Brief Clinical Note

Insulin Adsorbance to Polyvinylchloride Surfaces with Implications for Constant-infusion Therapy

Lance Peterson, M.D., Jeanne Caldwell, M.T., and James Hoffman, M.D.,†*
St. Paul and Minneapolis

SUMMARY

Because of the current interest in constant intravenous infusions of insulin for hyperglycemic conditions, we have re-examined the problem of insulin adsorption to the solid surfaces of commonly used infusion sets. Using both labeled and unlabeled insulin, we have compared solutions with and without albumin through various methods of delivery. An infusion system incorporating a 50-ml. wash-out with a solution of 25 U. regular insulin in 500 ml. normal saline permits delivery of at least 75 per cent of expected insulin for the first 50 ml. of the infusion and 100 per cent thereafter. After the first 20 ml. of the infusion, the per cent insulin recovered from the system is identical to that observed when albumin was added to the infusion solution at a concentration of 1.25 gm. per cent.

From these data, we conclude that if an insulin concentration of at least 25 U./500 ml. is used, and if 50 cc. is washed through the infusion apparatus before treatment of a hyperglycemic patient is instituted, no extra protein additives are necessary. DIABETES *25*:72-74, January, 1976.

Adsorption of insulin from solution to solid surfaces was first described in 1951.[1] The adsorption was shown to be greatest at neutral pH's and inhibited by the addition of albumin. In 1959, Hill found significant adherence of radiolabeled insulin to Pyrex, siliconized glassware, and polyethylene reagent bottles.[2] He reported decreased adsorption of tracer amounts of insulin with the addition of 5 per cent gelatin. Sönksen found that the addition of unlabeled insulin was an effective method of preventing the adsorbance of labeled insulin to glassware.[3] Weisenfeld subsequently confirmed these observations when she reported proportionately decreasing adsorbance of radiolabeled insulin with increasing quantities of carrier insulin.[4] Recently, however, Petty showed marked adsorption of insulin to glassware even in the presence of albumin.[5]

Interest in low-dose constant insulin infusion in the management of diabetic ketoacidosis has raised questions pertaining to the method of insulin administration. Most studies have included albumin in the infusion solution to minimize insulin adsorption by the infusion apparatus.[6-8] However, a clinical study using infusion protocols with and without albumin revealed no discernible differences in the recovery of these two patient groups.[9]

Because of the conflicting data on insulin adsorbance and the interest in the use of insulin infusions for ketoacidosis, we have evaluated several solutions for administration of insulin by slow intravenous infusion. This was done to determine the need for protein other than insulin in the infusion solutions used for the low-dose infusion therapy of ketoacidosis and other hyperglycemic states.

METHODS AND MATERIALS

The infusion solutions tested were 500-ml. samples of 0.9 per cent sodium chloride and lactated Ringer's

*Minneapolis Veterans Administration Hospital, Department of Medicine, Infectious Disease Section (111F), Minneapolis, Minnesota 55417.

†Minneapolis Veterans Administration Hospital, Assistant Chief—Medicine, Department of Medicine (111), Minneapolis, Minnesota 55417.

From the University of Minnesota, Department of Medicine, St. Paul Ramsey Hospital, St. Paul, Minnesota 55101.

Accepted for publication October 11, 1975.

solution‡ containing 25 U. regular insulin§ or 50 mU. ^{125}I radiolabeled insulin,[10] or both. Human serum albumin¶ was added to some experiments with each infusion solution at a concentration of 1.25 gm. per cent to allow comparison with solutions containing insulin alone. All infusion solutions were initially mixed in volumetric flasks and then placed in 500-ml. Travenol polyvinylchloride infusion bags.‡ The infusion bags were connected to 100-ml. burette solution administration sets// for collection of samples. One-milliliter samples taken from the initial volumetric flask mixture served as controls (100 per cent). One-milliliter samples were taken from the infusion solution one minute and 24 hours after placement into the polyvinylchloride bags to determine adsorbance to the bags. Consecutive one-milliliter samples were collected after the infusion solution had passed through the complete infusion apparatus. Sampling of the solution was begun either immediately as it passed from the infusion apparatus, or after a 50-ml. wash-out of the system with the infusion solution. All solutions containing ^{125}I-radiolabeled insulin were collected directly into counting vials in 1-ml. fractions on a Buchler 200 collector and counted on a Packard model 5120 gamma-counter for one minute. Two hundred samples were collected for each experiment with radiolabeled insulin. Solutions with only unlabeled insulin were collected directly into vials containing radioimmunoassy reagents plus albumin and assayed for insulin by radioimmunoassay.[11] Twelve to fifteen samples were collected over an eight-hour infusion for the radioimmunoassay experiments. Volumes in both collections were determined by an automatic drop counter. Infusion rates were held constant for each experiment with a constant-infusion pump. Experiments were run at flow rates of 10-50 ml./hr., which correspond to flow rates used to administer the quantity of insulin found to be clinically effective in the constant-infusion management of hyperglycemia.[6-9]

