A Brief Review On Various Devises Used In Tretment Of Diabetes Mellitus

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Abstract:
In 2021, 100 years mark to the discovery of insulin. The diabetes mellitus is disease increased worldwide day by day and they result in serious health complications. Now the disease affects most of the age groups. The most possible way of maintain the sugar level by using medication is insulin. It is most safe, potent and effective therapy to lower the high blood sugar level in blood. The major challenges of insulin despite its efficacy has result in low sugar level (hypoglycemia) which result in low level of dosage are prescribed in high majority people. In self care condition (self medication) administration of insulin very easy and it provide flexibility and freedom to patient with DM, the device provide good level dosing accuracy and improve patient compliance , the various popular device now days are use like insulin pen, syringe, pump, various calculator apps, artificial pancreas, insulin inhaler, jet injector, closed loop and continuous monitoring delivery systems are there and computer algorithms gain positive advancement in treatment of diabetes mellitus. So, this review is discussed about the various devices use in treatment of diabetes mellitus (DM) and their modifications.

Keywords: Diabetes mellitus, insulin, insulin devices, diabetic patient, self-care.

Introduction:
Diabetes mellitus is series of chronic disease that imposes substantial, social and economic Burdon around the world. The prevalence of diabetes for all age group worldwide is estimated to be 2.8% and is expected to be nearly double by 2030 (4.4%) [1]

In united state total almost 18 million people are diagnosed in 2007, an additional 5.7 million of people are diagnosed, which bring to total 8% of us population to have DM [2].Diabetes is associated with number of health related complication and the level of hyperglycemia and duration of disease is associated with increased risk of developing micro vascular and macro vascular complication such as neuropathy, nephropathy, myocardial infarction and stroke [3, 4]. the number of people are affect by this disease, including elderly patient "the prevalence of DM in patient 60 year of age or older was estimated to be grater then 12 million in 2007, which show that almost one fourth of elderly population and one half of overall DM population, the number surely increases. In 2020 an estimated 12% of US population was 65 year of age or older. This number is projected to grow over 16% by the year 2020 [5].

DM is endocrine disorder of pancreas. In which pancreas do not produce enough insulin for the body requirement. Diabetes is recognize exist in two forms- type 1 diabetes is insulin dependent diabetes mellitus (IDDM) it caused by failure of beta cells to produce adequate amount of insulin. Type 2 is non-insulin dependent diabetes mellitus (NIDDM)

it caused due to failure of insulin to facilitates the movement of glucose into cells. In this two condition blood sugar (glucose) level rise the above the normal range.

Gestational diabetes mellitus- it is type of diabetes .which present with hyperglycemia in pregnant women. It usually appears in 2-4% in pregnancies in 2nd and 3rd trimester [6].

