HYPOFIBRINOGENAEMIA IN ABRUPTIO PLACENTAE

by

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Introduction

In recent years the literature on bleeding problems in patients with abruptio placentae has been voluminous and most authors have attributed the bleeding diathesis to hypofibrinogenaemia.

In cases of abruptio placentae, there is sometimes a haemorrhagic syndrome, which results from a sudden fall in plasma fibrinogen level. This defibrination is probably due to escape of placental or decidual thromboplastin into the maternal circulation. This converts prothrombin to thrombin, and fibrin then is deposited spottily over large vascular lesions. (Page, Fulton and Glendening 1951) and (Schneider 1955 and 1956). Thus any alteration in haemostatic mechanism is believed to follow rather than to precede or initiate the placental separation. *(Ostreich, Veprovsky and Sawitskky in 1954).*

Pritchard and Wright in 1960-61, studied the pathogenesis of hypofibrinogenaemia in abruptio placentae. The fibrinogen lost from the circulation was found as fibrin in the blood clots obtained from the uterus. They concluded that the principal mechanism which contributed to the development of hypofibrinogenaemia in these cases was continued haemorrhage and coagulation within the uterine cavity at the sites of placental separation resulting in the local deposits of fibrin and progressive hypofibrinogenaemia.

In short, intra-vascular coagulation and then defibrination of the circulating blood is now widely accepted and supported as a mechanism of defibrination in abruptio placentae. Thus, if depletion of the fibrinogen has taken place, the patient's blood fails to clot, and haemorrhage uncontrollable by ordinary measures will take place from any raw surface—that is, placental site or episiotomy incision. Bleeding may even occur from the intact mucous membranes and subperitoneally, these latter are frequently apparent at caesarean section per-

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formed on cases of abruptio placentae, and constitute the classical Couvelaire lesions.

Material and Methods

This includes twenty cases of accidental haemorrhage. These cases were detected by performing a clot-observation test in all the cases of accidental haemorrhage from July 1962 to June 1965. Those cases which showed defective clot formation were further followed up by performing quantitative estimations of plasma fibrinogen by Quick's method. The clot observation test of Weiner served as a rough guide to diagnosis and evaluation of the degree of hypofibrinogenaemia as mild, moderate or severe. According to this criterion there were 11 cases of mild degree and 9 cases of moderate degree. There was not a single case of severe variety or complete afibrinogenaemia. (Moore, Mena, Perry, Greenberg and Crooks 1962) and (Pritchard, Dallas and Texas in 1955).

The test, first suggested by Page, rapidly indicated the rough estimation of the degree of hypofibrinogenaemia and is clinically most useful. The test is repeated as required depending upon the condition of the patient.

There is another method for bedside measurement of plasma fibrinogen levels. This is a qualitative test in which plasma is added to thrombin solution and calcium diluent. The resulting fibrin clot size gives a rough estimate of the amount of fibrinogen present. As thrombin was not available we have not followed this method.

Observations and Results

The average age of these patients was 29.1 years, varying from 18-38 years. There were two primigravidae and 18 multiparas, the average parity was 5.5 varying from primigravidae to 10th parity.

The average term of pregnancy was 37.6 weeks, varying from 34 weeks to 41 weeks.

In all cases there was a history of vaginal bleeding before admission to the hospital, the average duration of which was 8 hours, varying from 2 hours to 24 hours.

Other symptoms like pain in the lower abdomen and restlessness were present in 13 cases and absent in 7 cases. Toxaemia was present in 12 cases (60%).

On abdominal examination the uterus was found to be soft and the foetal parts were palpable in 9 cases (45%). The foetus presented by vertex in all of them and foetal heart sounds were present in 7 cases. In 11 cases (55%) in which the uterus was hard, rigid and tender, the foetal parts were not palpable and hence the presentation could not be made out, though the lie was vertical in all the cases. Foetal heart sounds were absent in all of them.

