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EFFECT OF RAW CAMEL MILK IN TYPE 1 DIABETIC PATIENTS: 1 YEAR RANDOMISED STUDY

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ABSTRACT

The efficacy of camel milk consumption as an adjunct to routine diabetic management in maintaining long-term glycaemia control in type I diabetes was assessed during a 52 week randomised study. Throughout the duration of the study, 12 randomly assigned patients underwent routine diabetic management (diet, exercise and parental insulin supplementation) and 12 randomly assigned patients additionally undertook daily consumption of raw camel milk (500ml/day). In both groups, the dose of parenteral insulin administration was adjusted to maintain an euglycaemic state. Glycosylated haemoglobin (HbA_1c) and body mass index (BMI) were measured at the initiation of the study and monitored at 3 monthly intervals. Additionally, plasma insulin, C-peptide and anti-insulin antibodies were measured at the beginning and end of the study. In the group receiving camel milk, there was a significant increase in MBI (17 ± 4.4 to 19.7 ± 2.97; $p < 0.001$) and a significant reduction in HbA_1c (7.8 ± 1.38 to 6 ± 0.96; $p < 0.001$), mean blood glucose (119 ± 19 to 95.42 ± 15.70; $p < 0.001$) and necessary insulin dose (32 ± 12 to 17.88 ± 12.40; $p < 0.005$) compared to the values at the initiation of the study. There was no significant change in c-peptide (0.18 ± 0.04 to 0.24 ± 0.07) or anti-insulin antibodies (22.92 ± 5.45 to 21.84 ± 7.34).

We have demonstrated that the consumption of camel milk in type I diabetes results in a significant reduction in the dose of insulin required to maintain long-term glycaemic control. Based on our results, camel milk consumption, may therefore, be considered as a useful adjunct to parenteral insulin administration in the management of type 1 diabetes.

Key words: Camel milk, glycaemic control, insulin, type 1 diabetic patients

Primary treatment of type 1 diabetes is insulin replacement. However, at present entire physiological insulin replacement cannot be achieved in clinical cases and metabolic disturbances cannot be normalised. The metabolic control in 2873 children and adolescents was studied at 21 centres of Europe, Japan and the United States (Moriensen and Hougaard, 1997 and Holl et al, 2003). In this large international study it was staggeringly obvious that despite unacceptable psychological emotional and social price, the level of glycaemic control achievable in children with modern insulin therapy is far from satisfactory. Insulin therapy is still the best treatment but in many countries needle phobia and cost of treatment forces these patients to adopt alternative therapies.

In this connection we have heard many anecdotal stories, which describe the use of camel milk in type-1 diabetes mellitus. There is also an account in memories of Emperor Jahangir (1579-1627 AD) about the usefulness and acceptability of camel milk (Rogers, 1989). It was found that one of the camel milk proteins has many characteristics similar to insulin (Beg et al, 1989). Furthermore, it does not form a coagulum in an acidic environment (Wangoh, 1993). This lack of coagulum formation allows the camel milk to pass rapidly through the stomach together with the specific insulin like protein/insulin and remains available for absorption in the intestine. Radioimmunoassay tests of camel milk has revealed high concentration of insulin i.e. 52 micro unit/ml. The concentration of insulin in human milk is also significantly higher (60.23 ± 41.05 micro unit/ml) whereas it is low in cow milk (16.32 ± 5.98 micro unit/ml) (Shehadeh et al, 2001). There is strong evidence that an oral insulin products would provide insulin in a more physiological manner, resulting in a decrease in peripheral insulin concentrations this “insulinsing” the live (Gwinup et al, 1991 and

Hoffman and Siv, 1997). Recently, scientists have developed hexylinsulin monoconjugate 2(HIM2), in which a single amphiphilic olignmer is covalently linked to the free amino group on the lys-ß 29 residue of recombinant human insulin via an amide bond (Still, 2002). HIM2 alterations in physio-chemical characteristics which resists the enzymatic degradation and facilitates absorption.

