Effect of uterine contractions on left atrial pressure in a pregnant woman with mitral stenosis

Peter Jakobi, Zvi Adler, Etan Z Zimmer, Simcha Milo

Rambam Medical Centre, Technion—Faculty of Medicine, Haifa, Israel 31096

Peter Jakobi, MD, senior registrar in obstetrics and gynaecology
Zvi Adler, MD, surgical registrar in cardiac surgery
Etan Z Zimmer, MD, consultant in obstetrics and gynaecology
Simcha Milo, MD, senior lecturer in cardiac surgery

Correspondence to: Dr Jakobi.

Br Med J 1989;298:27.

Several studies of peripartum haemodynamics in normal pregnancies have been performed.¹⁻³ The results, however, are somewhat confusing, probably because of methodological factors and the use of indirect methods to assess haemodynamic variables.³ We are aware of only one study on peripartum haemodynamics in parturients with mitral stenosis in which a pulmonary artery catheter was used, but measurements were made only between contractions.⁴ We present a case showing a relation between direct measurements of left atrial pressure and uterine contractions in a pregnant woman during and after a closed mitral valve commissurotomy.

Case report

A 32 year old woman in the 33rd week of her first pregnancy was referred for closed mitral valve commissurotomy after pulmonary oedema developed for no apparent cause after her admission to hospital with heart failure due to mitral valve disease. The area of the mitral valve on two dimensional echocardiography was only 1.1 cm². During and after the operation continuous external monitoring of fetal heart rate and uterine activity was performed. The direct left atrial pressure, which was 26 mmHg before the operation, dropped to 16 mmHg after it. As the left atrium was closed unexplained periodic increases in left atrial pressure were seen similar to the values before the commissurotomy. We then noticed that uterine contractions had started. On further observation it became obvious that the changes in left

Record from external monitor of fetal heart rate and uterine contractions. Left atrial pressure values were superimposed manually (paper speed 20 cm/min)

atrial pressure mimicked the contractions. The figure shows the left atrial pressure recorded on the printout from the fetal monitor.

The contractions occurred every three minutes. The left atrial pressure ranged from 13-19 mm Hg between contractions to 21-27 mm Hg during and immediately after contractions. The mean left atrial pressure measured during 17 contractions was 23.2 mm Hg, whereas the mean of the nadirs was 16.4 mm Hg. The average difference, 6.8 mmHg, was significant ($p < 0.001$). This association between left atrial pressure and uterine activity was also documented in the recovery room four hours after the operation.

Comment

In normal pregnancy maternal blood volume, heart rate, and cardiac output are considerably increased. During uterine contractions, depending on maternal posture, an additional increase in cardiac output and stroke volume has been found (W Lee, paper presented at 8th annual meeting of the Society of Perinatal Obstetricians, Las Vegas, 1988). In mitral stenosis the cardiac output is fairly fixed, and patients might be unable to cope with the increase in stroke volume that occurs during uterine contractions. Clark *et al* found a significant increase in the pulmonary capillary wedge pressure during the immediate postpartum period.⁴ No data were given, however, on the relation between haemodynamic changes and uterine contractions. In our patient, even after commissurotomy, the left atrial pressure during contractions was in the range at which pulmonary congestion or even pulmonary oedema occurs. As the uterine activity was monitored externally the exact intensity of contractions was unknown. The patient's cervical score, however, did not change, leading to the assumption that these contractions were ineffective and of fairly low intensity. Yet they were enough to cause haemodynamic impairments.

We suggest that in pregnant women with known mitral stenosis uterine activity (even premature or Braxton Hicks type) may cause acute heart failure and pulmonary oedema "of unknown origin." These contractions should be treated immediately and aggressively and be considered among possible trigger mechanisms for heart failure. An operation before delivery may be indicated in these patients.

- 1 Ueland K, Hansen JM. Maternal cardiovascular dynamics. II. Posture and uterine contractions. *Am J Obstet Gynecol* 1969;103:1-7.
- 2 Metcalfe J, Meanulity JH, Ueland K. Cardiovascular physiology. *Clin Obstet Gynecol* 1981;24:693-710.
- 3 Robson SC, Dunlop W, Hunter S. Cardiac output during labour. *Br Med J* 1987;295:1169-72.
- 4 Clark SL, Phelan JP, Greenspoon J, Aldahl D, Horenstein J. Labor and delivery in the presence of mitral stenosis: central hemodynamic observations. *Am J Obstet Gynecol* 1985;152:984-8.