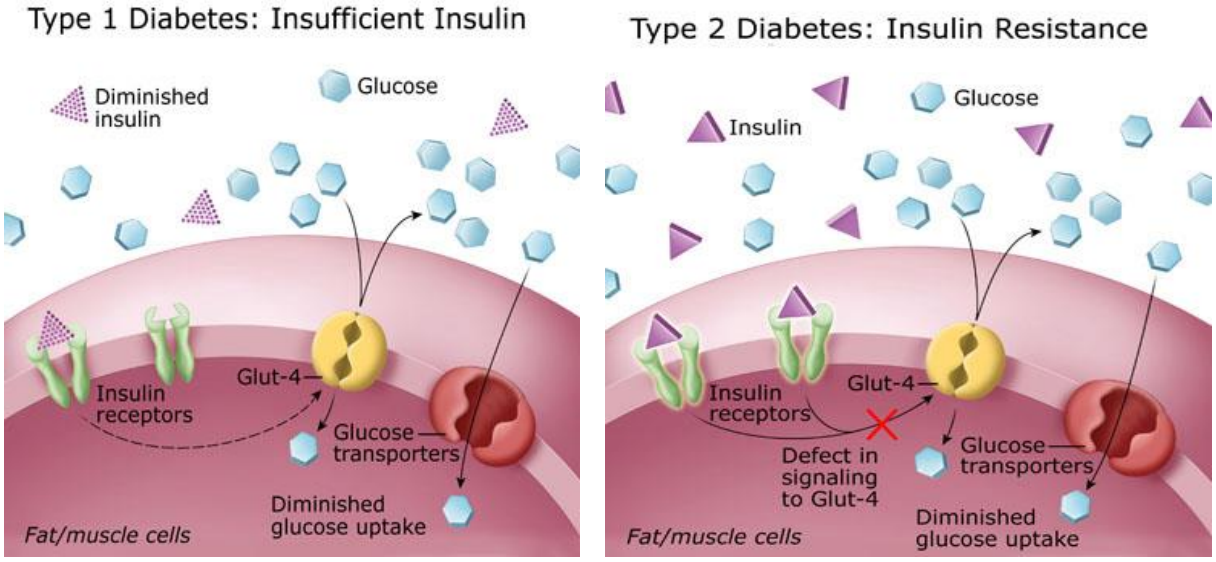

Fig. no.1: pathophysiology of Type 1(IDDM) and Type 2(NIDDM) diabetes mellitus

According to intentional diabetes federation (IDF) survey in 2016 diabetes is disorder which affects 415 million people in world and may increase to 642 million by the year 2040 [7]. According to aroma world record report 61.3 million people have diabetes in India and consist of 20-79 age group in the population. It may approx double by the year 2030 in India also known as diabetes capital of the world and mainly rural and urban people [8].

The frequency of diabetes in progressively increases in urban India. The frequency of diabetes is apporx 6 times more than compared to rural population. Decreased exercise, increasing weight indention, change in diet , malnutrition , alcohol consumption, viral infection are the major causes of diabetes mellitus in last 20 years[9,10]. Female diabetic patient are more compared to male diabetic patient because of hormone and inflammation act differently in women [11].
Insulin is hormone secreted in the pancreas by the beta cell of islets of langerhans. The discovery of insulin done in 1921 came from Frederik G. Banting in toranto [12]. All patients with type 1 diabetes (T1DM) require insulin because of its absolute deficiency with increasing longevity in type 2 diabetes mellitus (T2DM) patient. They will require insulin because of progressive beta cell failure. Even although insulin is a most powerful therapeutic option available to manipulate hyperglycemia, suffers with diabetes revel in diverse challenges consisting of, but no longer confined to interference with day by day dwelling, therefore addressing such diabetes with advanced and powerful technology for insulin transport is important to keep away from headaches associated with diabetes.

The advent of diabetes technology, the term used to describe hardware, devices and software use in diabetes has transformed the patient care [13]. starting with syringe for injecting insulin, graduating to insulin pen , pump , sensor augmented pump, the growth of diabetes technology accelerated with introduction of hybrid closed loop system, integration with consumer electronics and closed based data system[14,15]. The notable drawback of crude devises were poor dose accuracy, lack of social acceptance, prolonged training period and difficulty in convince. Continuous improvement and innovations in the design, technology and accessibility of insulin delivery devises helped overcome these limitations [16].The insulin transport devises accomplish insulin shipping in maximum specific way with minimal invasiveness. The device have favorably impacted sufferers perceptions approximately insulin therapeutic further to improving their satisfactory of lifestyle[17].The number of innovation have been done to improve ease and accuracy of insulin administration as well as to achieve tight glycemic control.

However, the proper choice and software of diabetes technologies are crucial for wonderful effects. Here, the aim of this review is to describe the various devises used in treatment of diabetes mellitus available today. The review will focus on now days which devises and how are they use in treatment of diabetes mellitus.

This article is based on previously conducted studies and not contains any study with human participants or animals performed by any of the authors.

