A 40-year-old pregnant female patient presented with malaise, sore throat, and cough with neither abdominal nor back pain at 36 weeks of gestation. She was in no acute distress. Her white blood cell count was 9.5×10^9/l, C-reactive protein 18 mg/l, plasma glucose 60 mg/dl, and serum amylase 683 IU/l. Ultrasonography yielded no medically or obstetrically abnormal findings. Lack of signs of acute pancreatitis suggested acute tonsillitis or a common cold as a preliminary diagnosis.

Five days after the initial visit, she was admitted to our hospital in a coma. Her blood pressure was 129/86 mmHg; her pulse was 70 bpm. Arterial blood gas analysis showed pH 7.055 and base excess = −17.6 mEq/l. Her marked elevation of ketone bodies reflected severe ketoacidosis. Plasma glucose was 936 mg/dl, HbA_{1c} 5.4%, serum C-peptide 0.15 ng/ml, and serum amylase 307 IU/l. Ultrasonography revealed an intrauterine fetal death and no abnormalities in her pancreas. After treatment for ketoacidosis improved her consciousness level, an emergent cesarean section was conducted. Serological testing for autoantibodies was later reported as negative for islet cell antibodies, glutamic acid decarboxylase autoantibodies, and insulinoma-associated protein 2 antibodies. Final diagnosis was made as fulminant type 1 diabetes.

A diagnosis of fulminant type 1 diabetes is not made without an initial occurrence of DKA (1–4). However, timely measurement of serum amylase in the appropriate high-risk group for fulminant type 1 diabetes might enable early diagnosis. Sekine et al. (3) recently reported the flare-up of trypsin, elastase I, and lipase before DKA occurrence in a patient who had never been diagnosed as having type 1 diabetes. In our case, the serum amylase concentration flared-up before DKA occurrence. It decreased gradually from 683 to 307 IU/l at the onset, which showed the same pattern of response as that reported by Sekine et al. (3), who provided no amylase levels. In patients with fulminant type 1 diabetes, hyperamylasemia at or after DKA onset is of diagnostic value (1–4). However, hyperamylasemia without the features of fulminant type 1 diabetes (absence of autoantibodies and normal HbA_{1c}) cannot be used to diagnose this disease because elevated amylase levels (although mostly of salivary gland origin) frequently accompany autoimmune DKA. On the other hand, we have also provided the time course of serum amylase before DKA onset, which might be of predictive value.

The cause of fulminant type 1 diabetes involves viral infection and pregnancy because flu-like symptoms are frequent (1,2), and some viral DNA have been detected in patients (2–4). Apparently, the disease's incidence increases in the latter term of pregnancy (2,4). In conclusion, pregnant women presenting with flu-like symptoms should have serum amylase levels measured. Subsequently, the time course of serum amylase concentration should be followed-up carefully to prevent this concealed life-threatening disease.

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Betel Nut Chewing Is Independently Associated With Urinary Albumin Excretion Rate in Type 2 Diabetic Patients

Betel nut chewing is associated with increased production of reactive oxygen species and inflammatory mediators (1), which could potentially cause kidney damage (2). This study investigated whether betel nut chewing could increase urinary albumin excretion rate (UAER) in 572 Taiwanese men (aged ≥45 years) with type 2 diabetes. Among them, 65 were chewers ≥5 years and 507 were nonchewers. Urinary albumin and creatinine concentrations, fasting plasma glucose and serum total cholesterol, triglycerides, and creatinine were measured as described elsewhere (3). Urinary albumin-to-creatinine ratio (ACR) ≥30.0 μg/mg was defined as albuminuria. Creatinine clearance (Ccr) was calculated from the Cockcroft-Gault formula (3). Statistical analyses were performed considering confounders including age, diabetic duration, smoking, BMI, blood pressure, metabolic control, and Ccr.

