

DERANGEMENT IN COAGULATION FACTORS IN HYPERTONIC SALINE-INDUCED ABORTION

by

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Of the different methods of MTP in second trimester, intra-amniotic instillation of hypertonic saline is quite popular, being effective, simple, quick and cheap. However, it is not free from complications like amniotic fluid embolism, pulmonary oedema, hypernatremia and consumptive coagulopathy.

A lot of work has been done on consumptive coagulopathy following the intra-amniotic instillation of hypertonic saline by various authors.

Edward Cohen *et al* (1974) studied 4112 patients receiving hypertonic saline and noted 5 cases of consumptive coagulopathy.

R. Rajan *et al* (1978) studied 88 cases of hypertonic saline and observed 7 cases of excessive blood loss per vaginum due to coagulation disorders.

In Sassoon General Hospital in last 8 years out of 1213 cases of intra-amniotic instillation of hypertonic saline, 5 developed consumptive coagulopathy.

This prompted us to undertake the prospective study of this problems.

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Material and Methods

One hundred and fifty cases between ages of 25-33 were studied during the period from January 1979 to June 1980. The cases were divided into three groups.

Group A

Twenty-five non-pregnant healthy women were studied in order to assess the normal values of different coagulation factors.

Group B

This included 25 pregnant healthy women between 16 to 20 weeks of pregnancy. They were studied to know the changes in coagulation factors in normal pregnancy.

Group C

Study group of 100 cases having pregnancy of 16 to 20 weeks and in whom termination of pregnancy was done by injecting 200 c.c. of 20% sodium chloride into the amniotic cavity by drip method.

The age groups were kept constant in all groups. Besides the routine investigations, the following investigations were done:

- (1) bleeding time, (2) clotting time, (3) prothrombin time, (4) platelet count, (5) plasma fibrinogen and (6) plasma fibrinogen degradation products.

In the study group C, the above investigations were done before the injection of hypertonic saline, 6 hours after the injection and 24 hours after the abortion.

Plasma fibrinogen estimation was done by sodium sulphate method. Quantitative estimation of fibrinogen degradation products could not be done due to the technical difficulties. So, qualitative estimation was done.

A comparison of the mean value of bleeding time, clotting time, prothrombin time, platelet count and plasma fibrinogen in group A and group B.

In study group C, there was a slight rise in the bleeding time, clotting time, prothrombin time, 6 hours after the instillation of hypertonic saline—rise was not statistically significant as the probability was greater than 0.05—All values came back to their original levels within 24 hours after abortion.

Platelet count and plasma fibrinogen levels showed a statistically significant

drop 6 hours after instillation (P 0.001). Both the levels returned to their pre-institution values 24 hours after abortion. Not a single patient showed presence of FDP before the procedure, but 12 patients demonstrated FDP 6 hours after the procedure which disappeared completely 24 hours after the abortion.

This drop in platelet and fibrinogen levels and appearance of FDP was studied according to weeks of gestation separately.

Drop in platelet and fibrinogen levels was maximum in patients with 16 weeks pregnancy. The appearance of FDP was almost same in patients with 16 and 20 weeks gestation.

This change was also noted according to injection/abortion interval.

It was observed that the maximum drop in mean platelet count per cu. mm. was in those patients who aborted between 11-20 hours ($t' = 2.53$ P 0.001). Patients aborting after 30 hours did not show any statistically significant drop in platelet count. Whatever the extent of the drop,

TABLE I
Non-pregnant and Pregnant Women

	Group A		Group B	
	Mean	S.D.	Mean	S.D.
Bleeding time (in seconds)	95	9.013	84.3	8.703
Clotting time (in minutes)	4	0.704	3.74	0.684
Prothrombin time (in seconds)	13/14	2.002	14.34/15	2.235
Platelet count (in cu. mm)	2,50,000	42,207.793	2,10,000	19,668.070
Plasma fibrinogen (in mgm%)	280	58.452	320	38.837

Comparison of A and B group i.e. non-pregnant and pregnant group showed there was no statistically significant change in the B.T., C.T. and prothrombin time during pregnancy. However, there was definite drop in the platelet count and rise in plasma fibrinogen levels. Both were statistically significant (P 0.001).

TABLE II
Mean Values of the Coagulation Factors on Admission, 6 Hours
After Intra-amniotic Saline Injection and 24 Hours After
Abortion in Group C.