Different devices used in treatment of Diabetes

1. Insulin pen:

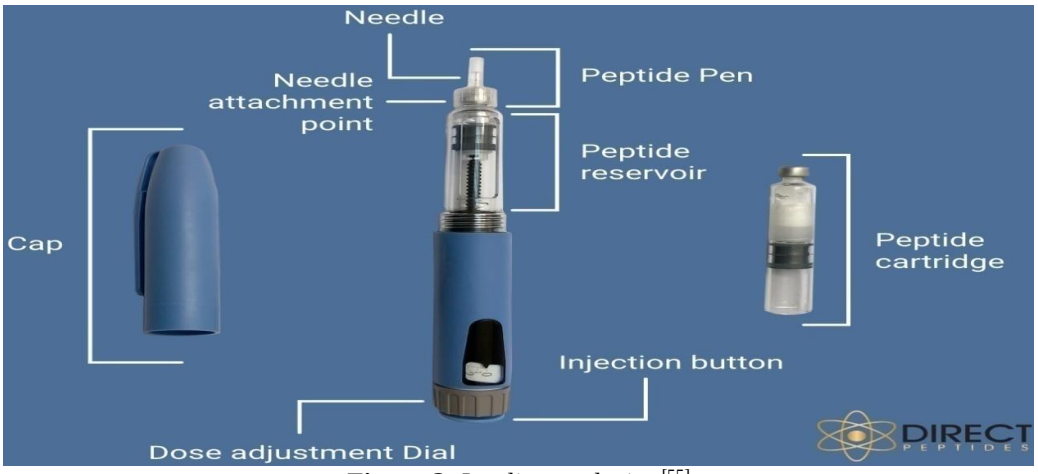

Fig. no 2: Insulin pen device [55]

An insulin pen is used to inject insulin for the treatment of diabetes .it consist of a cartridge (integrated or bought separately) and dial to measure the dose and use with disposable pen needles to deliver the dose. It changed into added and marked as novo Nordics, followed by novo pens 2 in 1988. Novo pen 2 has characteristics dial up setting to measure the required dose. [18].in general pens provide extra, easy, correct and handy insulin transport over syringes. An insulin pen has 3 component; insulin cartridge (a disposable short needle and on incremental "one click on in step with unit" dosing device can be both measurable and disposable. Reusable insulin pen have replaceable cartridge, a disposable pen have prefilled cartridge and are discarded after the use. In 1989 novo provide the global first disposable prefilled insulin pen "novolet" [19].insulin absorbed on plastic surface of those prefilled pens over the year and a specific awareness may be executed trough right mixing, therefore, those pens extended the dose accuracy and blood glucose among more cartridge modification[20].compared with syringe, pens offers more flexibility , accuracy, discreetness and lengthy time period , cost effective, contributing to improved remedy persistence and adherence. Therefore, the use of insulin pens demonstrates higher glycemic control and has wider popularity [21, 22].

In pediatric and aged population small insulin doses may be vital. Insulin pens allow for extra accurate shipping of the small doses (<5 Iu doses) [23] when using conventional vials and syringe strategies the aged (>60 years) are more likely to enjoy dose blunders [24]. This mistake can lead to over or under dosing insulin which can cause similarly complications. The insulin need to go into the fat layer under the skin.

The following steps are mainly use to inject insulin step by step using pen.

1. Remove the cover.
2. Attached the pen needle to the insulin pen.
3. Expel the air from the pen.
4. Pinch the skin and put the needle in at 45ºangle.
5. If the skin tissue are thicker then inject straight up and down (90º angle)
6. Leave the syringe in place 5 second after injecting.

