Fibrinolytic Activity and Capacity after Fracture of Femoral Shaft and Myocardial Infarction

	Mean Euglobulin Clot Lysis Time ($\pm$ S.E.) (Units)					
	After Fracture				After Infarction	
	2 Days	10 Days	2 Months	When Ambulant	2 Days	10 Days
Systemic fibrinolytic activity	1.6 $\pm$ 0.3	3.0 $\pm$ 0.4	3.3 $\pm$ 0.5	4.7 $\pm$ 0.6	1.7 $\pm$ 0.4	2.9 $\pm$ 0.4
Arm fibrinolytic capacity	14.2 $\pm$ 2.6	12.5 $\pm$ 1.9	14.3 $\pm$ 2.2	17.5 $\pm$ 2.3	16.8 $\pm$ 2.9	13.9 $\pm$ 2.5
Leg fibrinolytic capacity	3.2 $\pm$ 0.6	8.0 $\pm$ 1.0	9.1 $\pm$ 1.5	8.6 $\pm$ 2.0	3.1 $\pm$ 0.7	5.6 $\pm$ 0.7

occlusion is due to the release of plasminogen activator from the vein wall¹³ our findings may be explained in two ways: there may be a decrease in the leg vein wall activator early after tissue injury, or the release of activator from the wall may be impaired. Whatever the mechanism, however, the difference between the changes in the fibrinolytic capacities of the arm and leg may be one explanation for the relative frequency of venous thrombosis in the legs compared with the arms after fracture of the femoral shaft and myocardial infarction. The early depression of leg fibrinolytic capacity may also be relevant to the observation that deep venous thrombosis usually starts at the time of or very soon after tissue injury.^{1 3 4}

Our findings conflict with those of Karaca and Nilsson,¹⁴ who reported that the fibrinolytic capacity of the legs, in contrast to that of the arms, was increased after prolonged recumbency. One explanation for the differing conclusions is that these investigators studied different groups of individuals whereas we examined the same people sequentially.

The origin of the plasminogen activator responsible for the fibrinolytic activity of systemic blood is unknown. The close correlation between the fibrinolytic capacity of the legs and the systemic fibrinolytic activity suggests, however, that the leg veins are one important source of circulating plasminogen activator.

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Doppler Ultrasound and Fetal Activity

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Summary

The possibility that Doppler ultrasound, as used in routine fetal monitoring by external cardiotocography, might stimulate fetal activity was investigated. A mean increase in fetal activity of over 90% was found, as judged by the fetal movement count.

Introduction

Some patients undergoing antenatal external cardiotocography with Doppler ultrasound reported an increase in fetal activity during monitoring. We investigated whether this response was consistent and whether ultrasound was the likely stimulating agent.

Patients and Methods

Patients between 28 and 40 weeks of gestation were selected at random from inpatients used to counting fetal movements. The investigation was conducted in three parts—(1) assessment of fetal response to external cardiotocography using Doppler ultrasound with two different instruments to see whether it was due to an instrumental peculiarity; (2) a "sham" study to confirm objectivity; and (3) evaluation of the possibility that electrical currents from the apparatus stimulated fetal activity. This was achieved by occluding the transmission of ultrasound while retaining electrical contact.

In the first part of the study the Sonicaid FM2 and Hewlett-Packard 8025B cardiotocographs were used. Each has two abdominal inputs. One, the "tocograph head," detects the fetal heart beat using continuous Doppler ultrasound. The Sonicaid FM2 "ultrasonic head" consists of one transmitter and six peripheral ceramic receiving crystals; the Hewlett-Packard incorporates one transmitter and one receiving crystal. The ultrasonic energy output of the Sonicaid machine is about 12 mW/cm² of transducer head, and that of the Hewlett-Packard about 16 mW/cm² (manufacturers' data). In the second and third parts of the study only the Sonicaid FM2 was used.

Part 1—Fifteen patients were studied, eight with the Sonicaid FM2 and seven with the Hewlett-Packard 8025B. All rested before the investigation and were lying supine. The tocograph head was placed on the abdomen in the midline over the uterine fundus. The ultrasonic head was smeared with Aquasonic 100 gel and placed where the fetal heart was most clearly heard. Both heads of the monitor were held in position by Tubigrip bandage. Each patient was studied for 30 minutes. During the first 15 minutes uterine activity alone was recorded, and then, unknown to the patient, the ultrasonic head was

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activated. The patient counted the number of fetal movements during both periods. A high degree of correlation exists between electro-magnetic recording and the maternal assessment of fetal movements,¹ which was therefore used as the index of fetal activity.

