless administration.
There is physiological and psychological stress on patients.	No physiological and psychological stress on Patients.

High chances of transmission of blood-born Pathogens.	Fewer chances of transmission of the pathogens.
Insulin dose fluctuations may occur.	MNAIPs release the insulin constantly. There is no dose of fluctuations.
In some cases, Administration errors may occur.	No Administration errors are reported in previous studies.

Generally, two types of insulin Transdermal drug delivery systems are available. This includes insulin pump patches & MNAIPs. Transdermal drug delivery was severely restricted by the failure of most drugs to enter the skin at therapeutically helpful rates. For this reason, chemical penetration enhancer's [CPE] may be used to enhance the skin penetration of insulin through the skin while using insulin pump patches (11). While using the MNAIPs there is no need to use the CPE because the microneedles are directly entered into the skin. These microneedles directly release insulin into the skin. In MNAIPs the human recombinant insulin is encapsulated with glucose-sensitive materials like glucose oxidase enzyme and hypoxia-sensitive Hyaluronic acid (HS-HA) conjugated with 2-Nitroimidazole (12). These Glucose sensitive materials are highly sensitive to blood PH levels. The concentrations of blood glucose have a significant influence on the acid-base balance. The insulin encapsulated materials are easily oxidized under hyperglycemia conditions and then release the insulin directly into systemic circulation depends on blood glucose levels. Therefore the MNAIPs are acting as an external pancreas it stores the limited concentrations of insulin. It releases insulin continuously depends upon blood glucose levels. There are no blood glucose fluctuations may occur in diabetic patients. According to previous surveys, the MNAIPs are the best way to develop the treatment outcomes and prevent DKA.

There are distinct types of insulin's available for SC insulin administration, including quick-acting insulin, regular short-acting insulin, and long-acting and medium-acting insulin, ultra Long-acting insulin. According to previous studies, the subcutaneous administrations of insulin may cause the dose fluctuations that may occur and selection of a type of insulin and the number of units depends on patient demographics and blood glucose levels. In most clinical trials the researchers have proved too large fluctuations in insulin levels in diabetic patients. So finally the majority of the clinical trial studies of insulin SC administration are proved to be less safety and efficacy compared with the MNAIPs (12).

Conclusion

The Above review concluded that MNAIPs are loaded with human recombinant insulin and which can easily release the sufficient amount insulin into systemic circulation through the SC layer by creating the micro-channels using touch-actuated 'press and release' actions depend upon blood glucose levels in the body without pain. The MNAIPs are having good safety and efficacy compared with the insulin subcutaneous injections, Regardless of availability and cost.

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