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A Blood Cyanide Distribution Study in the Rabbits Intoxicated by Oral Route and by Inhalation

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Bestimmung der Blutzyanidkonzentration in oral oder inhalatorisch vergifteten Kaninchen

Zusammenfassung. Die Blutzyanidkonzentrationen wurden an Zyanid-vergifteten Kaninchen in Urethannarkose bestimmt. Die Kaninchen inhalierten HCN-haltige Verbrennungsgase durch die Trachealkanüle. Eine andere Gruppe von Tieren erhielt NaCN-Lösung per os. Während der Versuche wurden Blutproben aus einer katheterisierten Halsarterie gewonnen. Postmortale Blutproben wurden aus beiden Ventrikeln des Herzens und der kaudalen Hohlvene entnommen.

Der arterielle Blutzyanidspiegel der ersten Gruppe zeigte eine enge Beziehung mit der Ventilation auf. Nach einer Konzentrationszunahme im Anfangsstadium nahm der Blutspiegel mit einer vorübergehenden Apnoe ab. Mit der terminalen Atembewegung stiegen die Blutspiegel und erreichten ihre maximalen Werte. Die Blutzyanidwerte verminderten sich nach endgültiger Apnoe. Der Blutspiegel der per-os-Gruppe nahm stetig unabhängig von der Ventilationsgröße zu. Die „inhalatorische Gruppe" hatte niedrigere Zyanidwerte als die „orale Gruppe".

Schlüsselwörter: Blutzyanidspiegel, Verteilung des Blutzyanid – HCN-haltige Verbrennungsgase

Summary. Blood cyanide concentration was determined in rabbits intoxicated orally or by inhalation. Experiments were carried out under urethane anaesthesia. In the inhalation experiments, rabbits inhaled a combustion product containing HCN via the tracheal cannula and in the oral studies animals were administered NaCN solution into the stomach. In addition to the carotid artery and jugular vein blood samples, postmortem samples were obtained from both sides of the heart and the descending vena cava.

The arterial cyanide concentration in the inhalation group showed a close relationship with ventilation. After an initial rise, blood levels decreased a

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little, in some cases with transient apnea. At the last stage it again increased with gasping, reaching its maximal value. After ultimate apnea, the blood cyanide concentration declined. The blood cyanide values were higher in the oral group than in the inhalation group. The difference between the two groups became larger in the inferior order, the left heart blood—the right heart blood—blood in the descending vena cava. The left heart/right heart ratio of the inhalation group was significantly higher than that of the oral group (1.28 ± 0.28 vs. 0.95 ± 0.09). The coefficient of variation (c.v.) of the inhalation group was larger than that of the other group. Within the inhalation group, the left heart blood showed the largest c.v. values and this was probably due to redistribution of the cyanide by bloodstream after attainment of the maximal concentration.

Key words: Blood cyanide concentration, distribution – Combustion product containing HCN

An unequal distribution in the blood cyanide concentration was observed in the rabbits exposed to HCN or the combustion products containing HCN, the decreasing order of the concentrations being the left heart blood—the right heart blood—the blood in the descending vena cava [1]. A significant positive correlation between the blood cyanide and PO_2 levels strongly indicated a great effect of ventilation on the blood cyanide concentration [1].

The present study, the aim of which was primarily to elucidate the cause of the marked among-individual cyanide concentration differences, which remained unexplained in the previous report [1], is concerned with the determination of the blood cyanide concentration in the rabbits during exposure to the combustion products containing HCN. In addition to inhalation study, an oral study is included in the present report.

Materials and Methods

Male albino rabbits weighing about 2,000 g each were used. After intravenous injection of urethane (1 g/kg, 25% solution in saline), an animal was placed on its back and the polyethylene catheter was introduced into the carotid artery.

In the inhalation experiments, tracheal cannulation was made in addition to catheterization. The animal inhaled the combustion product from 20 g of polyacrylonitrile (PAN), the heating conditions of which were the same as the previous report [1], via the non-rebreathing valve.

In the oral experiments, rabbits fasted for 12 h prior to experiment were used. After catheterization into the carotid artery, NaCN solution in saline (CN radical 10–15 mg/kg, and dosis volume 10 ml/kg) was slowly administered into the stomach.

During the experiment about 1.5 ml arterial blood sample was collected frequently into the heparinized test tube by loosening the clamp placed around the carotid artery. Immediately after each sampling, small amount of heparin-saline solution was injected through the catheter. The venous samples were obtained by puncturing the jugular vein. The one sample volume was about the same as that of the arterial blood. As soon as it became difficult to collect adequate amounts of blood, the chest was opened and the blood samples were taken from the left heart, the right heart and the descending vena cava, respectively. Ultimate apnea preceded thoracotomy in all of the animals. The whole blood cyanide concentration determination was made by the method of Feldstein et al. [2]. In the per os group the PO_2 of the blood sample taken immediately after thoracotomy was determined by the Combianalyzer U (Eschweiler).

