Topically Applied Isophane Insulin (NPH) in Pluronic Lecithin Organogel

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When she was 17 years of age, a 24-year-old Caucasian woman was diagnosed as having insulin-dependent diabetes. For several years, her treatment consisted of isophane insulin (NPH) suspension at a dose of 10 to 15 units given subcutaneously in the morning and evening. About 9 months ago, subcutaneous lispro insulin (Humalog) was added to her therapy; it was prescribed as a sliding-scale dose of 3 to 5 units/dose based on the results of blood serum glucose testing 3 times a day before meals.

This patient became aware of a topically applied insulin in a Pluronic lecithin organogel (PLO) that had been used on a diabetic dog, as well as treatment with an insulin inhaler that was being studied in an investigational trial. In November 2000, she contacted us to discuss obtaining a topically applied insulin; she was tired of taking her daily insulin injections. After we had investigated the preparation of such an insulin, we explained the formulation and its use to the patient, whose physician agreed to prescribe it for her at her request. The physician was very interested in the outcome of treatment because of his large patient base of diabetics. This patient is very compliant and is diligent about following her protocol. She keeps a log of her diet and notes the doses of insulin she uses. She is not overweight. In September 2000, the result of this patient’s hemoglobin A1c (Hb A1c) test was 6.4%. The goal of therapy was to achieve (in a topically applied dosage form) the results provided by the subcutaneous maintenance dose of insulin.

We used a lipoderm base in our first compound of the NPH insulin. Lipoderm was used to help drive the large insulin molecule through the skin; the NPH insulin was at a concentration of 30 units/mL. The patient was instructed to rub the 30-unit (1 mL) dose in divided parts in the morning and in the evening on three areas of her body: the abdomen; the area just above the armpit and upper shoulder, which provides a long-acting effect; and the wrist, which provides an immediate effect. In the diabetic dog mentioned by the patient, the topically applied dose of insulin was found to be successful at 3 times the subcutaneous dose; for that reason, this patient’s dose of 30 units was prescribed. The patient’s blood serum glucose test results indicated that the topically applied 30-unit dosage of NPH insulin in a lipoderm base applied twice a day was effective and that she no longer had to use the subcutaneous lispro insulin. However, she complained that the lipoderm was watery to the touch and was difficult to rub into the skin. She asked if the preparation could be thickened. We tried compounding a stronger concentration of 60 units/mL; it was more watery than the formulation of 30 units/mL, so we did not dispense it to the patient.

Our second dispensed formulation was mixed at a concentration of 30 units/mL, but we used 20% PLO as a base. The patient complained that this formulation was too sticky. Our third formulation was mixed at the same concentration (30 units/mL) in a 1:1 base of 20% PLO and lipoderm. The insulin was dissolved in the PLO during the compounding process. In March 2001, after 5 months of this therapy, the patient began to experience an increase in her blood serum glucose level in the morning. Her doctor recommended that she add an additional dose of the 30 unit/mL compounded product of insulin in a 1:1 base of 20% PLO and lipoderm during the day. The patient was then applying 30 units 3 times a day.

At her annual appointment with her physician in June 2001, the patient’s Hb A1c level was 7.3%. At the time of that appointment, she had been experiencing a tremendous amount of stress as she completed her last college semester before graduation. Although her Hb A1c level had increased, her physician was pleased with her response to therapy. He instructed her to continue treatment and to return for re-evaluation in 6 months. At the time of this writing, she feels great and loves not hav-
Customized Hormone Replacement Therapy for Multiple Physical Complaints in a Middle-Aged Woman

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A 42-year-old woman presented to the clinic complaining of irregular menstrual cycles, arthritis of the knees, intolerance to cold, fatigue, and cramps in her legs and feet. Her physical examination was negative except for obesity (weight, 249 lb; height, 67 in.) Her medications at the time were as follows: The serum laboratory values for this patient were obtained on day 22 of her menstrual cycle, which were as follows:

