METABOLIC CHANGES DURING DOPAMINE INFUSION IN DOGS

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SUMMARY
The effects were investigated, in 12 dogs, of the infusion of dopamine 10 or 30 \( \mu g \) kg\(^{-1}\) min\(^{-1}\) on circulating glucose, glycerol, lactate and potassium concentrations. Both doses of dopamine produced an initial increase in blood glucose concentration \((P < 0.05)\) followed by hypoglycaemia \((P < 0.05)\). Lipolysis was stimulated as shown by an increase in plasma glycerol concentrations with dopamine 10 \( \mu g \) kg\(^{-1}\) min\(^{-1}\) \((P < 0.05)\) and dopamine 30 \( \mu g \) kg\(^{-1}\) min\(^{-1}\) \((P < 0.01)\). Blood lactate concentrations increased slightly in both groups, but this was significant \((P < 0.05)\) only in the dogs infused with dopamine 10 \( \mu g \) kg\(^{-1}\) min\(^{-1}\). Dopamine had no significant effect on the plasma potassium concentration.

It is well known that the inotropic agents adrenaline, noradrenaline and isoprenaline stimulate various aspects of metabolism (Himms-Hagen, 1967). Recent studies have shown also that salbutamol, administered i.v. in small doses to produce bronchodilatation, has significant metabolic activity (Neville et al., 1977). Goldberg (1977) claimed that dopamine has less effect on metabolism than adrenaline or isoprenaline, although no evidence was given to support this contention.

In this study we have examined the effects of the infusion in dogs of dopamine 10 and 30 \( \mu g \) kg\(^{-1}\) min\(^{-1}\) on circulating glucose, glycerol, lactate and potassium concentrations.

Such information is relevant to the management of patients receiving dopamine infusions, and is also of value in attempting to define the adrenoreceptor agonist activity of dopamine.

METHODS
The details of the anaesthetic technique and surgical preparation of the dogs, and the experimental procedure for the infusion of dopamine 10 and 30 \( \mu g \) kg\(^{-1}\) min\(^{-1}\), have been described in detail in the previous paper (Scott, Chakrabarti and Hall, 1979). Central venous blood samples were analysed in duplicate for blood glucose (Werner, Rey and Wielinger, 1970), plasma glycerol (Eggstein and Kuhlmann, 1974), blood lactate (Hohorst, 1962) and plasma potassium concentrations (flame photometry).

The results from the sample collected after 30 min of the initial saline infusion were used as the control values and statistical analysis of the results was undertaken as described previously (Scott, Chakrabarti and Hall, 1979).

RESULTS
The infusion of dopamine both 10 and 30 \( \mu g \) kg\(^{-1}\) min\(^{-1}\) produced a biphasic change in blood glucose concentration (fig. 1). There was an initial increase in glucose values after 45 min \((P < 0.05)\) followed by a decrease to control values. During the subsequent saline infusion, the glucose was decreased significantly \((P < 0.05)\) below control values.

Dopamine 10 \( \mu g \) kg\(^{-1}\) min\(^{-1}\) produced a significant increase \((P < 0.05)\) in plasma glycerol concentration after 60, 75 and 90 min (fig. 2). There was an even greater response to dopamine 30 \( \mu g \) kg\(^{-1}\) min\(^{-1}\), with a three-fold increase in glycerol concentration after 60 min \((P < 0.01)\). Furthermore, the stimulation of lipolysis with the larger dose of dopamine persisted into the second period of saline infusion, so that there was still a significant increase \((P < 0.05)\) in plasma glycerol concentration 45 min after the dopamine was discontinued.

Blood lactate concentration increased slightly with both doses of dopamine (fig. 3), but this was statistically significant \((P < 0.05)\) only with dopamine 10 \( \mu g \) kg\(^{-1}\) min\(^{-1}\) in the latter half of the period of infusion of catecholamine.

Plasma potassium concentration decreased by only 0.25 mmol litre\(^{-1}\) during the infusion of the small dose of dopamine and 0.5 mmol litre\(^{-1}\) with 30 \( \mu g \) kg\(^{-1}\) min\(^{-1}\) (fig. 4). Neither change was statistically significant.
Fig. 1. Mean (±SEM) blood glucose concentration (mmol litre⁻¹) in dogs infused with dopamine 30 μg kg⁻¹ min⁻¹ (closed circles) and dopamine 10 μg kg⁻¹ min⁻¹ (open circles). *P<0.05 compared with 30-min sample.

