The Correlation of β-Subunit Human Chorionic Gonadotropin Level in the Serum and First Morning Urine of Patients with Gestational Trophoblastic Disease

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Abstract

The purpose of this cross-sectional study was to determine the correlation of beta subunit human chorionic gonadotropin (β-hCG) level in the serum and first morning urine samples of patients with gestational trophoblastic disease (GTD). A total of 81 paired serum and first morning urine samples from 24 patients diagnosed with GTD, who had their follow-up at the Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital, Mahidol University. The paired serum and first morning urine samples were measured for β-hCG level, using enzyme-linked immunosorbent assay (ELISA). After logarithmic transformation, serum β-hCG level was strongly and significantly correlated to those of first morning urine samples, with the correlation coefficient of 0.97 ($p < 0.01$). Among the disease-remission group (serum β-hCG of less than 5 mIU/ml), the correlation coefficient was 0.52 ($p < 0.01$), which was still statistically significant. Stronger statistical significance was found in the disease-active group (serum β-hCG of 5 mIU/ml or higher), with the correlation coefficient of 0.95 ($p < 0.01$). We concluded that the level of serum β-hCG was strongly and significantly correlated with those of first morning urine samples, especially in patients with active disease. Determination of β-hCG level using first morning urine samples can be used as an effective mean in the follow-up of patients with GTD.

Key word : Human Chorionic Gonadotropin, Gestational Trophoblastic Disease, First Morning Urine

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Human chorionic gonadotropin (hCG) is a glycoprotein hormone, discovered in 1932[1]. It has been known as a valuable tumor marker for several tumors, especially gestational trophoblastic neoplasia (GTN). hCG has various subunits, and β-subunit is the most popular one in clinical practice[1]. The old assay for determining serum hCG has low specificity and may cross-react with other hormones, such as FSH, LH or TSH[2], so the value of the assay in following these patients was limited. Enzyme-linked immunosorbent assay (ELISA) was developed later, as well as the synthesis of high specific monoclonal antibody probe, making the test more sensitive, specific, and reliable[3]. It is possible to detect even very low titer of β-hCG in such a specimen as urine and saliva[4]. It was found that the amount of β-hCG in a 24-hour urine specimen had definite correlation with serum β-hCG concentration and could be used for monitoring progression of the disease as effective as its serum level[5,6]. Many studies showed that β-hCG was excreted in urine in a significant amount which could be used in clinical practice[7-10]. The objective of this study was to determine the correlation of β-hCG level in the serum and first morning urine samples of patients with GTD, treated at Siriraj Hospital.

MATERIAL AND METHOD

From June 1999 to February 2000, paired serum and first morning urine samples from patients with GTD, who had their follow-up at the Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Faculty of Medicine Siriraj Hospital, Mahidol University, were measured for β-hCG level, using the ELISA technique. Patients with renal diseases, abnormal renal function, urinary tract infection, diabetes mellitus, diabetes insipidus, and pregnancy were excluded from the study. The patients were divided into disease-remission and disease-active groups according to the level of serum β-hCG. Those with a serum β-hCG level of less than 5 mIU/ml were classified as disease-remission, while those with a serum β-hCG level of 5 mIU/ml or higher were the disease-active group.

Correlation coefficient of β-hCG level in serum and first morning urine of all patients, those with disease-remission, and disease-active were calculated. A $P < 0.01$ was considered significant.

RESULTS

A total of 81 paired serum and first morning urine samples from 24 patients with GTD were measured for β-hCG level. Of the 81 paired sam-

