EFFECT OF HALOTHANE ON OXYGEN UPTAKE BY MOUSE BRAIN COMPARED TO THAT OF CHLOROFORM AND ETHER

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Halothane had been introduced as a non-inflammable volatile anaesthetic. Its anaesthetic and hyperglycaemic properties have already been examined and compared with those of ether and chloroform (1). The present paper deals with the effect of halothane on mouse brain respiration as against the effects of ether and chloroform.

MATERIALS AND METHOD

Mice weighing between 20 to 27 gm were divided into 4 groups, one control and the three treated with 3 different anaesthetics i.e. ether, chloroform and halothane. The mice in the treated groups were anaesthetised for an arbitrary period of 15 minutes with the respective anaesthetics before they were guillotined and the whole brain of each mouse was dissected out as quickly as possible. The brains of two mice from each group including control, were weighed, homogenised in cold containers and then the oxygen uptake was measured by the manometric method of Warburg as quickly as possible. Three different substrates viz., glucose, sodium lactate and sodium succinate were employed. All the 4 groups were tested each day with the different substrates and experiments repeated for 3 days so that in all there were 12 determinations. At the end, results were pooled and calculated.

RESULTS

The effects on mouse brain respiration have been presented in the table below.

Each figure is the average of 3 determinations on three different days on 6 mice, each determination being done on brain homogenate from two mice.

It will be seen from the table that the uptake of oxygen by the normal mouse brain is different, depending on the substrate used. With succinate the uptake is the least, and with glucose the maximum. Irrespective of the type of substrate used, the oxygen uptake diminishes as a result of anaesthesia, and the order of this decrease is the same for each of the three substrates, that is, the greatest depression in uptake is found with halothane anaesthesia, and the least after ether anaesthesia irrespective of the substrate used. The variation from the control values is the least in presence of succinate and the highest with glucose as substrate.

The differences of these values when compared by statistical tests with respect to the control, show that the decrease in oxygen uptake following all the three anaesthetics is highly significant ($P<0.01$) when glucose and lactate are the substrates. On the other

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TABLE I

Oxygen uptake in μl. by mouse brain (0.5 g) in 30 min. at 37°C after 1 hour of auto-oxidation with different substrates.

Substrate Group	Glucose	Lactate	Succinate
Control ...	99.6± 3.5 (92.6—104.1)	82.5± 3.5 (76.0—88.1)	36.7± 1.9 (34.6—40.5)
Ether ...	**55.3± 3.3 (50.4— 61.5)	**44.4± 1.6 (41.5—46.8)	33.9± 0.8 (33.0—35.5)
Chloroform ...	**51.2± 2.1 (48.8— 55.3)	**41.5± 2.1 (38.6—45.5)	*30.1± 0.8 (28.6—31.3)
Halothane ...	**44.6± 2.1 (41.5— 48.5)	**38.2± 1.8 (35.0—41.2)	*29.0± 1.0 (27.1—30.6)

Values are the means±the standard errors; ranges of variation are given in brackets.

**P∠0.01 *P∠0.05

hand, when the substrate is succinate, the decrease in the oxygen uptake is significant ($P<0.05$) with chloroform and halothane anaesthesia, while that following ether is not significant.

DISCUSSION

Of the aerobic oxidative metabolisms in the body, the oxidation of glucose, lactate and pyruvate are the ones most sensitive to be affected by anaesthetics like chloroform even at a low concentration, whereas the oxidation of succinate is not so readily affected (2). On the basis of a similar finding, Quastel and his collaborators (3) opine that production of anaesthesia depends on some specific blocking of carbohydrate oxidative mechanism. The present findings with chloroform and ether used for comparison and control, are in agreement with the observations of the earlier workers viz., that oxidation of glucose and lactate are more easily and readily inhibited than that of the succinate. Moreover, the results obtained with halothane show similar inhibitory effect as are found with chloroform and ether towards aerobic oxidation of glucose, lactate and succinate.

In the present experiment, pyruvate was not available and therefore only glucose, lactate and succinate have been used.

The oxygen uptake in presence of succinate in control experiment is much less than the corresponding values of the controls with glucose and lactate. The values as obtained in presence of anaesthetics for succinate oxidation, are almost similar to the normal control figures (without anaesthetics). Quastel and Wheatley (4) and Greig (5) also failed to obtain any appreciable inhibition by narcotics of oxygen uptake of brain tissue of rats with succinate as substrate. The difference in values obtained with the three aneasthetic agents on their respective effects on succinate oxidation is not quite so remarkable as what are found with regard to oxidation of lactate or glucose. However, the oxidation of succinate in presence of chloroform and halothane in the present experiments, is found to be more reduced than that with ether.

SUMMARY

The effect of halothane, a non-inflammable volatile anaesthetic agent, has been studied on aerobic oxidation of three different substrates, glucose, lactate and succinate, by mouse brain, and has been compared with those of chloroform and ether studied under similar condition.

The results obtained show that halothane possesses similar inhibitory effects like chloroform and ether on aerobic oxidations of glucose, lactate and succinate by the mouse brain.

As regards the relative degree of depression caused by these three anaesthetic agents, the highest is caused by halothane and the least by ether, irrespective of the substrate used.

The oxidation of succinate appears to be more affected by halothane and chloroform than by ether.

The possible relation between the inhibition of carbohydrate oxidation and the production of anaesthesia has been discussed in the light of present findings.

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