All results were recorded as per cent of initial volumetric solution radioactivity or insulin level for each experiment. Ten experiments were run with an infusion solution of ^{125}I insulin in tracer amounts with 25 U. regular insulin in 500 ml. 0.9 per cent sodium chloride combined with a 50-ml. wash-out of the infusion apparatus with the infusion solution before any samples were collected. One to five experiments were performed with all other infusion solution and system combinations tested.

Significance was determined by Student's t test.

RESULTS

Infusion solutions containing no albumin and delivered without prior washout of the infusion system lost up to 70 per cent of the labeled insulin or assayable insulin in the initial 10 ml. collected. The recovery of insulin was greater than 90 per cent of control values in all studies when 100 ml. had passed through the infusion systems. When 50 ml. of the infusate was passed through the system prior to collection for assay, the loss of insulin in the first 10 ml. fell to 30 per cent that of control values and returned toward control levels, as seen in figure 1.

The addition of albumin to the infusate at a concentration of 1.25 gm. per cent prevented the loss of labeled insulin or assayable insulin without a wash-out of the infusion system. Recovery of insulin was enhanced by the presence of albumin in the solution over that of the insulin saline solution obtained following a 50-ml. washout. This difference became insignificant after an additional 20-ml. had passed through the system (figure 1).

No differences in recovery were observed when lactated Ringer's solution was substituted for normal saline.

The variance of flow rates in milliliters per hour within the ranges tested did not affect insulin recovery.

DISCUSSION

The apparent difference between our data and those of Petty, who found greater losses of insulin in infusions, is difficult to explain.[5] The direct collection of samples into the appropriate assay tubes may have eliminated some of the losses that occur during sample transfer and partially explain the differences in data. The use of direct measurements of labeled and nonlabeled insulin as controls rather than a calculated control based on a commercial preparation may also have contributed to the observed discrepancies. From our data, we conclude that the omission of albumin from infusion solutions is possible if the solution is comprised of regular insulin in normal saline at a

‡Travenol Laboratories 0.9 per cent sodium chloride injection (pH 5.0), U.S.P., and lactated Ringer's injection (pH 6.5), U.S.P., 500 ml. Viaflex containers.

§Eli Lilly beef and pork crystalline zinc insulin (U-100).

¶Armour Pharmaceutical Company human serum albumin 25 gm. per cent.

//Travenol Laboratories Buretrol 100-ml. burette solution administration set with membrane value minidrip.