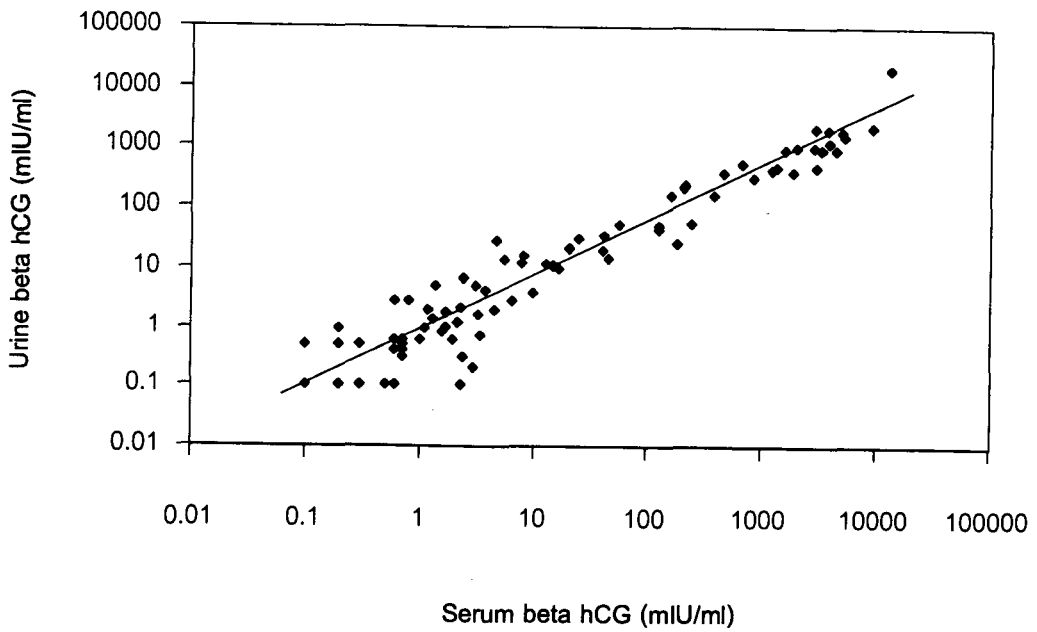

Fig. 1. Scatterplot of β-hCG level in serum and first morning urine of all patients (disease-remission and disease-active group).

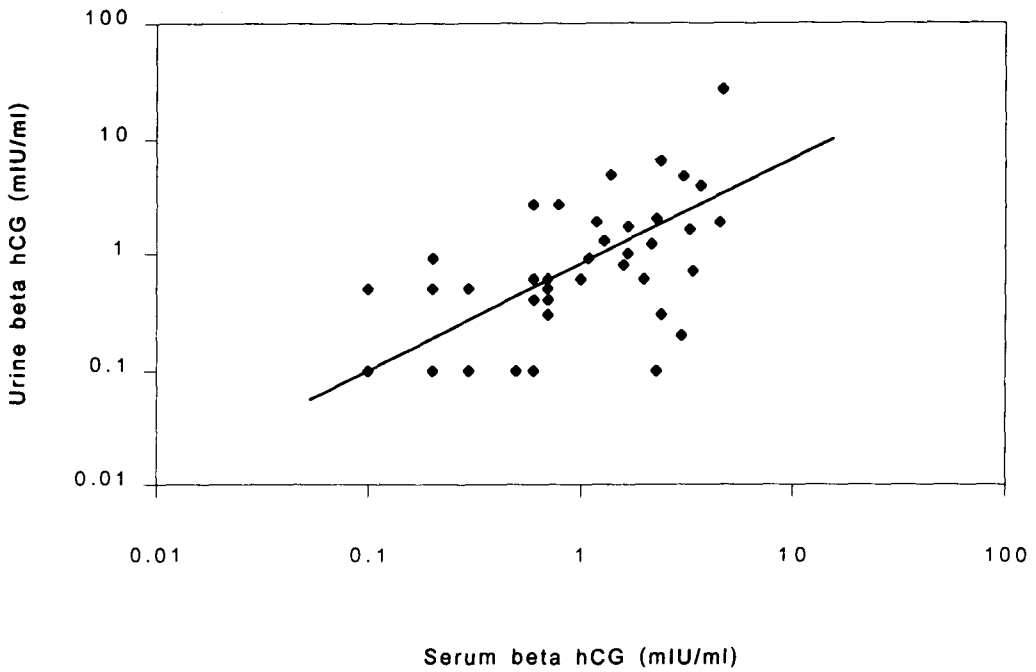

Fig. 2. Scatterplot of β-hCG level in serum and first morning urine of patients in disease-remission group.

ples, 41 were in the disease-active group and 40 were in the disease-remission group. The patients' ages ranged from 15 – 45 years with a mean age of 27.8±7.2 years. Eighteen patients were diagnosed with GTN, while 6 had hydatidiform mole. Of the 18 patients with GTN, 8 were treated with single agent chemotherapy and 2 were treated with combination regimens.