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Normal Value</th>
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<tbody>
<tr>
<td>Testosterone (total)</td>
<td>68 ng/dL</td>
<td>0.55 - 3.55 ng/dL</td>
</tr>
<tr>
<td>TSH</td>
<td>0.55 mIU/mL</td>
<td>0.89 - 4.0 mIU/mL</td>
</tr>
<tr>
<td>T4</td>
<td>3.2 pg/mL</td>
<td>1.14 - 4.9 pg/mL</td>
</tr>
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The patient was given the option of continuing her progesterone regimen or starting to take progesterone at the same dosage 2 days later in her cycle. As an alternative, the patient could stop the progesterone the day before menstruation and begin the regimen the day 26 instead of day 28. She opted to continue with her initial regimen because of the improved condition in her knees and ankles. No changes were made in her thyroid treatment because the symptoms of inadequate thyroid hormone had disappeared. Because of her eudystrophia, I anticipate an improvement in this patient's lipid values, which are to be evaluated 3 months after her follow-up appointment. Evaluations of thyroid hormones should be repeated 6 months after that follow-up appointment and every 6 to 12 months thereafter.

Prescriptions were written for progestrone 200 mg sustained-release SR capsules, which were intended to be ingested by the patient at bedtime on cycle days 12 and 13 and 2 capsules daily on cycle days 14 through the end of the menstrual cycle (10 mg/kg to be applied to the forearm or inner thigh in a dosage of 2 mg each morning) was ordered.

I usually evaluate the level of estradiol and sometimes the estrone level to determine the approximate ratio of estrogen to progesterone, which is deposited in the bone. This ratio is also important. The estradiol level of this patient was within normal limits. I did not obtain her estrone level because of her body composition. Obese individuals usually have an increase in aromatase activity because of increased body fat, as well as elevated insulin levels. This insulin-resistant state increases androgen levels as well as central body fat, which leads to a higher estradiol level.

Treatment was initiated with a split-dose regimen of thyroid replacement because the patient had a low estradiol level and normal T4 and T3 values. The 4.5 mg/day dose was lowered to 3 mg/day. This was decreased to 1.5 mg/day because of the patient's psychomotor retardation. At this time, the patient began to experience an improvement in her symptoms, and the treatment was continued. The patient was given the option of continuing her progesterone regimen or starting to take progesterone at the same dosage 2 days later in her cycle. As an alternative, the patient could stop the progesterone the day before menstruation and begin the regimen the day 26 instead of day 28. She opted to continue with her initial regimen because of the improved condition in her knees and ankles. No changes were made in her thyroid treatment because the symptoms of inadequate thyroid hormone had disappeared. Because of her eudystrophia, I anticipate an improvement in this patient's lipid values, which are to be evaluated 3 months after her follow-up appointment. Evaluations of thyroid hormones should be repeated 6 months after that follow-up appointment and every 6 to 12 months thereafter.

Adequacy of Slow-Release Morphine Sulfate Capsules Variates with Formulation


Pharmacists are often asked to compound slow-release morphine sulfate capsules in dosages that are not commercially available to treat severe pain. However, that practice is controversial. Bogner and colleagues used a United States Pharmacopeia (USP) type II dissolution apparatus to evaluate the release of six formulations of 300-mg morphine sulfate sustained-release capsules. Two formulations (formulations I and II) were prepared to the protocol of this patient

<table>
<thead>
<tr>
<th>Literature Summaries</th>
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<tr>
<th>Premedication with Oral Ketamine Is Unsuitable for Upper Airway Procedures in Children</th>
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Orally administered ketamine has been used as a premedication in adults and children because it attenuates pain and produces a tranquilizing effect.

However, when the level of hydroxypropyl methylcellulose (Methylcellulose) was increased to the level of morphine sulfate was prolonged and the amount of drug released during the first hour was reduced. One formulation of encapsulated capsules varied with the type of drug used, and the release could be sustained significantly beyond that of the original formulation. The authors concluded that because the release rate was increased agitation that occurs in the gastrointestinal tract when medication is taken after a meal reduces the rate of dissolution and that formulations were superior, but the preparation of encapsulated compressed pellets may be too labor-intensive for most compounding pharmacies.