Fig. 2. Mean (±SEM) plasma glycerol concentration (mmol litre⁻¹) in dogs infused with dopamine 30 μg kg⁻¹ min⁻¹ (closed circles) and dopamine 10 μg kg⁻¹ min⁻¹ (open circles). *P<0.05; **P<0.01 compared with 30-min sample.
Fig. 3. Mean (± SEM) blood lactate concentration (mmol litre⁻¹) in dogs infused with dopamine 30 μg kg⁻¹ min⁻¹ (closed circles) and dopamine 10 μg kg⁻¹ min⁻¹ (open circles). *P < 0.05 compared with 30-min sample.

Fig. 4. Mean (± SEM) plasma potassium concentration (mmol litre⁻¹) in dogs infused with dopamine 30 μg kg⁻¹ min⁻¹ (closed circles) and dopamine 10 μg kg⁻¹ min⁻¹ (open circles).
DISCUSSION

The biphasic response of the blood glucose concentration to infusion of dopamine (fig. 1) has not been reported previously. Leblanc and others (1977) showed that, in man, the glycaemic response was not sustained when dopamine 4 \( \mu g \cdot kg^{-1} \cdot min^{-1} \) was infused i.v. for 2 h, but they failed to continue their observations after the dopamine was discontinued. However, their results suggested a possible mechanism for the biphasic response. Dopamine was found to stimulate a rapid but transient increase in glucagon secretion from the \( \alpha \) cells of the pancreas, followed by a slower but more sustained secretion of insulin. Thus, the increase in blood glucose is probably caused by the effect of glucagon in stimulating hepatic glycogenolysis, although it is not possible to exclude a direct action of dopamine on glycogenolysis. The failure to sustain the hyperglycaemia and the occurrence of subsequent hypoglycaemia are the results of the persistent hyperinsulinaemia. Chideckel and others (1977) have suggested that the effect of catecholamines on hepatic glucose metabolism is always mediated indirectly via changes in secretion of pancreatic glucagon and insulin. This indirect effect of catecholamines may explain the difficulty in ascribing the stimulation of hepatic glycogenolysis to either \( \alpha \) or \( \beta \) adrenoreceptors.

It is possible that the results obtained in the dog may not be applicable directly to man, but the results of Leblanc and others (1977) and our findings of unstable glucose values during infusions of dopamine (authors' unpublished observations) suggest that the biphasic glucose response has important clinical implications. We recommend that frequent monitoring of the blood glucose concentration is undertaken not only during the infusion of dopamine but also after the catecholamine is discontinued, to detect possible hypoglycaemia.

We chose to measure plasma glycerol rather than plasma free fatty acid (FFA) concentrations to indicate changes in fat metabolism, as we consider the former to be a more accurate indicator of lipolysis (Hall et al., 1978). The significant increase in lipolysis observed with both doses of dopamine (fig. 2) showed that the catecholamine was a potent stimulator of the adrenoreceptors in the adipose tissue. Fain (1973) has demonstrated that lipolysis is subserved by \( \beta_2 \)-adrenoreceptors in all animal species, so that we would predict similar changes in man. Random estimations of plasma FFA values in the dogs confirmed the increase in lipolysis, and when dopamine 30 \( \mu g \cdot kg^{-1} \cdot min^{-1} \) was infused individual values greater than 2 mmol litre\(^{-1} \) were found. It is possible that high FFA values predispose to cardiac arrhythmias (Oliver, 1972), although this is disputed by most cardiologists (Opie, 1972). It is usually considered that the infusion of dopamine has little effect on heart rate or myocardial irritability, but recent studies by Chauve, Castro and Fontan (1977) and Miller (1977) have reported the occurrence of tachyarrhythmias. Although it has been assumed that this represents a direct effect of dopamine on the myocardium, a secondary effect from the stimulation of lipolysis may be contributory.

The cause of the statistically significant, but metabolically small, increase in lactate concentration observed with the administration of dopamine 10 \( \mu g \cdot kg^{-1} \cdot min^{-1} \) (fig. 3) is obscure, particularly as oxygen availability increased more than oxygen consumption (Scott, Chakrabarti and Hall, 1979). However, the failure of the larger dose of dopamine to increase blood lactate concentration significantly showed that there was unlikely to be an important contribution from the stimulation of \( \beta_2 \)-adrenoreceptors responsible for lactate production in muscle (Brody and McNeill, 1970). Dopamine had little effect on plasma potassium concentration (fig. 4), but if the associated haemoconcentration was a result of a diuresis (Scott, Chakrabarti and Hall, 1979) this may prevent the full extent of the hypokalaemic response from being recorded.