(Accepted 19 September 1988)

Increased plasma concentration of von Willebrand factor in insulin dependent diabetics with incipient nephropathy

Tonny Jensen

Steno Memorial Hospital, DK-2820 Gentofte, Denmark
Tonny Jensen, MD, research fellow

Br Med J 1989;298:27-8.

Much of the excess mortality in diabetics with clinical nephropathy is caused by cardiovascular disease,¹ but despite the presence of known cardiovascular risk factors, such as raised blood pressure and atherogenic lipoprotein abnormalities, this increase in mortality

has not been fully explained. According to the response to injury hypothesis, "injury" to the endothelium is the initiating event in atherogenesis, and an increased plasma concentration of von Willebrand factor possibly reflects generalised endothelial cell injury. Moreover, increased release of this factor from endothelial cells provides opportunities for thrombosis. We therefore investigated whether diabetics with increased urinary albumin excretion had an increased plasma concentration of von Willebrand factor.

Patients, methods, and results

We studied 75 non-obese patients with insulin dependent diabetes (onset before age 31). They had no

history of non-diabetic renal disease and for all of them bacterial culture of the urine yielded negative results. None were taking drugs other than insulin or had any disease other than diabetes.

The patients were recruited from three groups according to their albuminuria. Group 1 comprised 28 patients with normal urinary albumin excretion (<30 mg/24 h); group 2 comprised 25 patients with increased excretion (30-300 mg/24 h)—that is, with incipient diabetic nephropathy; and group 3 comprised 22 patients with increased excretion (>300 mg/24 h—that is, with clinical diabetic nephropathy. Seventeen healthy non-diabetic people served as controls.

The table gives details of the findings. The plasma concentration of von Willebrand factor, measured by microenzyme linked immunosorbent assay (ELISA),² was similar in controls and patients in group 1 but was significantly increased in groups 2 and 3 ($p<0.05$). The difference in concentration between groups 1 and 2 was 0.29 mU/l (95% confidence interval 0.09 to 0.49) and between groups 1 and 3, 0.36 mU/l (0.14 to 0.58 mU/l). In multivariate analysis of the logarithmically transformed urinary albumin excretion (ELISA), haemoglobin A_{1c} (chromatographic technique), serum creatinine concentration (reaction rate kinetic principle), and mean blood pressure (diastolic blood pressure plus 1/3 (systolic minus diastolic)), only the logarithmically transformed urinary albumin excretion was independently associated with the plasma concentration of von Willebrand factor. There was no independent association with retinopathy.

Results and clinical data on patients and controls. Values are means (confidence intervals) unless stated otherwise

Variable	Controls (n=17)	Group 1. Normal urinary albumin (<30 mg/24 h) (n=28)	Group 2. Incipient nephropathy (urinary albumin 30-300 mg/24 h) (n=25)	Group 3. Clinical nephropathy (urinary albumin >30 mg/24 h) (n=22)
No of men:	7	11	13	10
Median (range) age (years)	33 (22-47)	31 (19-48)	33 (22-53)	33 (19-48)
Blood pressure (mm Hg)	86 (92 to 90)	87 (84 to 90)	97 (92 to 102)	102 (97 to 107)
Serum creatinine (μmol/l)	76 (71 to 81)	78 (75 to 81)	82 (74 to 90)	90 (82 to 98)
Blood glucose (mmol/l)	4.2 (3.4 to 5.0)	9.7 (8.0 to 11.4)	8.6 (6.6 to 10.6)	10.9 (8.8 to 13.0)
Haemoglobin A _{1c} (%)		7.6 (7.2 to 8.0)	8.9 (8.1 to 9.7)	9.6 (8.9 to 10.3)
Insulin dose (IU/kg)		0.64 (0.57 to 0.71)	0.63 (0.55 to 0.71)	0.70 (0.59 to 0.81)
No of patients with:				
<3 Microaneurisms		23	11	1
Simplex retinopathy		4	10	9
Proliferative retinopathy		1	4	12
Mean (range) urinary albumin (mg/24 h)		8 (3-16)	96 (39-299)	638 (310-6000)
Plasma von Willebrand factor (mU/l)*	0.96 (0.79 to 1.13)	0.94 (0.83 to 1.05)	1.23 (1.06 to 1.40)	1.30 (1.11 to 1.49)

*Plasma concentration of von Willebrand factor was significantly increased in groups 2 and 3 compared with group 1 and normal subjects (multiple range test followed by unpaired *t* tests) $p<0.05$.

