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INVESTIGATION OF THE ROLE OF PLACENTA IN TRANSFER OF BROMINE CONTAINING DRUGS TO INFANTS

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Bromine containing drugs have long been administered as laxatives and sedatives. Continued use of bromine causes symptoms such as drowsines,coma or psycotic behaviour, but acute poisoning is rare. Skin eruptions have also been observed with the chronic use of bromine (1). Bromide ions is distributed in body fluids much like chloride ion (2), bromide ion is ssecreted in all body secretions(3).

An interesting case of bromine poisioning was observed in a child born and breast fed by an epileptic mother treated by bromine compounds during pregnancy and in the post-partum period (3). Bromine is secreted in breast milk (3), but the high blood level of bromine in the child could not be accounted solely through intake by milk. The role of placental transfer of bromine from maternal to fetal blood was therefore investigated.

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EXPERIMENTAL PROCEDURE

Sample collection

Twenty pregnant women at their last days of gestation were given polassium bromide orally 500 mg/50 Kg body waight. It was desirable to administer bromine 10 hours before the delivery, but this could not be controlled due to unexpected deliveries. During the delivery, blood samples were taken from mother and child (via umbilica Vein), the serum was cellected after centrifugation at 2000 rpm at room temprature. Serum samples were stored at 5^{o} C until analysis.

Source preparation

About 50 µg of each serum was placed in a highly pure polyethylene vial and heat sealed. They were then irradiated together with the bromine standards(10-50 µg Br) in Tehran Research Reactor at a flux of $2x10^{13}$ n S^{-1} cm^{-2} for a period of one hour. After allowing a cooling period of 24h the vials were washed in dilute acid to remove the surface contamination and prepared for analysis.

Counting procedure

A Ge(Li) detector with a full width at half maximum (FWHM) of 2.98 Kev for 1.33 MeV γ-ray of ^{60}CO attached to an 800 channel analyser was used to register the photopeaks of 554 and 777 KeV of ^{82}Br.

Data analysis and results

The method used for the analysis was a non-destructive activation analysis. Therefore it was neccessary to establish the amount of bromine in the polyethylene vials used for irradiation. The empty vials were irradiated along with the standards and their bromine con-

tent was estimated to be 0.096± 0.005 ppm.

In 20 cases under study the bromine concentration of serum before the oral administration of bromine was 4.32± 1.7 ppm.

As is shown in Table 1 the time difference between the intake of bromine and delivery varies between 5 and 83½ h, but in most cases this difference is 5-10h.

Investigation of the results shown in Table 1 reveals that 8h after bromine intake the bromine level in serum of mothers rises 7-9 fold. Considering the mean value of bromine in serum before the administration of bromine this value is comparable with the resuls previousely mentioned (3).

In serum collected 24h after intake of bromine this rise is 5 fold.

The bromine concentration in serum of the new-borns was similar to the concentration of bromine in mother's serum. This was oberved in 72% of the cases.

CONCLUSION

Placental transport mechanisms from maternal to fetal blood occurs via five different pathways (4).Simple diffusion is the most likely mechanism for bromine (5,6,7). The rate of transfer across the placental membrane is dependent on lipid solubility, molecular size and degree of ionization. Drugs with a molecular weight of 600 or less cross the placenta readily (8). Other factors such as changes in uterine blood flow,contraction of uterine musele affect the transfer of substances across the placenta.

As it is shown in Table 1 in most cases (72%) the distribution of bromine in serum of both mother and

Table 1. Bromine Concentration in Different Serum Samples Before and After Bromine Intake

No of the case	Time pf delivery after bromine intake(h)	amount of bromine in serum of mother (ppm)	bromine conten. of mother's serum after bromine intake (ppm)	Bromine content of child's serum (ppm)
1	4.15	--	21.00	22.5
2	5.10	2.83	19.30	14.90
3	5.30	--	46.4	50.0
4	5.30	10.90	31.4	41.3
5	5.45	2.03	11.90	8.70
6	6.10	--	76.6	19.1
7	7.00	4.80	5.28	17.05
8	7.45	5.57	34.10	32.40
9	7.45	4.10	29.40	124.70
10	8.00	--	22.40	23.40
11	8.20	5.40	37.30	24.60
12	8.30	--	31.40	47.50
13	8.30	1.11	39.20	53.00
14	10.00	3.92	23.10	26.80
15	10.20	--	26.80	20.00
16	11.30	5.83	51.10	51.10
17	21.00	6.10	33.3	60.5
18	26.00	6.65	23.4	20.7
19	39.30	12.30	20.00	16.30
20	83.30	3.47	19.50	22.7

seen in other cases could not be easily interpreted due to the lack of enough information regarding the history of the mothers.

After intake of bromine the concentration in the blood of mother increases repidly and after 8 hours reaches a value of 7-9 times the original figure. After 24h this value declines to 5 times. At term,the infant's blood levels are similar to the mother's levels. Placental transport of bromine is a potential source of bromine toxicity in the new born.

SUMMARY

A study was undertaken to investigate the role of placenta in transferring drugs containing bromine to the infant. 20 pregnant subjects were given bromine as KBr (500 mg/50 Kg weight) 10h before the delivery the bromine content of the serum in the mother and the child was estimated by neutron activation analysis. Samples were irradiated at $2x10^{13}$ n $cm^{-2}s^{-1}$ for a period of one hour. A Ge (Li) detector connected to an 800 channel analyser was used for measuring ^{82}Br photopeaks. In 72% of the cases the distribution of bromine in both mother and child was equal, revealing a transfer across the placenta of the intaken drug.

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