2. Next generation insulin pens:

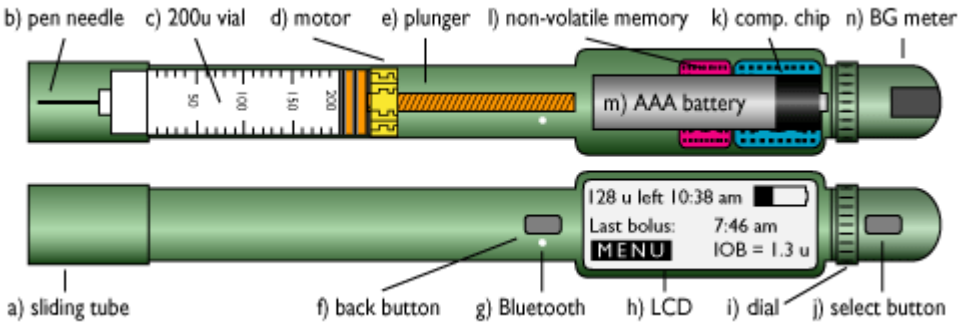

Fig. no.3: Next generation insulin pens [56]

This generation technology pen devises or "smart pens" with a reminiscence characteristic had been on the scene because in 2007 the multi dose reminiscence characteristic allows these gadgets to keep the date, time quantity of

previous dose [25, 26]. The gadgets are integrated with USB or Bluetooth feature for efficient tracking and statistics management. Future refinement on this subject consist of "clever pens"

With in- built calculators to provide proper strange to sufferers regarding the insulin dosage, reminiscence features to show quantity and time of injection as well as automated transmission trough Bluetooth to produce computer generated review [27].

3. Connected pens:

The connected pens are subsequent era-insulin pen with capabilities that pass past the memory function in pen system. A Bluetooth enabled Wi-Fi insulin pen with a cell phone interface and bolus advisor, is the forerunner of this type and become launched by using companion medical in 2000[28].according to pens website, this tool is "reusable injector pens plus an initiative cell phone interface equal smart insulin transport"[29] A Bluetooth internet related insulin pen cap that support the technology smart dosing structure trough a mobile app for the convent of T1DM suffers who do not longer use an insulin pumps is another coming near near innovation in pen era[30].

4. Insulin syringes:

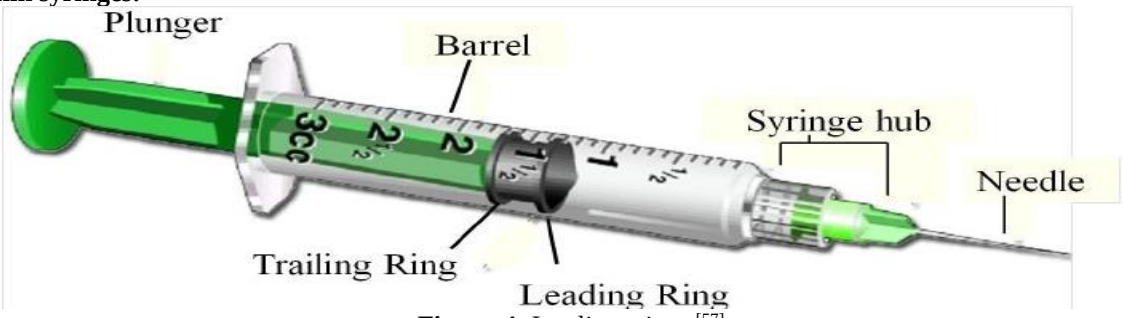

Fig. no.4: Insulin syringe [57]

The insulin syringes are prefilled disposable contain specific type or mixture of regular and modified insulin. It is common way of administration of via syringe, it came in range capacities of (0.3ml, 0.5ml, 1ml) and with range of needle type gauges , initially large and heavy reusable syringes with plungers, barrels and long bore needles have been used for insulin delivery. These syringes and reusable needles had to be sterilized through boiling to insure green reuse. The first specialized syringe for insulin injection become manufactured via Becton Dickinson (BD) in 1924[31] in 2016 the FDA approved U-500 precise insulin syringe design via BD to cope with the dosing errors while administering doses from U-500 vial with a U-one hundred insulin syringe [32] even although "traditional" syringe generation has become much less famous in present day era, vials and syringe have delivery for more than 50 years.