Part 2—Sham studies were performed on a further six patients under conditions identical with those in part 1 but without activating the ultrasonic head.

Part 3—A further 15 patients were studied for three successive 15-minute periods. A circular brass collar was fitted to the ultrasonic head, so that though the collar was in contact with the abdomen an "air cell" existed between the skin and the transmitter and receiver. This was packed with polyvinyl foam (see fig.). The brass collar allowed electric currents if any to be conducted between the ultrasonic head and the skin, and the air cell impaired the transmission of ultrasound. During the first period the ultrasonic head with the intervening air cell was placed on the abdomen but the head was not activated. In the second period the ultrasonic head with the intervening air cell was activated. Finally, the activated ultrasonic head without the air cell was used. The fetal movement count was recorded for each period.

In all cases the recording face of the monitor was out of sight of the patient. The procedure was evaluated by a clinical psychologist to ensure that no observer bias was introduced.

Method of shielding ultrasonic head of Sonicaid FM2 fetal monitor to prevent passage of ultrasound but permit electrical conduction.

Results

The first 15 patients were divided into two groups according to the apparatus used (tables I and II). In each group the use of the activated ultrasonic head was associated with an increase in fetal activity. For both groups combined the mean numbers of movements were 8.1 ± 1.2 without ultrasound and 15.6 ± 1.8 with ultrasound, an increase of over 90% ($P < 0.001$, paired t test).

The results of the six sham studies (table III) were consistent with a random distribution (paired t test).

The results of the third part of the study were as follows (table IV). In the first 15-minute period (non-activated ultrasonic head with air cell) the mean number of fetal movements was 4.6 ± 1.35 ; in the second period (activated ultrasonic head with air cell) 4.5 ± 0.87 ; and in the third period (activated ultrasonic head without air cell) 10.1 ± 1.69 . Statistically there was no difference in fetal activity between the first and second periods. The increases in fetal activity between periods 1 and 3 and periods 2 and 3 were significant ($P < 0.001$ and $P < 0.01$ respectively, paired t test).

Discussion

Our results show that Doppler ultrasound as used in obstetrics increases fetal activity. So far as we are aware this has not been reported previously.

The fetal excitatory response to exogenous stimuli such as sound and vibration has been known for over 40 years.² The fetal response in terms of movement and alterations in heart rate pattern is depressed by narcotics administered to the mother.³ A brisk increase of fetal heart rate in response to sound was thought to reflect good fetal condition, but a non-reactive fetus might be asphyxiated, asleep, or under the influence of narcotics.⁴ Thus, though fetal arousal (when brisk) may predict good fetal outcome, the reverse is not necessarily true.

TABLE I—Fetal Movement Counts before and after Activation of Ultrasonic Head Using Sonicaid FM2 Monitor

Case No.	Maturity (Weeks)	No. of Fetal Movements			Parity	Obstetric Disorder
		Non-activated Ultrasonic Head (15 Min)	Activated Ultrasonic Head (15 Min)	Difference*		
1	36	4	5	+1	M.	Cervical incompetence
2	38	9	10	+1	M.	Diabetes
3	38	13	13	0	M.	Bad obstetric history
4	27	6	16	+10	M.	Antepartum haemorrhage
5	28	3	9	+6	M.	Raised B.P.
6	35	5	12	+7	M.	Bad obstetric history
7	29	2	8	+6	P.	Raised B.P.
8	38	6	16	+10	M.	Raised B.P.
Mean		6.0	11.1	+5.1		

*Mean increase 85.4% ($P < 0.01$)

TABLE II—Fetal Movement Counts before and after Activation of Ultrasonic Head Using Hewlett-Packard 8025B Monitor

Case No.	Maturity (Weeks)	No. of Fetal Movements			Parity	Obstetric Disorder
		Non-activated Ultrasonic Head (15 Min)	Activated Ultrasonic Head (15 Min)	Difference*		
9	39	15	27	+12	M.	Mild hypertension
10	38	11	17	+6	P.	Antepartum haemorrhage
11	35	1	27	+26	P.	Raised B.P.
12	39	15	18	+3	M.	Cardiac
13	33	11	11	0	M.	Small-for-dates
14	35	11	26	+15	M.	Large-for-dates
15	38	10	19	+9	M.	Raised B.P.
Mean		10.6	20.7	+10.1		

*Mean increase 100% ($P < 0.05$)

TABLE III—Results of Six Sham Experiments Showing Random Distribution of Fetal Activity between First and Second 15-minute Periods of Observation