Coagulation factors	On admission		6 hours after procedure		24 hours after abortion	
	Mean	S. D.	Mean	S. D.	Mean	S. D.
Bleeding time (in secs.)	80.3	8.705	86.7	12.998	81.9	8.013
Clotting time (in mins.)	3.74	0.684	4.77	1.207	3.44	0.592
Prothrombin time (in secs.)	14.34/15.12	2.36	15.21/15.12	2.762	14.01/15.20	2.018
Platelet count (per cu. mm)	2,26,000	17325.08	2,04,000	18356.211	2,25,000	17145.56
Plasma fibrinogen (in mgm.%)	316	44.042	180	54.223	311	43.864
Fibrinogen degradation levels	Absent		Present in 12%		Absent	

TABLE III
Relation of the Drop in Mean Platelet Count, Mean Plasma Fibrinogen Level and
Appearance of Fibrinogen Degradation Products to Period of Gestation

Period of gestation in weeks	Drop in coagulation factors 6 hours after instillation		Appearance of FDP in %
	Mean platelet count/cu. mm	Mean fibrinogen level in mgm%	
16	29,687.50	48.44	15.06
18	15,882.36	30.00	5.71
20	14,857.15	33.05	15.15

TABLE IV

Relation of the Drop in Mean Platelet Count per cu.mm. Mean Fibrinogen in mgm% and Appearance of FDP to Induction/abortion Interval

Induction-abortion interval (in hours)	Drop in mean platelet count per cu.mm.	Drop in mean plasma fibrinogen level in mgm%	Presence of FDP in %
0-11			
11-20	39,412.37	81.17	41.01
21-30	19,655.18	33.45	7.0
31-40	16,363.64	22.64	4.54
41-50	02,500.00	2.50	—

the values had come back to their original levels 24 hours after abortion. Definite drop was observed in mean concentration of plasma fibrinogen 6 hours after the instillation of hypertonic saline in all cases. It was statistically highly significant in patients who aborted between 11-20 hours ($t = 3.34$ $P 0.001$). The patients aborting after 20 hours did not show any statistically significant drop in the plasma fibrinogen.

The percentage of appearance of fibrinogen degradation products in patients aborting between 11-20 hours was maximum.

The 'Fishser's' exact Test of Significance' gave a probability of less than 0.05 which showed that it was statistically highly significant. They had totally disappeared in all cases 24 hours after abortion.

Patients with 16 weeks of pregnancy had aborted within 20 hours of induction, while patients with 18 and 20 weeks had aborted after 30 hours of induction.

Of the 100 patients in group C, 4 showed significant haemorrhage per vaginum in whom drop in the platelet count as well as the plasma fibrinogen was more marked

Discussion

Many theories have been put forward to explain the coagulation disorder which develops after intra-amniotic instillation

of hypertonic saline R. W. Stander *et al* (1971) studied coagulation factors in patients undergoing intra-amniotic instillation of hypertonic saline. Their studies indicated that the intra-amniotic injection of hypertonic saline initiated a disseminated intravascular coagulopathy though process appeared to be self limited. They postulated that the tissue thromboplastin of placental or amniotic fluid origin released into the maternal circulation after the injection of hypertonic saline, triggered off the conversion of prothrombin to thrombin which in turn converted fibrinogen to fibrin, other factors factor VIII and IX and platelets gradually decreased. Fritz K. Beller *et al* (1972) studied coagulation system in 25 patients of intra-amniotic hypertonic saline—induced abortions and noted maximum drop in coagulation factors at the time of abortion.

Since there was no evidence of intravascular fibrin deposition or glomerular damage Beller (1972) named this pathophysiology by the term consumptive coagulopathy rather than disseminated intravascular coagulopathy. Jerry L. Sprak *et al* (1972) studied a series of coagulation factors in 12 patients of abortion by the intra-amniotic hypertonic saline. They postulated that the injection of hypertonic saline either produces placental abruption or permitted the release of thromboplastin material into the circulation. Lonnie S.

Burnett *et al* (1974) found that there was some evidence that hypernatremia itself may play atleast a partial role in some cases.

Whatever the mechanism, it seems that the coagulation process is activated to some degree in all patients—receiving intra-amniotic hypertonic saline. In some, it is sufficient to cause bleeding problems. Bleeding always results when the plasma fibrinogen level drops below 100 mg%. But between 100-300 mg%, it is not certain which patients will bleed.