However, a few people get a difficulties and no longer very convent for this cause a range of different transport devises where advanced, consisting of insulin pens, jet injector and pumps.

5. Insulin pumps:

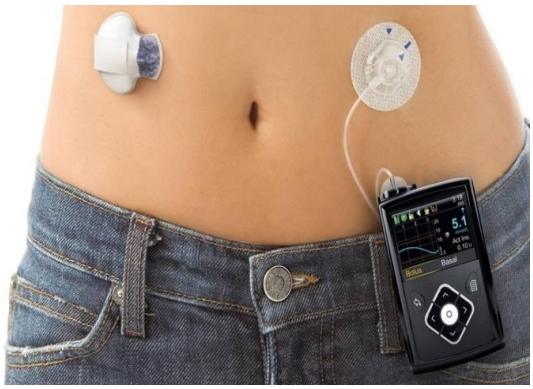

Fig. no.5: Insulin pumps [58]

The insulin pump are small electronic gadgets, in that size of plunger that may attached on belt or placed on (near abdomen) pocket. They run off batteries. They are made up of an insulin reservoir related to tube, finishing in cannula or catheters that inserted under the pores and skin of abdomen. They can be set to supply insulin at continuous charge in course of day or to release larger portion at meal instance or white blood sugar level are excessive.

Portableinfusiin devices connected to subcutaneously placed cannula to provide continuous subcutaneous insulin infusion (CSII) only regular insulin is used. They can be programmed to deliver insulin at low basal rate (apporx 1U/hr)

and premeal boluses. (4 to 15 time the bolus rate) to control post prandial glycemia though theoretically more appealing. No definite advantage of CSII over the multi dose, SC injection has been demonstrated.

Moreover, cost, strict adherence to diet, exercise care of the device and cannula, risk of pump failure, site infection are the demanding the patient. The first wearable pump called as "blue bricks" and later the 'Auto syringe' turned into designed via Dean Kamen in 1976 and brought about the advent of insulin pump therapy in the equal year [33]. according to endocrine society guidelines, the patient must be assess before his or her psychological repute, previous complication with diabetes self care, willingness and motivation to attempt the tool, and comfort of the required comply with up visits before suggesting CSII[34] insulin pump are specially used for insulin substitute in T1DM patient. But it has been widely accepted via T2DM patient as properly [35] Diabetes management with CSII affords better glycemic and metabolic manipulate (reduce HbA1C glycemic variant and glycemia) in patient with diabetes [36, 37]. the clinical trial, the exploratory CSII randomized controlled trial on Erectile dysfunction in T2DM patients. (ECSIITED) carried out by means of our organization, discovered, improved efficiency of CSII within the remedy of erectile dysfunction and diabetic peripheral neuropathy in T2DM patient [38].

6. Patch pumps:

The barriers of infusion set have brought about the important of "patch pumps" ; pump that are free of infusion sets, small, light in weight and connected to skin trough an adhesive. Patch pumps offer extra comfort and versatility to the users. Mainly while traveling from one place to another. In 2011 insulate introduce omniped (the primary tubeless insulin pump) it accommodates an included infusion set and automatic inserter that converses on wirelessly with an incorporated BG meter. The omniped patch pump gets entire freedom to the users to have interaction in recurring activities [39]. It is completely disposable and waterproof, lasting 72 hours and the body mention up to 200 units of insulin, the second version of omniped of patch pump was launch in 2013 with an advance future this pump is more accurate and helps to better manage of blood sugar level, it may improve A1C level. Dosing for meals and snacks are easer due to these pumps.