Speculum examination was done to confirm the intrauterine source of bleeding. Clot observation test on admission showed following results:

1. *Mild Cases:*

1. Firm clot resulted in 12.1 minutes on an average, varying from 8-20 minutes.

2. No lysis occurred in any of the cases.

II. *Moderate Cases:*

1. Poor clotting occurred within 20.4 minutes on an average, varying from 13-30 minutes.

2. In all cases the clot was abnormally small and poor.

3. In all cases partial lysis occurred, varying from 20 minutes to 2 hours with 1 hour and 22.2 minutes, on an average.

These cases were further followed up by repeated clot observation test and plasma fibrinogen estimated as found necessary in each individual case.

Mild Cases: 11 cases.

Plasma fibrinogen estimation was done immediately after admission, within the first twenty-four hours after delivery and on the 3rd post-partum day. The levels were as follows:

	Average	Maximum	Maximum
On admission.	190.2 mgm%	206.4 mgm%	174.6 mgm%
Within first 24 hours after delivery.	201.8 mgm%	208.0 mgm%	186.0 mgm%
Third post-partum day.	257.9 mgm%	284.6 mgm%	234.0 mgm%

Moderate Cases: 9 cases.

The results of plasma fibrinogen levels at various periods in these cases are shown in the following table:

Case No.	Level on admission in mgm%	Level during observation period in mgm%	Level immediately after delivery in mgm%	Level after first 24 hours after delivery in mgm%	Level on 3rd post partum day in mgm%
1.	146.4	—	142.4	186.6	260.0
2.	186.5	Pt. got second bout of bleeding 8 hours after admission-162.4	—	196.4	264.0
3.	184.6	—	156.4	186.4	266.4
4.	164.6	132.6 (Before caesarean section)	—	184.4	204.6
5.	142.0	—	125.0	174.0	285.0
6.	154.0	126.4 (Before caesarean section)	—	164.0	236.4
7.	164.0	—	146.0	198.0	254.6
8.	146.4	126.0 (Before caesarean section)	156.4 (12 hours after caesarean section)	194.0	246.4
9.	158.4	—	164.0	184.0	218.0

In three cases (Nos. 4, 6 and 8) artificial rupture of membranes was done and syntocinon drip (1.5000) started. During this period there was a fall in plasma fibrinogen. As these patients did not show any progress within 4 hours lower segment caesarean section was done in all the three cases.

Case No. 2 was kept under observation for 8 hours as there was only slight bleeding. The clot observation test after the second bout of bleeding revealed a lowering of coagulation capacity of blood and hence plasma fibrinogen was estimated. The level after the second bout fell from 186.5 mgm% to 162.4 mgm%. In this case labour was induced by artificial rupture of membranes and syntocinon drip 1.5000) started.

Management

Routine anti-shock therapy was immediately given to patients who needed it. Close and careful watch was kept on these patients in order to prevent further lowering of their general condition.

Mild Cases

In all the mild cases artificial rupture of membranes was done, intravenous syntocinon drip in 5 per cent dextrose solution was started in 10 cases, while in one case (No. 3) drip was not given as patient was getting good uterine contractions. The average duration of labour after starting syntocinon drip was 2 hours and 15 minutes, varying from 1-4 hours. All the patients delivered spontaneously. There were 5 live born infants and 6 stillbirths, in two of which foetal heart sounds were absent at the time of admission.

Retroplacental blood clots and liquid blood were present in all cases, the amount of which was as follows:

Blood Loss	Few small retroplacental clots	200 — 300 c.c.	300 — 400 c.c.	About 700 c.c.
No. of Cases	4	4	2	1

There was mild post-partum haemorrhage in one case and moderate post-partum haemorrhage in 3 cases. Syntocinon drip was continued for sometime after delivery in all cases till there was no fear of further bleeding.