The aim of the present study was to determine the long-term efficacy and safety of camel milk as an adjunct to insulin therapy in patients with type 1 diabetes.

Material and Methods

A total of 24 type 1 diabetic patients were randomly recruited from the outpatient diabetic clinic in PBM Hospital, Bikaner, India. Ethical committee of S.P. medical College, Bikaner approved the protocol and all subjects gave written consent before participation in this study. The patients were advised to follow a strict t diet, exercise and insulin treatment regime for 1month. During this period frequent monitoring of blood sugar was done to maintain euglycaemia. After a one- month period these patients were randomly divided into two groups. Group 1 patients (N=2) received usual care i.e diet, exercise and insulin and group 2 patients (N=12) received 500ml of fresh camel milk daily for 12 months in addition to the usual care. Patients with any acute metabolic complications like hypoglycaemia, ketoasidosis, cardiovascular event, renal or acute infections were not included in the study.

Blood sugar was measured twice weekly before breakfast and dinner, and insulin doses were titrated weekly according to the blood sugar levels. All patients were provided with a one touch profile memory glucometer (life Scan), along with strips for self monitoring of blood glucose concentrations. They were also instructed to record the glucose readings and insulin doses in diaries. Vital signs, body weight, haematologic and laboratory parameters, glycosylated haemoglobin (HbA_1c) were monitored throughout the study. Patients also monitored symptoms of hypoglycaemia and, if possible, obtained glucose readings when hypoglycaemia symptoms occurred. Anti-insulin antibodies were measured at the beginning and end of the study. Safety evaluations included vital signs and laboratory parameters. Severe hypoglycaemia was defined as an event requiring the assistance of another individual or the administration of glucagons or intravenous glucose and was expressed as event rate per patient year of exposure, thus accounting for multiple events in the same patients and for differences in time of exposure to study medication.

Plasma glucose concentration was measured using the glucose oxidise method. Lipid profile was estimated by a fully automated Biochemistry Analyser Hitachi 717. Plasma insulin and C-peptide were estimated by chemiluminescence (CLIA test) using an automated chemiluminescence analyser (Imulite, DPC, USA). Anti-insulin antibodies were estimated by radioimmuno assay HbA_1c was measured by high performance liquid chromatography (HPLC), variant Boiorad, USA.

The baseline difference between the two groups were analysed using the t-test for independed samples assuming heteroscedastic variance. Changes from baseline to end point were analysed using MANCOVA. Age, sex and body mass index (BMI) were taken as covariates. The groups were taken as independent variables. Insulin dose, fasting blood sugar (FBS) and HbA c were taken as dependent variables and analyse independently.

Results

Demographic characteristics of both the group were comparable. The group 1 (control group) and group 2 (camel milk group) were similar in age (years ±7.5 vs 15 years ± 9.4), Sex (10M. 2F in both groups), BMI (17± vs 17 ±4.4), FBS (121 + 17 VS 119 + 19), plasma insulin (7.73 ± 2.42 vs 6.91 2.13), c-peptide (0.22 ±0.03 vs 0.18 ± 0.04), and insulin antibody (22.20 ± 7.69 vs 22.92 ± 5.45) at mean dose of insulin required (33±11 vs 32±12).