7. Sensor Augmented therapy:

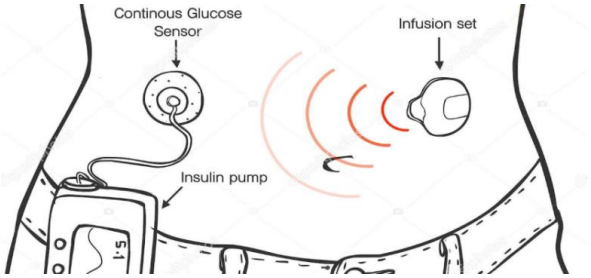

Fig. no.6: sensor augmented therapy [59]

All sensor augmented pump allow patient to see their glucose level on their insulin pump or a separate device and alert them, when their blood sugar level are low or high. However, Medtronic sensor augmented pump are the future called "smart guard". In 2009 Medtronic launched the minimedvio system with low glucose future that automatically halts the insulin shipping when sensor glucose degrees hit a present low threshold; this tool has been considered the first stepping stone to an SAP system [40].

8. Bolus calculator apps:

Fig. no.7: image of bolus calculator app. [60]

Bolus calculator app/ bolus for insulin dose calculation available in smart phones these can characteristic independently or can be include into pump to calculate the accurate insulin dose by incorporating predicted carbohydrates intake, measured blood glucose values and previous insulin doses[41]. it is promising equipment to help human being with diabetes administer insulin appropriately and feature capability to decorate glycemic control, while big quantity of app which assist with insulin dosing are to be had. There can be restricted record evaluating their efficacy, safety and price. Recently a need for regulatory oversight has been identified. However, few app meet federal necessities, thus deciding on perfect app is difficult for both patients and providers [42]. Carbohydrates counting using bolus calculator app has been found to improve glycemic control. There is lot of evidence for improving the quality of life and metabolic control of diabetes. It is advice to use BC app from the bigning of therapy with PIP, diabetes; mellitus, mysuger (Roche) and predict BGL are the number of mostly used bolus calculator apps. The bolus wizards ere the integrated automated bolus calculator precise to insulin dose recommendation. The use of bolus wizards has been related to better glycemic control and treatment pleasure [43].

9. Artificial pancreas (AP):

The artificial pancreas (AP) device system is devise that closely mimics the glucose regulating feature of healthful pancreas. The most AP system consist of 3 style of devices

1. Open app
2. Android app
3. Loop system

A continuous glucose monitoring system (CGM) and insulin infusion pump. A blood glucose device (which include a glucose meter) is use to calibrate CGM. A controlled algorithms connect the CGM and insulin infusion pump to permits continuous verbal exchange among two gadgets sometime as an AP tool system is known as 'closed loop machine' or an "automatic insulin delivery machine"

An APDS (artificial pancreas device system) will not only monitor glucose level in the body but also automatically adjust the delivery of insulin to reduce high bold glucose level (hyperglycemia) and minimize the incidence of low blood glucose level (hypoglycemia) with real lifestyle studyor no input from the patient [44]. Real lifestyle studies from patient and caregiver's anecdotal information and posted review from selected cohorts have highlighted the clinical blessing and reduction in self management Burdon with APS [45].

10. Bionic pancreas (BP):

The bionic pancreas is type of closed loop gadgets including two infusion pumps (one by one for insulin and glucagon) and linked to CGM trough a phone app, the first bionic pancreas "I Let" (bets bionics), exclusively for T1DM treatment changes into invented with the aid of DR. Edwarddamianoin 2015. In this system automatic dosing tests of insulin and glucagon degrees are made every 5 minute primary based on the appraised CGM data. These statistics are transmitted to pump to adjust insulin or glucagon shipping the previous research in home use and outpatient setting indicate higher glycemic low and positive psychological impacts related to use of bionic pancreas [46, 47].