All the 11 cases required blood transfusion. Fresh whole blood was given whenever it was available. The number of transfusions required was as follows:

No. of blood transfusions	One	Two	Three	Four	Five
No. of cases	5	1	3	1	1

Moderate Cases

Besides routine anti-shock therapy blood transfusion was required in all 9 cases. In 8 cases labour was induced by artificial rupture of membranes and syntocinon drip. Five cases delivered spontaneously. In 3 cases, Nos. 3, 4 and 8, there was no progress even after continuing the drip for 4-6 hours. Lower segment caesarean section was therefore done. Plasma-fibrinogen level was found to have lowered in all the three cases. This was first judged by clot observation test and later on confirmed by quantitative estimation of plasma fibrinogen level.

Case 2 was kept under observation for eight hours as there was only slight bleeding. The clot observation test after a second bout revealed a lowering of coagulation capacity of blood and hence plasma fibrinogen was quantitatively estimated. The level after the second bout fell from 186.5 mg% to 162.4 mg%. Hence labour was induced by artificial rupture of membranes and syntocinon drip.

The foetus was stillborn in all 9 cases. Retroplacental bleeding was present in all cases. Its quantity estimated roughly was as follows:

Blood Loss	200-300 c.c.	400-600 c.c.	600-800 c.c.	800-1000 c.c.
No. of cases	2	3	3	1

Blood transfusion requirements were as follows:

No of blood tansfusions	4	5	6	7	8
No. of cases	1	1	5	1	1

Thus 17 patients out of 20 had vaginal delivery after artificial rupture of membranes with or without oxytocin drip. Three patients required caesarean section. In no case was hysterectomy necessary.

The foetal salvage rate was 25%. All the cases who had live infants were of mild variety.

There was not a single maternal death in this series.

Discussion

Management of this condition differs widely and hence no one form of management is entirely acceptable. Majority of patients who die from this complication do so from immediate and excessive blood loss. Evidence is accumulating that haemorrhagic deaths result from a defect in the clotting mechanism.

Hypofibrinogenaemia must be suspected, recognised and treated properly in managing premature separation of placenta. Simple clot observation test is best for this purpose. Once the patient is safely delivered, there is no further fall in fibrinogen level. Once the source of thromboplastin, i.e. the placenta, is removed, the fibrinogen level will start rising progressively and in roughly linear fashion and comes to normal within 24 hours after delivery. (Pritchard in 1958).

Following methods are known to

have been used in the treatment of hypofibrinogenaemia.

1. *Fibrinogen therapy:*

When should it be given? This is not a simple matter. First the diagnosis of hypofibrinogenaemia must be well established in bleeding patients and then fibrinogen is administered, otherwise it should not be given.

Intravenous fibrinogen isolated from human plasma in a dose of up to 8-12 gms. is ideal. In severe cases it is very important to transfuse large doses of fibrinogen. (Paranjothy 1959). Usually patients with severe degree of hypofibrinogenaemia recover with 6-8 gms. Some haematologists have expressed a fear of subsequent homologous serum jaundice in its use, this being as high as 20% according to many and hence they advise to withhold fibrinogen therapy in borderline cases of clotting defect. Thus fibrinogen therapy is not mandatory in all cases of abruptio placentae with hypofibrinogenaemia.

But, if any operative interference is contemplated, if an anaesthetic agent which might contribute to decreased myometrial tone is to be administered, if extensive genital tract incisions are encountered, or if the uterus does not remain firmly contracted with all routine treatment after delivery, fibrinogen therapy is highly indicated. (Pritchard 1958) (Benweth R. C. 1963).

Blood transfusion

As fibrinogen therapy is not mandatory in all cases of hypofibrinogenaemia, patients can be treated with blood transfusions alone or with syntocinon drip.

If the cause of post-partum haemorrhage is atonic uterus, no amount of fibrinogen will control haemorrhage. Ample blood transfusions to replace total blood loss must be given. In many instances, maintaining a well contracted uterus and replacing blood loss will be adequate therapy for hypofibrinogenaemia.