Comment

We found an increased plasma concentration of von Willebrand factor in diabetics with persistently but only slightly increased urinary albumin excretion but a normal concentration in those with normal urinary albumin excretion.

The von Willebrand factor is a glycoprotein synthesised by endothelial cells, and an increased plasma concentration indicates endothelial damage.³ Our findings suggest that an increased influx of the factor to the plasma is possibly caused by generalised endothelial damage in patients with early diabetic nephropathy. An increased concentration has been associated with diabetic microangiopathy (defined as retinopathy),⁴ though no information on urinary albumin excretion was given. As proliferative retinopathy is seen predominantly in patients with proteinuria the results reported by Porta *et al* could be explained by a higher prevalence of proteinuria among patients with retinopathy. This assumption is supported by our finding of no independent association between retinopathy and the plasma concentration of von Willebrand factor.

The relation of the increased plasma concentration of von Willebrand factor to the development of cardiovascular disease is uncertain, but the presence of this factor is essential for platelet adhesion to subendothelium.⁵ This adhesion is an important step in the first phase of the formation of a haemostatic plug, and increased platelet adhesion has been found in diabetic microangiopathy.

We believe that the increased plasma concentration of von Willebrand factor is due to a generalised vasculopathy in diabetics with albuminuria. Our study suggests that young diabetics with persistently increased urinary albumin excretion suffer not only from early renal disease but also from widespread vascular disease, which is possibly important for the development of macroangiopathy.

This study was supported by the Danish Diabetes Association and the Foundation of Merchant V Foersom and wife T Foersom.

- 1 Borch-Johnsen K, Kreiner S. Proteinuria: a predictor of cardiovascular mortality in insulin-dependent diabetes mellitus. *Br Med J* 1987;294:1651-5.
- 2 Ingerslev J. A sensitive ELISA for von Willebrand factor (vWt:Ag). *Scand J Clin Lab Invest* 1987;47:143-9.
- 3 Boneu B, Abbal M, Plante J, Bierne R. Factor-VIII complex and endothelial cell damage. *Lancet* 1975;i:1430.
- 4 Porta M, Townsend C, Clover GM, *et al*. Evidence for functional endothelial cell damage in early diabetic retinopathy. *Diabetologia* 1981;20:597-601.
- 5 Sakariassen KS, Bolhuis PA, Sixma JJ. Human blood platelet adhesion to artery subendothelium is mediated by factor VIII-von Willebrand factor bound to subendothelium. *Nature* 1979;279:636-8.

(Accepted 19 August 1988)

Hidradenitis suppurativa associated with use of oral contraceptives

1 Sheringham Ave, London N14 4UB

A J Stellon, MRCP, general practitioner trainee

Lewisham and North Southwark Health Authority, London SE1 9RY
M Wakeling, DPM, family planning instructing doctor

Correspondence to: Dr A Stellon, 110 London Rd, Dover, Kent CT16 3AB.

Br Med J 1989;298:28-9.

A J Stellon, M Wakeling

Hidradenitis suppurativa is a disorder affecting the axillary apocrine sweat glands, anogenital regions, and breasts, resulting in recurrent boils at these sites.¹ We report seven cases that occurred in patients taking the combined oestrogen-progestogen pill.

Seven women, who had attended one of three family planning clinics or a general practitioner's surgery from February 1987 to December 1987 were identified in whom hidradenitis suppurativa had developed while

they were taking the contraceptive pill. The table gives details of the use of the pill in these patients and its temporal relation with the development and exacerbation of hidradenitis suppurativa. We have described one case in detail to illustrate the salient features of this association.

Case report

A 23 year old women was prescribed Conova-30 (ethinylloestradiol 30 μg-ethynodiol 2 mg) in 1981. One month later she developed hidradenitis suppurativa of the anogenital region and was treated with antibiotics. A further three episodes occurred up until October 1982, when Conova-30 was changed to Eugynon-30 (ethinylloestradiol 30 μg-levonorgestrel 250 μg) because of mid-cycle bleeding. Between October 1982 and June 1987 another eight episodes