After 1 year of treatment with fresh camel milk there were a statistically significant change in both (17± 4.4 to 19.7 ±2.97, p<0.001), FBS (119 ± 19 95.42 ± 15.70 P<0.001), and in HbAıc (7.8 ± 1.386 ± 0.96, p<0.001), in group 2. But when MACOVA for FBS was used, we observed significant variance (Fig 1). Similarly when MANCOVA for HbAıc was used we observed overall a significant variance in HbAıc (Fig 2). The parameters were either unchanged or there was slight increase in group 1 patients (table 1). There was no significant change in fasting plasma insulin and c-peptide levels in either group. There was significant reduction in the mean doses of insulin (32±12 vs 17.83 ± 12.40, p<0.005) in patients receiving camel milk (table 1, fig 3). When MANCOVA was used for insulin dose there was overall significant variance in insulin doses. There was no significant reduction in mean doses of insulin in individual patients not receiving camel milk (N=12. Fig 4). While in the camel milk consuming group every patient had a significant reduction in the doses of insulin. In one patient there was no requirement for insulin therapy after 8 months of camel milk consumption (fig 5). There were no significant changes in anti insulin antibodies (22.92 ± 5.45 to 21.84± 7.34).

Nausea, flatulence and diarrhoea were the only treatment-emergent adverse events which disappeared spontaneously. No severe hypoglycaemic event or DKA were reported in either group. Anti insulin antibody titres were around 20% even after 1 year i.e. insignificant.

Table 1. Effect of camel milk on glycaemic control and insulin requirement in type 1 diabetic patients

Group 1: Control group			
Variables	**Before Treatment**	**After Treatment**	**P value**
BMI (Kg/ m²)	17 ± 5.2	18.2 ± 3.8	NS
HbAıc (%)	7.54 ± 1.38	7.63 ± 1.03	NS
Dose of Insulin (units/ day)	33 ± 11	30.16 ± 8.45	NS
Mean Blood Sugar (mg/ dl	121 ± 17.3	105.25 ± 14.50	0.041
Plsama Insulin (Uiu/ ml)	7.73 ± 2.42	19.54 ± 0.43	0.041
C.Peptide (ng/ ml)	0.22 ± 0.03	0.21 ± 0.06	NS
Anti Insulin Antibody (%)	22.20 ± 7.69	19.70 ± 8.40	NS
Group 2: Camel Milk Group			
Variables	**Before Treatment**	**After Treatment**	**P value**
BMI (Kg/ m²)	17 ± 4.4	19.7 ± 2.97	0.001
HbAıc (%)	7.8 ± 1.38	6 ± 0.96	0.001
Dose of Insulin (units/ day)	32 ± 12	17.83 ± 12.40	0.005
Mean Blood Sugar (mg/ dl	119 ± 19	95.42 ± 15.70	0.001
Plsama Insulin (Uiu/ ml)	6.91± 2.13	18.17 ± 7.12	0.03
C.Peptide (ng/ ml)	0.18 ± 0.04	0.24 ± 0.07	NS
Anti Insulin Antibody (%)	22.92 ± 5.45	21.84 ± 7.34	NS

NS = Not Significant

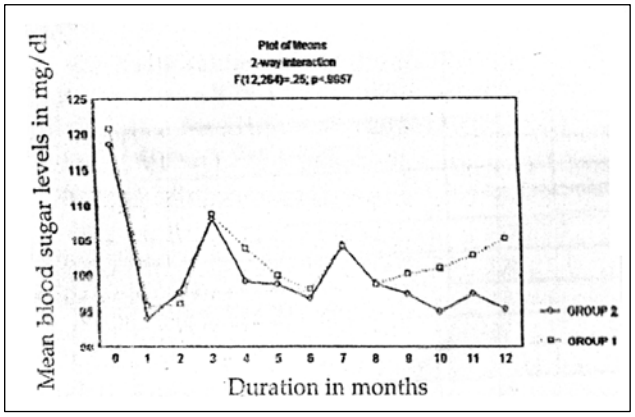

Fig. 1. Mean blood sugar levels measured over 12 months in patients given fresh camel milk (group 2) and no camel milk (group 1).