The logarithmic scale was used to show the distribution and correlation of β-hCG level in all serum and first morning urine samples with the correlation coefficient of 0.97 ($p < 0.01$). (Fig. 1)

Fig. 2 and 3 show the distribution and correlation of β-hCG level in serum and first morning urine samples in the disease-remission and disease-active groups, respectively. The correlation coefficient of β-hCG level in serum and first morning urine in the disease-remission group was 0.52 ($p < 0.01$), and in the disease-active group was 0.95 ($p < 0.01$).

DISCUSSION

hCG was the first major tumor marker, used in many areas of oncology, especially GTD[1]. The specificity of serum hCG assay was low due to cross-reaction of hCG and some pituitary hormones[2]. The distinction between pituitary hormones and hCG became possible with the production of antisera predominantly direct at the beta subunit of hCG. Monoclonal antibody against β-hCG, using ELISA technique was produced and proved its specificity and reliability for monitoring β-hCG producing tumors before and after therapy [3]. Serum β-hCG has been widely used as clinical assay to follow-up patients with GTD. The regression curve of serum β-hCG has been used clinically not only to discriminate persistent GTD from uneventful hydatidiform mole, but also to determine the success of therapy in patients with GTN who receive chemotherapeutic agents[11,12].

Bagshawe et al used radioimmunoassay for urinary hCG to follow their patients after molar evacuation[5]. In the series of Wehmann et al, the amount of β-hCG in 24-hour urine specimens had significant correlation with serum β-hCG concentration and could be used in the management of patients with GTD[6,7]. Despite the fact that the molecular structure of β-hCG in urine is somewhat different from that in serum, there is no significant effect on the accuracy of the assay[13].

During the past decade, there have been many attempts to develop more sensitive and speci-

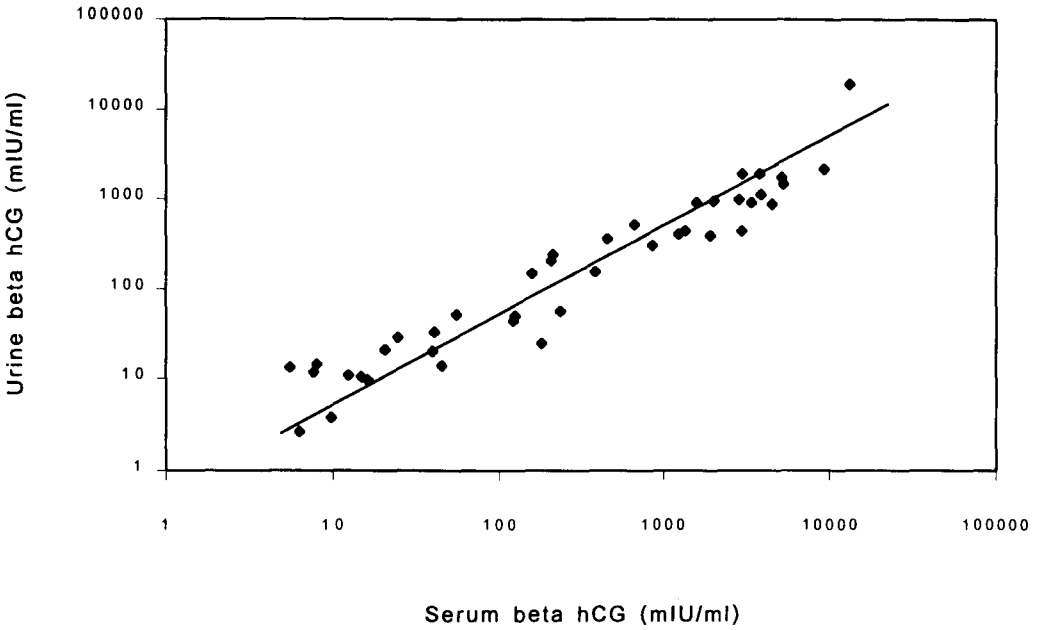

Fig. 3 Scatterplot of β-hCG level in serum and first morning urine of patients in disease-active group.

fic techniques for determining urinary β-hCG level, leading to wider clinical utilities[14-18]. Urinary β-hCG level determination may be preferable to serum β-hCG since collection of urine specimens usually is more convenient and less invasive to patients than venipuncture, especially patients with chemotherapy-induced thrombocytopenia.