Case No.	Maturity (Weeks)	No. of Fetal Movements			Parity	Obstetric Disorder
		Non-activated Ultrasonic Head (15 Mins) 1st Period	Non-activated Ultrasonic Head (15 Min) 2nd Period	Difference		
16	38	14	1	-13	M.	Raised B.P.
17	36	8	6	-2	M.	Cervical incompetence
18	28	11	16	+5	M.	Antepartum haemorrhage
19	33	16	2	-14	M.	Small-for-dates
20	36	32	36	+4	M.	Raised B.P.
21	30	2	5	+3	M.	Raised B.P.
Mean		13.8	11.0	-2.8		

TABLE IV—Fifteen-minute Fetal Movement Counts with Inactivated and Activated Ultrasonic Heads with Intervening Air Cell and Activated Ultrasonic Head without Air Cell

Case No.	Maturity (Weeks)	No. of Fetal Movements			Parity	Obstetric Disorder
		Non-activated Ultrasonic Head with Air Cell (15 Min)	Activated Ultrasonic Head with Air Cell (15 Min)	Activated Ultrasonic Head Without Air Cell (15 Min)		
22	33	1	4	11	M.	Placenta praevia
23	36	0	0	5	P.	Placenta praevia
24	36	0	4	5	M.	Raised B.P.
25	38	4	3	3	M.	Rhesus isoimmunization
26	40	2	1	5	P.	Anaemia
27	38	0	0	2	M.	Placenta praevia
28	38	7	9	11	P.	False labour
29	36	4	6	16	M.	Antepartum haemorrhage
30	38	10	5	7	P.	Raised B.P.
31	35	0	6	7	P.	Raised B.P.
32	38	8	4	23	M.	Diabetes
33	32	5	6	18	P.	Antepartum haemorrhage
34	33	8	2	13	P.	Raised B.P.
35	33	19	13	20	P.	Urinary tract infection
36	36	1	5	6	P.	Raised B.P.
Mean		4.6	4.5	10.1		

During the past 12 months in our unit four infants have died antenatally. Each mother had reported absent fetal movements for at least 12 hours before the fetal heart became inaudible. During this time each patient underwent external cardiotocography using Doppler ultrasound without fetal response. Other patients who recorded low daily fetal movement counts (below 11/24 h) and in whom the fetal outcome was satisfactory showed an increase in fetal activity during the 24 hours after a one-hour exposure to Doppler ultrasound; however, the reverse was not always true. Though we do not know why the fetus responds to Doppler ultrasound, it is a procedure without known risk,⁵ and we think that with further development the study of this response might provide further information about the fetus.

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Accumulation of Storage Iron in Patients Treated for Iron-deficiency Anaemia

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Summary

The repletion of iron stores after treatment was studied in 38 patients with uncomplicated iron-deficiency anaemia. The serum ferritin concentration rose significantly when oral treatment was continued for two months after the attainment of a normal haemoglobin concentration. Patients treated with a total-dose infusion of iron dextran had the highest final serum levels, which were significantly greater than in patients given Ferro-Gradumet. Oral ferrous sulphate was almost as effective as parenteral iron in producing iron stores.

Introduction

In the management of patients with iron-deficiency anaemia it is generally recommended that oral treatment should be

continued for several weeks after the peripheral blood has returned to normal so that iron stores are adequately replenished.¹⁻³ The validity of this concept remains unproved as the repeated measurement of body iron stores during treatment has not previously been feasible. Measurement of the serum ferritin concentration, however, provides a simple and accurate means for assessing iron stores,³ and we have used this in patients being treated for simple iron-deficiency anaemia as a guide to the rate at which storage iron accumulates.

Patients and Methods

All the patients studied had iron-deficiency anaemia with a haemoglobin concentration of less than 10 g/dl, a mean corpuscular volume (M.C.V.) of less than 75 fl, and a mean corpuscular haemoglobin concentration of less than 25 pg. The peripheral blood films all showed hypochromic, microcytic red cells. In all cases the serum iron concentration was less than 7 $\mu\text{mol/l}$ (39 $\mu\text{g}/100\text{ ml}$), the total iron binding capacity greater than 70 $\mu\text{mol/l}$ (390 $\mu\text{g}/100\text{ ml}$), and the transferrin saturation less than 10%. The patients were allocated at random to four treatment groups. Group 1 received a total-dose infusion of iron dextran (Imferon) according to the manufacturer's instructions; group 2 ferrous sulphate tablets (200 mg three times daily); group 3 Ferro-Gradumet one tablet daily; and group 4 Ferrograd C one tablet daily. Ferro-Gradumet is a controlled-release preparation containing 525 mg ferrous sulphate in each tablet, while Ferrograd C also contains 500 mg ascorbic acid in each tablet. All patients except those in group 1 were treated until two months after

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