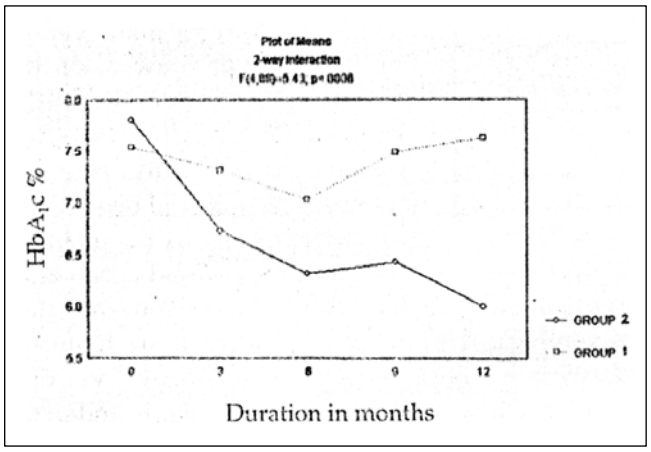

Fig. 2. HbA_1c results measured over 12months in patients given fresh camel milk ((group 2) and no camel milk (group 1).

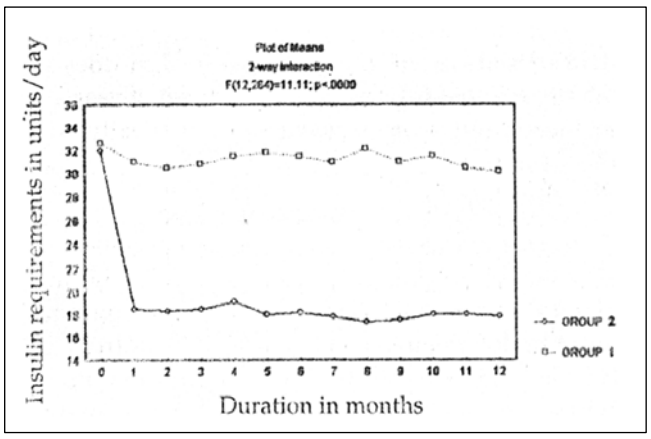

Fig. 3. Insulin requirements measured over 12months in patients given fresh camel milk ((group 2) and no camel milk (group 1).

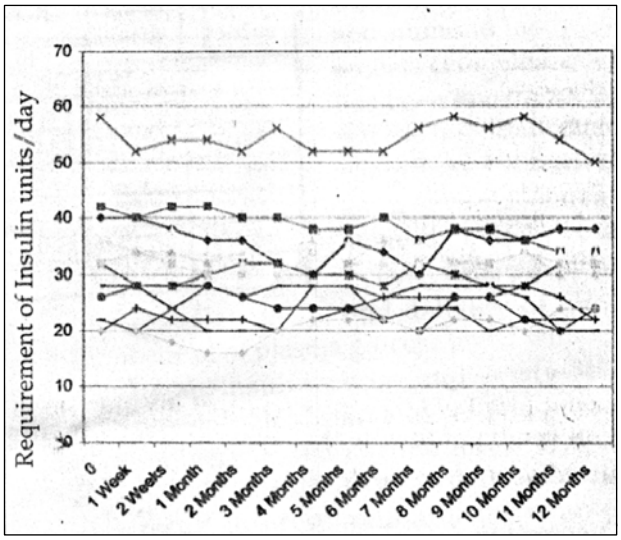

Fig. 4. Mean insulin doses per day in individual patients of control group 1 (n = 12).

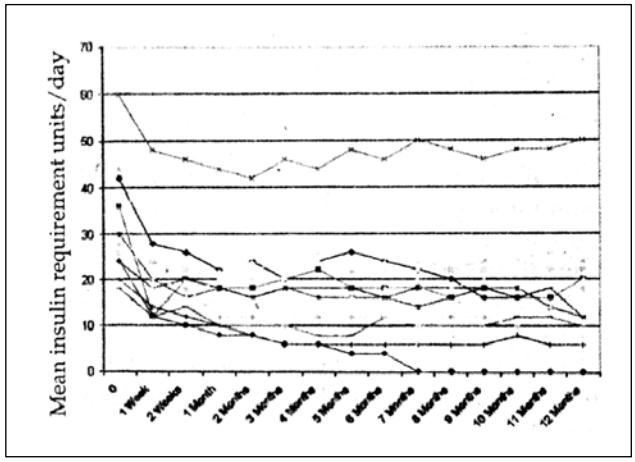

Fig. 5. Mean insulin doses per day individual patients of camel milk consuming group 2 (n = 12).