Results showed that chewers were significantly younger (56.4 ± 8.6 vs. 65.0 ± 9.5 years), had higher prevalence of smoking (89.2 vs. 62.2%), higher BMI (25.7 ± 3.5 vs. 24.8 ± 3.2 kg/m^2), poorer glycemic control (176.0 ± 71.9 vs. 158.8 ± 61.6 mg/dl), higher ln(ACR) (4.0 ± 1.7 vs. 3.5 ± 1.5 μg/mg), and higher prevalence of albuminuria (61.5 vs. 47.5%). However, diabetic duration, systolic and diastolic blood pressures, cholesterol, triglycerides, and Ccr were not significantly different. In multiple linear regression, the adjusted regression coefficient for ln(ACR) associated with betel nut chewing was 0.427 ($P < 0.05$). The multivariate-adjusted odds ratio for albuminuria in chewers versus nonchewers was 2.024 (95% CI 1.129–3.630). In stepwise models of multiple linear and logistic regression, betel nut chewing was selected as an independent variable associated with elevated ln(ACR) and albuminuria, respectively. Therefore, the kidney-damaging effect of betel nut chewing was consistent and independent of confounders.

Constituents of areca nut and *Piper betle* flower may exert sympathomimetic effects (4), which might elevate blood pressure leading to increased UAER. However, because the effect was independent of blood pressure, other mechanisms should have been in play. Reactive oxygen species and *N*-nitroso compounds can be formed in the oral cavity during betel nut chewing, and in vitro studies also demonstrated that betel nut components increased the release of inflammatory mediators including prostanoids, interleukin-6, and tumor necrosis factor-α (1). Increased oxidative stress and inflammation are also associated with glomerular damage and increased UAER (2). Therefore, the inflammatory mediators produced with betel nut chewing could be responsible.

In conclusions, betel nut chewing is independently associated with increased UAER and albuminuria in Taiwanese type 2 diabetic male patients in this cross-sectional observation. However, future prospective longitudinal studies are warranted for confirmation.

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Effect of Multifactorial Intervention on Diabetic Macular Edema

Clinical trials (1,2) have shown that intensive control of blood glucose and hypertension reduce development of clinically significant macular edema (CSME). Elevated HbA_{1c} (A1C) is a risk for persistent CSME (3). Gross proteinuria is associated with a 95% increase in the incidence of macular edema (4). However, the effect of control of systemic factors before focal laser photocoagulation is not known. We aimed to determine whether multifactorial intervention over 4–6 weeks before focal laser photocoagulation would reduce macular thickness.

In a prospective nonrandomized pilot study, 14 consecutive patients (10 men and 4 women, aged 44–65 years) with type 2 diabetes presenting with nonproliferative diabetic retinopathy and CSME underwent multifactorial interventions including single or multiple modifications in oral hypoglycemic agents (n = 10), atorvastatin (n = 11), antihypertensive drugs (n = 12), and losartan (n = 4) to control A1C, fasting and postprandial blood glucose, systolic and diastolic blood pressure, lipid profile, and 24-h urinary proteins. Detailed ocular examination at recruitment and 6 weeks after interventions included fundus fluorescein angiography and measurement of macular thickness using stratus optical coherence tomography done between 12:00 P.M. and 3:00 P.M. Quantitative data are shown as means ± SD. Intergroup comparison was performed by unpaired t test.

At 6 weeks postintervention, we found a statistically significant decrease in mean A1C (8.3 to 7.62%, $P < 0.01$), LDL (125.14 to 99.5 mg/dl, $P < 0.001$), fasting blood glucose (142.07 to 117.5 mg %, $P < 0.01$), systolic blood pressure (141.43 to 126.43 mmHg, $P < 0.002$), and diastolic blood pressure (87.14 to 81.54 mmHg, $P < 0.001$). There was significant decrease in mean retinal thickness in both central 1 mm (244.20 ± 64.30 to 220.30 ± 59.68 μm, $P < 0.001$) and 6 mm (282.87 ± 51.09 to 261.65 ± 40.08 μm, $P < 0.001$) of the macula that resulted in a trend toward improvement in visual acuity (logarithm of minimal angle of resolution 0.53 ± 0.29 to 0.52 ± 0.27).

Decreasing macular edema on optical coherence tomography with multifactorial control before laser photocoagulation is encouraging in the management of CSME. Reducing macular thickness facilitates application of a low-energy laser beam. Previously, we found that atorvastatin 6 weeks before focal laser photocoagulation reduced subfoveal migration of lipids in patients with macular edema and dyslipidemia (5). We propose larger studies to determine the role of optimizing systemic factors before laser in CSME.

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