Savitri Agrawal and Samen Kumar Bash (1979) studied 400 cases with intra-amniotic 20% saline and found that no coagulation disorder was noted in any of their cases.

Mrs. Jalajakshi Kothandarum (1981) has studied 200 cases of transvaginal intra-amniotic hypertonic saline but she did not encounter any coagulation disorder in her series.

K. K. Deshmukh, R. Anjaneyullu *et al* (1979) studied coagulation factors in 33 cases of hypertonic saline induced abortions and found that there was fall in mean fibrinogen level after 6 hours of intra-amniotic injection and levels came back to preinjection blood levels.

They also noted that the prothrombin time after the intra-amniotic injection was definitely prolonged from 25.42 seconds to 44.94 seconds even at the end of 48 hours.

In the study group, though each and every patient demonstrated change in the coagulation factors, only 4 cases had clinically

significant haemorrhage per vaginum and recovered with 1 or 2 blood transfusions. Patients who aborted between 11 to 20 hours demonstrated more drop in coagulation factors. In them drop in mean plasma fibrinogen was 81.17 mg% as compared to 19.56 mg% who aborted after 24 hours. Drop in mean platelet count was 39,412.37 as compared to 12,836.271 cu. mm, who aborted after 21 hours.

This group mainly includes the patients at 16 weeks of pregnancy. This obviously shows the danger of instilling at 16 weeks and when injection abortion interval is shorter, there are more pronounced changes in the coagulation factors.

Conclusion

1. The drop in coagulation factors was more pronounced in patients undergoing termination of pregnancy at 16 weeks of gestation.

2. The shorter the induction abortion interval more marked were the changes in the coagulation factors.

3. As all the patients with 16 weeks of gestation aborted within 20 hours of instillation it is very obvious that the interruption of pregnancy at 16 weeks by intra-amniotic hypertonic saline injection is rather dangerous procedure.

4. Considering the amount of liquor at 16th, 18th and 20th weeks gestation when a fixed amount of 200 ccs. of 20% saline is instilled the resultant concentration of sodium chloride varies in these three different groups, as shown in Table V.

TABLE V
Concentration of Sodium Chloride in Amniotic Fluid After the Intra-amniotic Instillation of 20% Saline

Period of pregnancy	Quantity of liquor	Quantity of hypertonic saline injected	Concentration of solution
16 weeks	175	200 (20%) ccs.	11.3 gm%
18 weeks	275	"	8.4 gm%
20 weeks	375	"	7.6 gm%

More concentration of sodium chloride at 16 weeks could cause more cellular destruction and release of more tissue thromboplastin and that too over a shorter period as compared to other groups. Thus, the coagulation changes are more marked in the patients at 16 weeks gestation. This shows the need to delay the termination by intra-amniotic hypertonic saline till 18th or 20th week of pregnancy. If one wants to induce abortion at 16th week instillation of lesser amount e.g. 160 ccs. of 20% saline may be advisable.

References

1. Agrawal, S., Samar Kumar Bash: J. Obstet. Gynec. of India, 29: 784, 1975.
2. Beller, K. K. et al: J. Obstet. Gynec. 112: 534, 1972.
3. Burnett, L. S. et al: Obstet. Gynec. Survey, 29: 6, 1974.
4. Cohen, E. and Ballard. C.: Obstet. Gynec. 43: 300, 1974.
5. Gillman, T., Naidu, S. S. and Micheel, H.: Lancet, 2: 70, 1959.
6. Kamble, S. T., Deshmukh, K. K. and Anjaneyulu, R.: J. Obstet. Gynec. of India, 30: 59, 1980.
7. Jaljakshi Kothandarum, 1981. Ind. J. Obstet. Gynec. 31: 377, 1981.
8. Rajan, M., Subhadra, Nair and Usha Devi, L.: J. of Obstet. Gynec. India, 28: 785, 1978.
9. Saxena, S. C. and Gaur: Ind. J. Obstet. Gynec. 28: 980, 1978.
10. Sprak, J. L. et al: New England J. Medicine, 287: 321, 1972.
11. Stander, R. W., Herbert, C. F., Helen, I. G. and Thomas, K.: Obstet. Gynec. 37: 660, 1971.