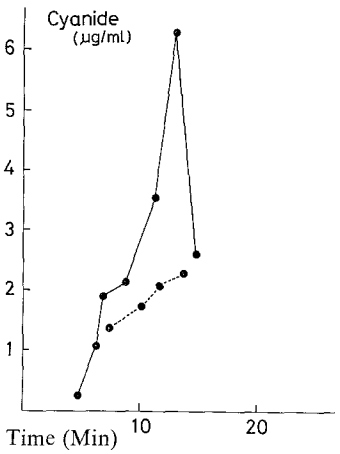

Fig. 1. A typical time-course curve of the blood cyanide concentration in the inhalation group. Solid and dotted lines indicate the arterial and venous blood, respectively. With transient apnea (at about 7 min after exposure), the increasing rate of the arterial concentration became less. At the last stage, the blood level again began to increase with gasping (at about 11 min), reaching its peak concentration. Following ultimate apnea (at about 13 min), the concentration began to decrease. Note a strong relationship between the arterial cyanide level and the state of ventilation

Table 1. Summarized data. The figures are expressed in means ± s.d. The c.v. values are given in the brackets under each figure. Note the larger c.v. values in the inhalation group. Within the inhalation group, left heart blood showed the largest value

Groups	Number of animals	Blood cyanide concentration (μg/ml)					
		(1) Left heart	(2) Right heart	(3) Descending vena cava	(4) Maximal arterial concentration	(4)/(1)	(1)/(2)
Inhalation	10	3.14 ± 2.03 (65)	2.31 ± 0.96 (42)	1.65 ± 0.47 (28)	5.84 ± 1.70	2.16 ± 0.66 (31)	1.28 ± 0.28 (22)
Oral	5	3.78 ± 0.52 (14)	4.04 ± 0.53 (13)	5.40 ± 0.97 (18)	3.62 ± 0.53	0.96 ± 0.08 (1)	0.95 ± 0.09 (1)

Results

Inhalation Group. The time to ultimate apnea (the survival time) ranged 12–16 min. Cyanide concentration began to increase several minutes after the start of experiment. With transient apnea, which occurred about 8–10 min after exposure, the rate of increase became less and the concentration decreased a little in some cases. At the last stage of exposure, with the occurrence of gasping, the blood cyanide level again began to rise, reaching its peak level. Following ultimate apnea, blood cyanide concentration began to decrease in all of the 6 rabbits, from which blood sampling was still possible. The concentration in the venous blood was lower than that in the arterial blood. Figure 1 shows a typical time-course curve of the blood cyanide concentration.

Table 1 gives the summarized data of the 10 rabbits. The left heart blood showed the highest cyanide level, and the right heart blood followed it. The former values were higher than the latter values in all of the rabbits, the ratio

being 1.28 ± 0.28 (mean $\pm$ s.d.). The coefficient of variation (c.v.) was the highest in the left heart sample. A cyanide concentration ratio of the arterial blood to the left heart blood was maximally 2.16 ± 0.66. The cyanide concentration, at which transient apnea and gasping began to occur, were 1.5–2.6 μg/ml and 1.7–3.0 μg/ml, respectively. When the chest was opened, 3 of the 10 rabbits showed no heart beat.

Oral Group. The survival time of this group ranged 14–30 min. In this group, transient apnea was not observed so clearly as in the former group. Blood cyanide level increased with time independent of the state of ventilation.

The summarized data of this group are given in Table 1. This group showed the higher postmortem cyanide values than the inhalation group in all of the sampling sites, and the difference was the greatest in the descending vena cava, the mean concentration ratio being 3.3. The cyanide concentration of the left heart blood was nearly equal to that of the right heart. The left/right ratio (0.95 ± 0.09) of this group was significantly lower than that of the inhalation group. The maximal arterial concentration of this group was low in comparison with the inhalation group. There was not significant difference between the both groups in the cyanide concentration, at which gasping occurred. The blood PO_2 values of the left heart, the right heart and the descending vena cava were 74 ± 14 mm Hg, 45 ± 7 mm Hg, and 39 ± 6 mm Hg, respectively.

Discussion

The time-course curve of the blood cyanide concentration of the inhalation group showed a close relationship between the arterial blood cyanide and the state of ventilation. At relatively low blood cyanide concentration, animals showed transient apnea and the cyanide concentration decreased a little in some animals. With gasping at the last stage, the blood cyanide level again began to increase, attaining to its peak value which was followed with a decrease after ultimate apnea. This decrease was considered to be due to the redistribution of cyanide by bloodstream.

Marked among-individual difference was present as to both the maximal arterial cyanide concentration and the left heart blood concentration, and the c.v.s. were 29% and 65%, respectively. The redistribution of the cyanide by blood flow after the attainment of the peak levels was considered to contribute greatly to the among-individual variation, especially, of the left heart blood cyanide concentration. The cyanide concentration ratio of the left to right heart blood in the inhalation group was considered to depend on the state of circulation after ultimate apnea. In the present study, this ratio of the negative heart beat group consisting of 3 animals, 1.54 ± 0.32, was significantly higher than that of the positive group of 7 rabbits, 1.17 ± 0.16.

In addition to the difference in the concentration, the distribution pattern was different between the two experimental groups. It is pointed out that the cyanide

concentration in the gastric content is a useful criterion, as to whether a cyanide intoxication under consideration is due to per os route or inhalation [3, 4]. We also confirmed that the cyanide concentration in the gastric content of the rats exposed to the combustion product from PAN was, though not negative, very low in comparison with the blood level (unpublished data). From the above it is considered that the present study restressed the importance of examining the cyanide concentration distribution [5].

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