We conclude that the administration of dopamine i.v. is associated with significant changes in glucose and fat metabolism. The stimulation of lipolysis shows that dopamine is an agonist for \( \beta_1 \)-adrenoceptors and this catecholamine appears to be unique in stimulating \( \alpha \), \( \beta_1 \) and dopaminergic receptors.

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REFERENCES


METABOLIC EFFECTS OF DOPAMINE


CHANGEMENTS METABOLIQUES PENDANT L'INFUSION DE DOPAMINE A DES CHIENS

Resume
On a etude sur 12 chiens, les effets de l'infusion de dopamine, a raison de 10 et de 30 \( \mu g \) kg\(^{-1} \) min\(^{-1} \), sur les concentrations de glucose, de glycerol, de lactate et de potassium dans la circulation. Ces deux doses de dopamine ont produit a l'origine une augmentation de la concentration de glucose dans le sang (\( P<0.05 \)) et celle-ci a ete suivie d'une hypoglycémie (\( P<0.05 \)). La lipolyse a ete stimulee, comme on a pu le voir par une augmentation des concentrations de glycerol dans le plasma, par de la dopamine a 10 \( \mu g \) kg\(^{-1} \) min\(^{-1} \) (\( P<0.05 \)) et de la dopamine a 30 \( \mu g \) kg\(^{-1} \) min\(^{-1} \) (\( P<0.01 \)). Les concentrations de lactate dans le sang ont augmente legerelement dans chacun des deux groupes, mais cela n'a ete significatif (\( P<0.05 \)) que chez les chiens soumis a une infusion de 10 \( \mu g \) kg\(^{-1} \) min\(^{-1} \). La dopamine n'a eu aucun effet sur les concentrations de potassium dans le plasma.

STOFFWECHSELÄNDERUNGEN WÄHREND DOPAMIN-INFUSION BEI HUNDEN

ZUSAMMENFASSUNG
Bei 12 Hunden wurden die Wirkungen einer Infusion von 10 oder 30 \( \mu g \) Dopamin auf zirkulierende Konzentrationen von Glucose, Glycerol, Laktat und Kalium untersucht. Dopamin bewirkte einen anfänglichen Anstieg der Blut-Glukosekonzentration (\( P<0.05 \)), gefolgt von Hypoglykämie (\( P<0.05 \)). Lipolyse wurde stimuliert, wie durch einen Anstieg der Blut-Glycerolkonzentrationen mit Dopamin 10 \( \mu g \) kg\(^{-1} \) min\(^{-1} \) (\( P<0.05 \)) und Dopamin 30 \( \mu g \) kg\(^{-1} \) min\(^{-1} \) (\( P<0.01 \)) gezeigt wurde. Blut-Laktatkonzentrationen stiegen leicht, doch war dies nur bei Hunden wesentlich (\( P<0.05 \)), die eine Infusion von 10 \( \mu g \) kg\(^{-1} \) min\(^{-1} \) erhalten hatten. Auf die Plasma-Kalium-konzentrationen hatte Dopamin keinen Einfluss.

CAMBIOS METABOLICOS DURANTE LA INFUSION DE DOPamina EN PERROS

SUMARIO
En 12 perros, se averiguaron los efectos de la infusion de 10 y 30 \( \mu g \) kg\(^{-1} \) min\(^{-1} \) de dopamina en las concentraciones circulantes de glucosa, glicerol, lactato y potasio. Ambas dosis de dopamina causaron un aumento inicial de la concentración de glucosa en la sangre (\( P<0.05 \)), seguido por hipoglucemia (\( P<0.05 \)). Se estimuló la lipólisis, tal como indicado por un aumento en las concentraciones de glicerol en el plasma, con 10 \( \mu g \) kg\(^{-1} \) min\(^{-1} \) (\( P<0.05 \)) y 30 \( \mu g \) kg\(^{-1} \) min\(^{-1} \) de dopamina (\( P<0.01 \)). Las concentraciones de lactato en la sangre aumentaron ligeramente en ambos grupos, pero fueron significantes únicamente (\( P<0.05 \)) en perros infusados con 10 \( \mu g \) kg\(^{-1} \) min\(^{-1} \) de dopamina. La dopamina no tuvo ningún efecto significativo en la concentración de potasio en la sangre.