Discussion

The present study was performed to observe the role of camel milk in achieving glycaemic control in type –1 diabetic patients. We observed a significant improvement in mean BMI (17±4.4 to 9.7 ± 2.97, $p<0.001$) after 1 year of camel milk treatment. The positive effects in weight gain may be because of good nutritional value of camel milk.

The important observation of this study was the significant reduction in insulin doses to obtain glycaemic control along with significant improvement in HbAıc level at the end of 1 year in patients taking camel milk. The requirement for mean doses of insulin/ day before treatment in patients of group 2 was 32 ± 12. It came down rapidly initially and then gradually to a mean level of 17.83±12.40, ($p<0.005$). Only one patient out of 12 required the same doses of insulin and the other 11 patients had a reduction in the required amount necessary to maintain euglycaemic blood level.

Camel Milk was found to contain approximately 52 micro unit/ml insulin and it may be the reason for a lesser requirement of insulin in diabetic patients receiving camel milk. In one patient there was no requirement for insulin therapy after 8 months of camel milk consumption. The therapeutic efficacy of camel milk observed in the current study is consistent with earlier clinical trials in this area (camel milk + insulin therapy) (Agrawal et al, 2003a,b). Breitling (2002) believed that camel milk had an anti-diabetic activity possibly because of insulin-like activity, regulatory and immuno modulatory effect on beta cells. Oral insulin therapy has been known for many years but the important drawback is its coagulum formation in acidic environment such as the stomach, thereby neutralising its potency. The potential benefits of oral delivery of insulin include control of plasma glucose levels without peripheral hyper-insulinnaemia and restoration of the physiological pathway of endogenous insulin. Delivery of therapeutic levels of insulin via the portal route decreases hyperinsulinaemia and more result in preservation of the counterrgulatory responses to hypoglycaemia, with a concomita reduction in hypoglycaemic events (Davis et 1993; Oskarsson et el, 200 and Wan et al, 2000 Pozzilli et al (2000) in IMDIAB VII study indicates that an addition of 5 mg of oral insulin does not modify the course of the disease in the first year after diagnosis and probably does not statistically effect the humoral immune response against insulin (Pozzilli et al, 2000).

The lack of coagulum formation of camel milk may act as an effective vehicle to take the milk insulin unchanged to the intestine, and from that it can be absorbed even if some of it is destroyed in the passage. Beg et al (1986) has found that any acid sequence of some of the camel milk protein rich in half systine, which has some similarities with the insulin family of peptides.

The data of this study confirms a significance hypoglycaemic effect of camel milk when given an adjunctive therapy, presumably due to presence of insulin/insulin like proteins therapeutic efficacy may be due to lack of coagulum formation of camel milk in an acidic environment.

There is no doubt that the discovery and development of oral insulin for therapeutic use is a difficult task. It has been observed that oral administration of insulin did not prevent the deterioration of beta cell function in type –1 diabetic patients (Chaillous et al, 2000).

The main problem of using insulin viz bovine and porcine is that there are some possibilities of developing immunogenicity t that insulin, so further development has taken place to check this side effect in the form of human recombinant insulin. We also estimated change in this variable throughout the treatment period.

In conclusion. Camel milk, as an adjunct to insulin therapy, appears to be safe and efficacious in improving long-term glycaemic control, and helps in the reduction of insulin requirement in type 1 diabetic patients. Camel milk was well tolerated and its use was not associated with an increase in hypoglycaemic events.

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