The concentration of plasma fibrinogen in blood from normal donors after collection is as follows:

	Immediate	1-7 days	8-14 days	15-21 days
Average	194 mgm%	194 mgm%	198 mgm%	192 mgm%
Range	164-234 mgm%	170-226 mgm%	169-243 mgm%	152-238 mgm%

It can be seen that whether the blood is fresh or stored, it is of little value when used for the specific purpose of attempting to raise the plasma fibrinogen level. (Pritchard in 1958). Each bottle of blood transfused, whether it is fresh or stored, contributes less than 0.3 gm of fibrinogen. (Pritchard in 1958). Similarly Hsu and Momá in 1960, had also to restrict their therapy to fresh blood transfusion because of poor economic status, without any supplement of fibrinogen, but they found that fresh blood was important and it elevated the patient's fibrinogen above the critical level and controlled bleeding in a matter of hours. Similarly Masani also believes in giving fresh blood transfusion when fibrinogen is not

available (Masani 1964). Paranjothy also believes that fibrinogen at present is very expensive and not available in our country, so massive blood transfusion may be given to correct the coagulation defect (Paranjothy D. 1959).

In the present series we had to restrict only to blood transfusions because of unavailability of fibrinogen and poor economic status of our patients. As far as possible we had given fresh blood transfusions (from the patient's relatives) but in cases where relatives were absent or not ready to donate, we had to depend on stored blood. In such cases we had tried to give the blood which was donated within 24 to 48 hours.

Dried plasma

This retains a high fibrinogen content even if stored for as long as 3 years and if it is reconstituted in double strength, it promotes a solution containing approximately 0.7 gm% of fibrinogen. One or two pints of this is sufficient to enable the patient to survive the crisis and may be very valuable while waiting for blood. Paranjothy believes that in the absence of fibrinogen, the next best substitute is dried plasma. This is an excellent source of fibrinogen, and plasma contains 0.35% of fibrinogen. Triple strength plasma therefore contains 1 gm% or 4 to 5 gms per pint. Masani also believes in transfusing multiple strength plasma in the absence of fibrinogen.

When the patient is in a state of shock, and condition calls for intravenous fluids, it is wise never to administer an artificial plasma expander of polysaccharide type. Coagulation failure develops rapidly after the administration of Dextran or Polyvinylpyrrolidone and convert a sub-clinical blood change into a state of uncontrollable bleeding (Jeffcoate and Scott 1955-56).

Induction and hastening of labour

Artificial rupture of membranes

This is an important adjunct to the management of abruptio placentae of milder variety. Here one should do prompt rupture of the membranes, irrespective of the condition of the cervix or the station of the presenting part. Labour and delivery are usually hastened by this manoeuvre and there is lowering of intrauterine pressure, which appears to have a beneficial effect in minimising maternal vascular infiltration with thromboplastin, Longo, Caillonette and Russel 1959, Masani (1964), and hence it has an almost immediate good effect on coagulation of blood. It moreover brings on and hastens labour and helps to control the amount of retroplacental bleeding. The old fear that the uterus may fail to retract and thus allow more bleeding is unfounded. (Jeffcoate and Scott in 1955-56).

Fish and Grimes in 1961 stated that conservative treatment and vaginal delivery are preferable to caesarean section, not only from the standpoint of immediate risk but also of further risk in childbearing. After measures have been taken to prevent shock and to combat it promptly by sedation and blood transfusion, labour should be induced or stimulated by artificial rupture of membranes and, if necessary, syntocinon drip may be started. An unripe cervix with little

or no dilatation is no more a contra-indication to conservative treatment, and does not necessarily constitute an indication for caesarean section.

Labour, either spontaneously occurring or induced and maintained with syntocinon drip, does not cause a significant change in the level of circulating fibrinogen, even when there is pre-existing hypofibrinogenaemia (Pritchard and Dallas 1956).