The implemented artificial pancreas;

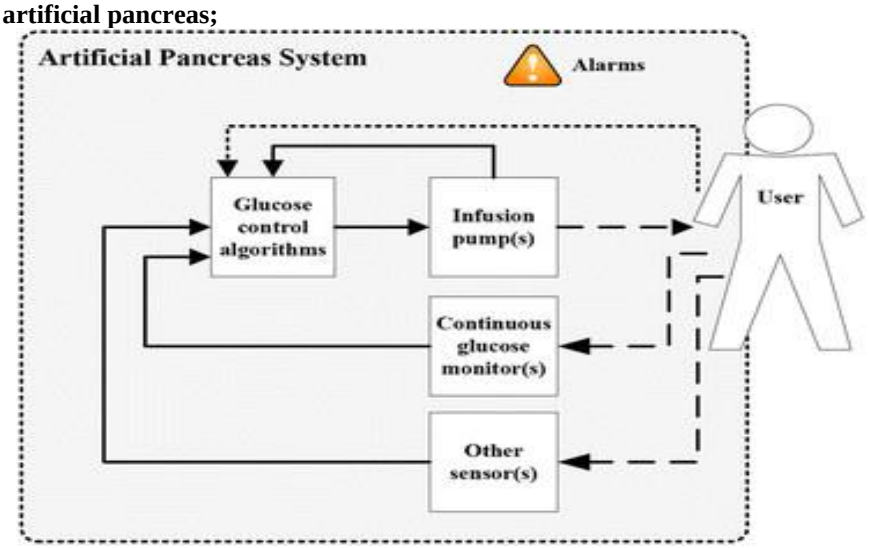

Fig. no.9; working flow chart of implemented artificial pancreas. [61]

It is completely insulin shipping tool, is every other novel app era under development at demon Fort University. It is primary gel based gadget that responds to BG version by using changing the insulin transport charge. The overall performance of this machine in glycemic control is nicely examined in diabetic pig [48]. The work of implantable

pancreas as simple as the blood sugar level fluctuates. A signal tell the pump how much insulin to deliver it is also known as “all in one” diabetes management system.

11. Insulin inhalers:

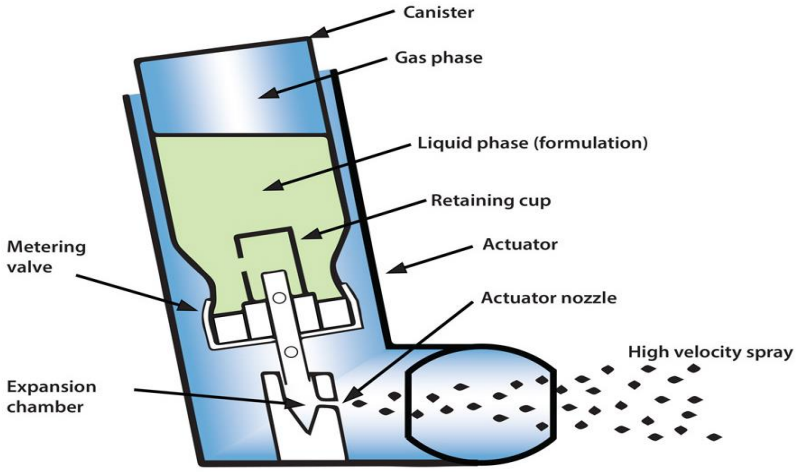

Fig. no.10: Insulin inhaler[62]

Insulin inhaler had been used to deliver pre-mealtime insulin. Insulin inhaler work like an asthma inhaler. However, it supply drug powder insulin into the bloodstream trough the lungs. However, because the device can most effective be used to supply speedy performing insulin, lengthy_ appearing insulin need to nonetheless be injected. Large are dose are needed because only around 10% of dose actually reaches to the bloodstream and that amount may range for instance. If you have cold or asthma when it added to market place in 2006 inhalable insulin become taken into consideration a giant innovation to address needle phobia and incorrect insulin injection technique, the effectiveness of inhaler insulin in diabetic treatment especially for postprandial hyperglycemia has already been validated [49]. The first inhalable insulin, exabera was approved by FDA in 2006 for the treatment of T1DM and T2DM. Its real advantage it is work quickly and goes into action for short term (12 to 15 minute) and it have lower risk of hypoglycemia and weight gain. The acceptance of inhalable insulin is further limited by insurance barrier, safety concern and completing product [50].