First morning urine was used in this study because its high concentration might provide a substantial amount of β-hCG and collection is more convenient than a 24-hour urine specimen. Our study showed significant correlation of β-hCG level in serum and first morning urine samples, however, correlation coefficient in disease-remission ($r = 0.52$) was lower than that of the disease-active group ($r = 0.95$). We concluded that the level of serum β-hCG was strongly and significantly correlated with that of first morning urine samples, especially in patients with active disease. At present, measurement of β-hCG level by the ELISA technique is widely available in Thailand, and first morning urine can be used as an effective mean to determine β-hCG level in following patients with GTD.

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ความสัมพันธ์ระหว่างระดับเบต้าซับยูนิตของฮอร์โมนฮิวแมน โคริโอนิก โกนาโดโทรปินในซีรั่มและในปัสสาวะที่เก็บเป็นครั้งแรกของวันในผู้ป่วยตั้งครรภ์ไข่ปลาอุกและมะเร็งเนื้อรก

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ทำการวิจัยแบบตัดขวางเพื่อศึกษาค่าสัมประสิทธิ์ความสัมพันธ์ของระดับ β-hCG ในซีรั่มและในปัสสาวะที่เก็บเป็นครั้งแรกของวันในผู้ป่วยตั้งครรภ์ไข่ปลาอุกและมะเร็งเนื้อรก ส่งตัวอย่างซีรั่มและปัสสาวะที่เก็บเป็นครั้งแรกของวันจากผู้ป่วยตั้งครรภ์ไข่ปลาอุกและมะเร็งเนื้อรกที่กำลังติดตามการรักษาที่สาขาวิชามะเร็งนรีเวชวิทยา ภาควิชาสูติศาสตร์-นรีเวชวิทยา คณะแพทยศาสตร์ศิริราชพยาบาล มหาวิทยาลัยมหิดล จำนวน 81 ตัวอย่าง เพื่อตรวจหาระดับ β-hCG โดยวิธี enzyme-linked immunosorbent assay (ELISA) แจกแจงข้อมูลใน logarithmic scale พบว่าระดับ β-hCG ในซีรั่มมีความสัมพันธ์กันอย่างมีนัยสำคัญทางสถิติกับระดับ β-hCG ในปัสสาวะที่เก็บเป็นครั้งแรกของวัน โดยมีค่าสัมประสิทธิ์ความสัมพันธ์เท่ากับ 0.97 ($P < 0.01$) เมื่อพิจารณาเฉพาะในกลุ่มที่โรคสงบ (ระดับ β-hCG ในซีรั่มน้อยกว่า 5 mIU/ml) พบว่าค่าสัมประสิทธิ์ความสัมพันธ์เท่ากับ 0.52 ($P < 0.01$) และในกลุ่มที่ยังมีการดำเนินของโรค (ระดับ β-hCG ในซีรั่มมากกว่าหรือเท่ากับ 5 mIU/ml) พบว่าค่าสัมประสิทธิ์ความสัมพันธ์เท่ากับ 0.95 ($P < 0.01$) ซึ่งมีนัยสำคัญทางสถิติทั้งสองกลุ่ม สรุปว่าระดับ β-hCG ในซีรั่มมีความสัมพันธ์กันอย่างมีนัยสำคัญทางสถิติกับระดับ β-hCG ในปัสสาวะที่เก็บเป็นครั้งแรกของวัน โดยเฉพาะในกลุ่มผู้ป่วยที่ยังมีการดำเนินของโรค การตรวจหาระดับ β-hCG ในปัสสาวะที่เก็บเป็นครั้งแรกของวันสามารถนำมาใช้ติดตามการดำเนินโรคของผู้ป่วยตั้งครรภ์ไข่ปลาอุกและมะเร็งเนื้อรกได้อย่างมีประสิทธิภาพ

คำสำคัญ : ฮิวแมน โคริโอนิก โกนาโดโทรปิน, ครรภ์ไข่ปลาอุก, มะเร็งเนื้อรก, ปัสสาวะที่เก็บเป็นครั้งแรกของวัน

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