Oxytocin drip

It is often given after artificial rupture of membranes in order to induce and hasten labour. There is a theoretical disadvantage in that by raising the intra-uterine pressure, it may drive thromboplastin into circulation. Labour either spontaneous or induced and maintained with syntocinon, does not cause a significant change in the level of circulating fibrinogen, even when there is pre-existing hypofibrinogenaemia (Pritchard and Dallas in 1956). Masani believes that when patients fail to respond to artificial rupture of membranes, oxytocin drip with 5 units to 10 units in one pint of 5% glucose is very useful and most of the patients respond well and in very rare cases it fails. (Masani 1964).

Caesarean section

This ensures quicker delivery and a greater chance of securing a live baby. In milder forms it is performed primarily in the interest of the patient. The prognosis for the baby is already poor and the choice of treatment should not be unduly influenced by consideration for its safety. With a severe case, with a hard uterus, marked shock and a long closed cervix, and if the uterus is so damaged that it can no longer evacuate by its own intrinsic contractile powers, a caesarean section is performed. But prior to it one should first give blood. (Stevenson, Braden R. G., Schneider and Johnson 1953).

Alben Weiner in 1953 advocated caesarean section in the group with milder separation when effective labour failed to set in 6-12 hours after artificial rupture of membranes, while, Reid, Roby and Weiner in 1952 advocated to restrict caesarean section to patients in whom labour does not ensue within 6-8 hours after artificial rupture of membranes and before intra-uterine infection becomes an added hazard.

In the present series, in mild cases of hypofibrinogenaemia we had tried artificial rupture of membranes and intravenous syntocinon drip in 10 cases and all responded well. In one case patient had good pains so we did not need syntocinon drip.

In our nine moderate cases, labour was induced by artificial rupture of membranes and then syntocinon drip was started; 5 cases delivered spontaneously. In 3 of our cases there was no progress even after 4-6 hours, lower segment caesarean section was therefore done.

In short, caesarean section is not to be preferred as a method of treatment for the control of bleeding, and a more conservative approach has been suggested in the overall management of the severe cases. As such in severe cases foetal death in utero has already occurred when the patient is first seen. Likewise, at the time the diag-

nosis of accidental haemorrhage is made, the clotting mechanism is already disturbed. In case surgery is preferred, one should know the status of the clotting mechanism prior to surgery (Heaton, Solomon and Happel 1955).

Masani believes in a conservative approach and in cases where neither spontaneous labour sets in nor is it possible to initiate uterine contractions after artificial rupture of membranes and an oxytocin drip the decision to do an abdominal section is difficult. He believes that abdominal section is more difficult in a shocked patient and carries a great risk. (Masani 1964).

Paranjothy believes that in such cases surgery is not effective and even dangerous if coagulation defect has not first been corrected. (Paranjothy 1959).

Hysterectomy

The place of hysterectomy for controlling post-partum haemorrhage in the condition is questioned. Weiner, Reid and Roby in 1953 did not prefer this measure to prevent post-partum haemorrhage because it transfers the bleeding tendency to areas outside the uterine corpus, that means the ovarian pedicle, cervical stump and incised viscera and parietal peritoneum. Oozing occurs from these raw areas in spite of ligature. In these cases the cause of post-partum haemorrhage is a defect in the clotting mechanism of blood rather than uterine atony. Correction of this deficiency will displace hysterectomy from its place as a method of choice for the treatment of post-partum haemorrhage associated with premature seperation of placenta.

Murphy, Picot and Thompson in 1956 were of the opinion that in cases of post-partum haemorrhage due to hypofibrinogenaemia, the treatment will be specific and hysterectomy will not be needed. Also, Jeffcoate and Scott in 1955-56 told that hysterectomy so often advised is contra-indicated. It cannot help and it only provides further sources of bleeding from all lines of incision and suture.

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