

REVERSAL OF INSULIN LIPOATROPHY BY MONOCOMPONENT INSULIN

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SYNOPSIS

Lipoatrophy is a common complication over the site of insulin injection. Until fairly recently, no effective treatment was available for this unsightly complication. With the introduction of purified insulins (monocomponent, single-peak, rare-immunogenic) encouraging reports have appeared on the improvement and disappearance of lipoatrophy. This paper documents our initial experience with monocomponent (MC) Lente insulin (Novo, Copenhagen, Denmark), in reversing lipoatrophy caused by ordinary insulin injection in a female diabetic patient.

The literature on this subject is briefly reviewed.

INTRODUCTION

Since the use of insulin injections in the treatment of diabetes mellitus (Banting and Best, 1922), a variety of local skin reactions have been documented. Insulin-induced lipoatrophy has remained one of the more difficult and disfiguring problems. Lipoatrophy (fat atrophy or dystrophy) is a "sharply defined disappearance of the subcutaneous fat without exudative reactions and appreciable fibrosis" (Marble and Simith, 1942; Marble and Renold, 1949). It was first reported in 1926 (Depisch). Further reports appeared soon after (Mentzer and DuBray 1927; Rabinowitch, 1928). After this early interest, enthusiasm waned, and up till the early seventies there was sparse reference to this phenomenon in the medical literature.

The incidence of lipoatrophy has been variously reported from 24% to 50% (Renold et al, 1957; Knowles, 1971; Teuscher, 1974; Ferland and Ehrlich, 1975). It is more frequent in females (Watson and Vines, 1973; Teuscher, 1974; Ferland and Ehrlich, 1975; Hulst, 1976). The fat atrophy develops within a few months of starting insulin therapy and can last for many years.

Until recently, no truly effective treatment was available; even a recent work of reference declares that there is no specific therapy (Moschella et al, 1975).

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The term "monocomponent insulin" (MC insulin) was introduced by Schlichtkrull et al (1972), to designate insulin that has been purified to become the sole component, with little or no immunogenic activity when used for therapy. In 1973, reports that these purified insulins, injected directly into the atrophic patches, produced striking improvement and reaccumulation of fat, appeared (Wentworth et al, 1973; Korp and Levett, 1973; Bruni et al 1973). Enthusiastic accounts on the use of purified insulins in lipoatrophy have since surfaced (Teuscher, 1974; Ferland and Ehrlich, 1975; Teuscher, 1975; Hulst, 1976).

This paper describes our initial success in the treatment of lipoatrophy with MC Lente insulin (Novo, Copenhagen, Denmark).

CASE REPORT

The patient (T.E.E.), a 22 year old Chinese girl, presented in February 1976 with polyuria and polydipsia. Physical examination was normal. Her fasting blood sugar was 98 mg/100 ml. Following a 50 gm glucose load, the blood sugar at 1 hour and 2 hours was 278 and 206 mg/100 ml respectively; thus confirming the diagnosis of diabetes. She was advised on a 1,800-calorie diabetic diet and Lente insulin zinc suspension (LZS) 16 units daily was given. On this treatment, her symptoms were relieved and her postprandial blood sugar was 107 mg/100 ml.

The patient had been injecting insulin over each deltoid on alternate days. She had noticed progressive loss of tissue bulk at the injection sites. By March 1977 (13 months after insulin therapy), she had severe lipoatrophy over both deltoids (Fig. 1) and this distressed her as it was unsightly.

She was started on monocomponent (MC) Lente insulin (Novo, Copenhagen, Denmark), 16 units daily, injected directly into the atrophic areas. After 2 weeks of treatment, the lesions had begun to show improvement. By 4 weeks, there was fairly complete resolution of lipoatrophy in the injected areas (Fig. 2).

A year later (May, 1978), the patient is well and continuing daily injections of MC Lente insulin, 16 units daily. The previous sites of lipoatrophy have completely disappeared. The tissues in these sites look and feel normal without any caving-in of the overlying skin (Fig. 3).

DISCUSSION

The exact aetiology of lipoatrophy remains obscure. Among the factors which have been implicated include the pH and temperature of the insulin preparation, the angle of injection, local inflammation, in-



Fig. 1 Lipoatrophy over deltoid region after ordinary insulin injections.

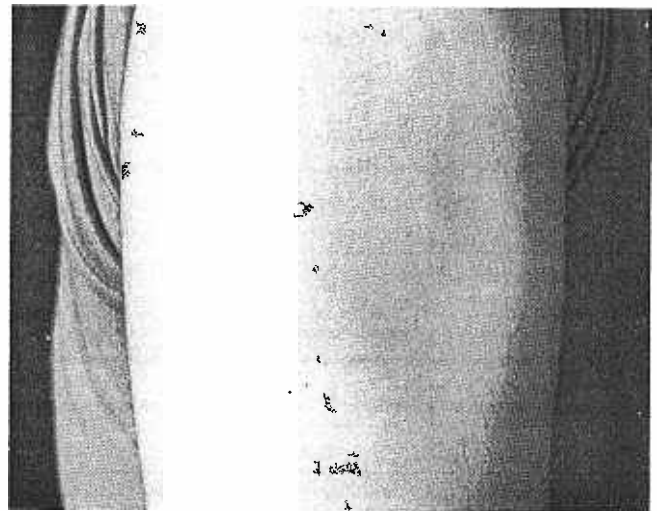


Fig. 2 Marked improvement in lipoatrophy, one month after changing to monocomponent (MC) Lente insulin injections.