12. Insulin jet injector:

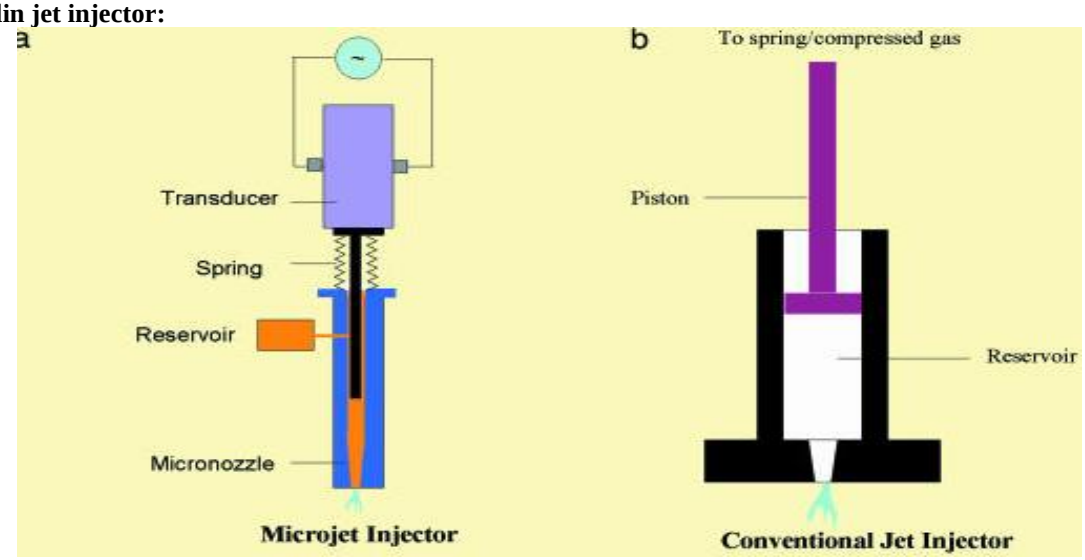

Fig. no. 11 insulin jet injector [63]

Insulin jet injector is the device which allows injecting insulin without using needle .it give fast delivery of insulin into the bloodstream. An insulin jet injector allow the insulin to spread over a large area in the lower layer of skin than typical needle, would as result the insulin move in bloodstream faster than it would from needle injection to say the jet injector are the solution for the patient with needle phobia [51] recent safety and feasibility research have evaluated in treatment per formal and pharmacokinetic and pharmacodynamic (PK-PD) profile of insulin administered by way of new generation jet injector [52, 53].

It is use pressure from a spring loaded piston to create fine stream of insulin trough a small bore nozzle, delivering insulin to the subcutaneous layer.

Future prospects:
The insufficient insulin secretion is a core pathogenic mechanism of diabetes mellitus, therefore, insulin therapy remain the cornerstone of management.

From the past 100 years various progresses has been done in development of insulin and delivery system of insulin therapy. With this advancement and never changing delivery system of insulin go through various changes and uncertainties to overcome this challenge the next generation insulin therapy best represent which give delivery according to endogenous glucose sensing feedback mechanism[@]

The advancement and digitalization marks tremendous changes in past few years and to overcome the accuracy of doses, safety therapeutic efficacy of insulin delivery therapy with the help of various devises like insulin pen, pump, artificial pancreas inhaler and jet injector will most probably make even in more so in near future.

The significant changes in newer technology help patient to choose best option to deliver insulin. Each device has their unique dosing advantage.

Conclusion:
From the past years tremendous evaluation and modification has been done to improved insulin delivery method and route easy to accessible are rapidly becoming effective and also has great potential to improve delivery of insulin and give good quality of life to patient suffering diabetes mellitus.

The aim of this newer generation delivery system is to give maximum therapeutic efficacy with more patient compliance.

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