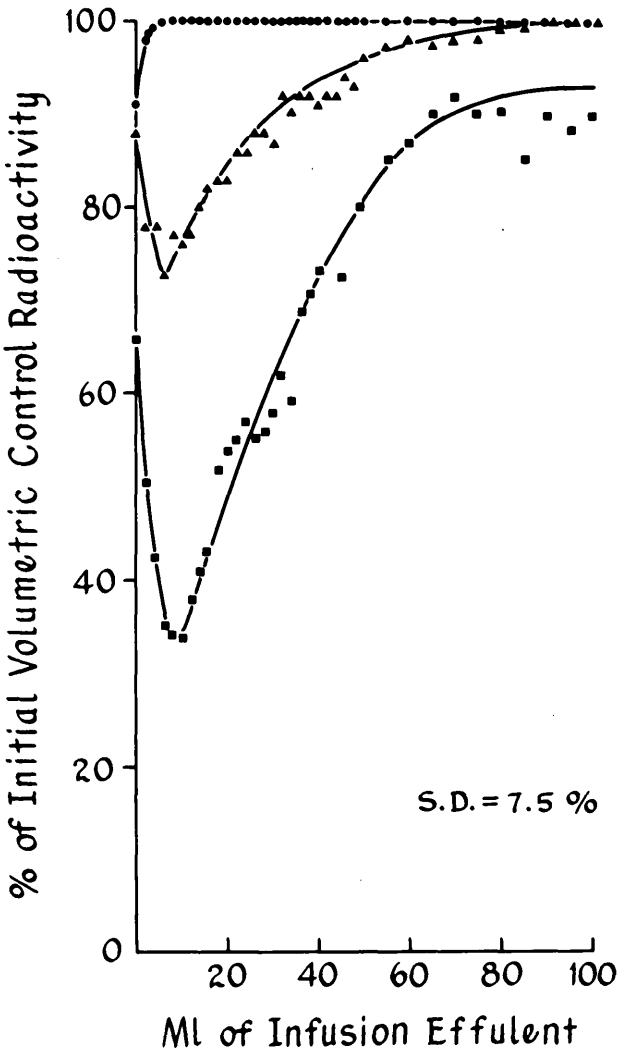

FIG. 1. Insulin recovered from the infusion apparatus for 50 mU. ^{125}I-insulin plus 25 U. regular insulin in 500 ml. normal saline with a 50-ml. wash-out prior to the start of sample collection (●-●); the same solution without a 50-ml. wash-out (■-■); and the same solution with 1.25 gm. per cent albumin added, with no washout prior to sample collection (▲-▲). Each figure represents a 1-ml. sample, with radioactivity in each sample represented as per cent of radioactivity in a 1-ml. sample of the initial volumetric control.

concentration of 25 U./500 ml. or greater and a 50-ml. "wash-out" of the entire infusion apparatus is done prior to patient infusion. From the passage of 50-ml. through the entire apparatus prior to patient infusion, we presume that the sites of nonspecific binding are saturated and that further loss of insulin through adsorbance is minimal.

REFERENCES

[1]Ferrebee, J. W., Johnson, B. B., Mithoefer, J. C., and Gardella, J. W.: Insulin and adrenocorticotropin labeled with radioiodine. Endocrinology *48*:277-83, 1951.

[2]Hill, J. B.: The adsorption of I^{131}-insulin to glass. Endocrinology *65*:515-17, 1959.

[3]Sönksen, P. H., Ellis, J. P., Lowy, C., Rutherford, A., and Nabarro, J. D. N.: A quantitative evaluation of the related efficiency of gelatine and albumin in preventing insulin adsorption to glass. Diabetologia *1*:208-10, 1965.

[4]Weisenfeld, S., Podolsky, S., Goldsmith, L., and Ziff, L.: Adsorption of insulin to infusion bottles and tubing. Diabetes *17*:766-71, 1968.

[5]Petty, C., and Cunningham, N. L.: Insulin adsorption by glass infusion bottles, polyvinylchloride infusion containers, and intravenous tubing. Anesthesiology *40*:400-04, 1974.

[6]Kidson, W., Casey, J., Kraegen, E., and Lazarus, L.: Treatment of severe diabetes mellitus by insulin infusion. Br. M. J. *2*:691-94, 1974.

[7]Genuth, S. M.: Constant intravenous insulin infusion in diabetic ketoacidosis. J.A.M.A. *233*:1348-51, 1973.

[8]Semple, P. F., White, C., and Manderson, W. G.: Continuous intravenous infusion of small doses of insulin in treatment of diabetic ketoacidosis. Br. M. J. *2*:694-98, 1974.

[9] Page, M. McB., Alberti, K. G. M. M., Greenwood, R., Gumaa, K. A., Hockaday, T. D. R., Lowy, C., Nabarro, J. D. N., Pyke, D. A., Sönksen, P. H., Watkins, P. J., and West, T. E. T.: Treatment of diabetic coma with continuous low-dose infusion of insulin. Br. M. J. *2*:687-90, 1974.

[10]Hunter, W. M., and Greenwood, F. C.: Preparation of iodine-131 labelled human growth hormone of high specific activity. Nature *194*:495-96, 1962.

[11]Yalow, R. S., and Berson, S. A.: Immunoassay of endogenous plasma insulin in man. J. Clin. Invest. *39*:1157-75, 1960.