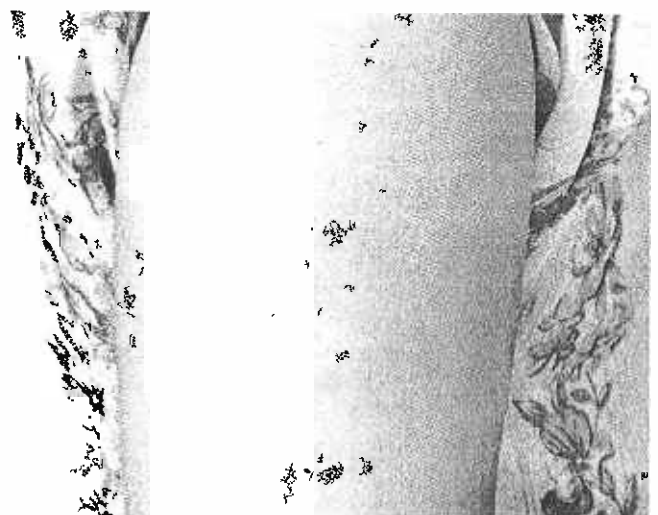


Fig. 3 Maintenance of complete reversal of lipoatrophy, 14 months after monocomponent insulin injections.

complete removal of surface alcohol, contamination by pancreatic exocrine secretions and mechanical trauma of injections (Mentzer and DuBray, 1927; Rabinowitch, 1928; Marble and Smith, 1942; Marble and Renold, 1949); but none of these have been proven. The condition may be related to the zinc content of the insulin preparation (Watson and Vines, 1973).

The pathogenesis of lipoatrophy involves lipolysis, but the fat cells obviously remain intact since lipid can reaccumulate with time, or by the use of purified insulins. It is probable that the usual insulin preparations are lipolytic, lipolysis being a direct effect, or mediated by other mechanisms (Ferland & Ehrlich, 1975).

Injections of insulin directly into the lipoatrophic regions have been reported to improve healing of the lipoatrophy (Collens, 1949; Watson and Calder, 1971). But these were still doubted up till recently. For even in 1970, Marble recommended that one should avoid giving insulin injections into the atrophic regions.

The highly purified insulins were introduced in 1970 (Levett and Korp, 1971; Levett and Korp, 1972; Galloway and Root, 1972; Galloway et al, 1975; Yue and Turtle, 1977; Caterson and Turtle, 1978). These are insulins purified to 99% by anion-exchange chromatography, which removes high molecular-weight components. They have been found to be less allergenic than the regular insulins. Among the purified insulins in the market include "single-peak" (SP) and "single-component" (SC) by Lilly, "rare-immunogenic" (RI) by Nordisk and "monocomponent" (MC) by Novo.

Successful therapeutic trials with highly purified insulins in lipoatrophy was first reported in 1973 by Wentworth et al, Korp and Levett, and Bruni et al. Subsequently, other reports have followed (Teuscher, 1974; Teuscher, 1975; Ferland and Ehrlich, 1975; Hulst, 1976). Our experience with this case illustrates the usefulness of monocomponent (MC) Lente insulin in the treatment of lipoatrophy. When purified insulins are injected directly into the lipoatrophic areas, the change is rapid and usually permanent. However, in some cases, there was caving-in again when injection sites were changed (Ferland and Ehrlich, 1975). In a fairly large series (Wentworth et al, 1973), treatment with purified insulins resulted in improvement of the lipoatrophy in 90% of the cases, while the remaining 10% showed no improvement even after a year of treatment. The treatment failure may be due to factors other than the purity of the insulin preparation.

It is significant that lipoatrophy occurs more frequently in females, as is our patient. It has been sug-

gested (Hulst, 1976) that insulin-induced lipoatrophy is related to the subcutaneous fat mass. As the subcutaneous fat mass is greater in females, they are more prone to lipoatrophy as a consequence. This is an interesting proposition which remains to be tested.

The non-development of lipoatrophy in patients using purified insulins (Teuscher, 1974; Teuscher, 1975; Ferland and Ehrlich, 1975; Hulst, 1976) is noteworthy. In addition, due to the increased tendency of antibody formation to insulin, and the longer duration of insulin therapy in younger individuals, it is logical to use an insulin preparation which is not antigenic at all or only slightly so (Teuscher, 1975). A strong case therefore exists, for the routine use of purified insulin in all juvenile diabetics, particularly females, as they are more prone to lipoatrophy. Thus, this disfiguring side-effect of insulin therapy can be prevented or minimised.

It is interesting to note that a case of hypertrophy of the adipose tissue at the injection site has been recorded with the use of single-peak insulin (Ferland and Ehrlich, 1975).

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