PROCaine DOSAGE AND INTERACTION WITH GALLAMINE IN CHILDREN

by

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SUMMARY

The dose of procaine (in mg/kg/min) necessary to obtain a satisfactory light level of general anaesthesia in children from 18 to 168 months old, diminishes with increasing age. There is no difference in the procaine requirement between sexes. When higher doses of procaine are injected, greater amounts of gallamine are needed to maintain satisfactory relaxation. Young children require higher doses of gallamine than the older ones. A curvilinear regression has been constructed so that mg/kg/min doses of procaine in relation to sex and age can easily be found.

It is known that the level of cholinesterase is high in young children and decreases with age (Hutchinson and Widdowson, 1952). On the other hand, since procaine is hydrolyzed by cholinesterase (Hazard, Nicaud and Lafitte, 1949) it might be advanced that young children should need higher doses of procaine.

To test this hypothesis a series of anaesthesias with intravenous procaine was studied and the doses correlated with age.

Incidentally the interaction between procaine and gallamine was also investigated.

METHOD

The subject matter of this work is a series of healthy children (80 girls and 79 boys), their ages ranging from 18 to 168 months, who were submitted to general anaesthesia with intravenous procaine, for the performance of dental procedures. The operations lasted from 65 to 295 minutes, with a mean duration of 192 minutes.

Anaesthesia was induced in each case by the intravenous injection of a 2.5 per cent solution of sodium thiopentone in doses ranging from 12.05 mg/kg (mean) for children in the lower ages, to 9.49 mg/kg (mean) in the older. This dose was generally used for induction, but sometimes part of it was employed for this purpose and the remainder injected during the operative procedure.

Immediately after induction, an intravenous procaine drip was started (2 per cent procaine in 5 per cent dextrose in water) and regulated so as to obtain a steady light level of anaesthesia.

Procaine is a weak general anaesthetic agent and should be used as such. Therefore only light or medium plane anaesthesia should be intended. In this way it is similar to nitrous oxide, oxygen and pethidine anaesthesia because only analgesia is to be provided by the agent, while relaxation is obtained through the use of a muscle relaxant. In light general procaine anaesthesia the corneal reflex is merely obtunded, the eyes are humid, pupils are medium sized (excepting children, whose pupils quickly become wider), and the light reflex is present. Small movements of the arms or legs can be observed on occasions in response to painful surgical stimuli when insufficient procaine is being injected. Some of these signs can be more or less altered by the degree of curarization (Stilmann Salgado, 1953, 1959).

Gallamine triethiodide was employed for relaxation until apnoea ensued, and was followed by controlled ventilation of the lungs.

Pethidine in fractional doses was used to reinforce analgesia in doses ranging from 1.33 mg/kg for the younger children to 1.4 mg/kg for the older ones.

All children were intubated intratracheally by the nasopharyngeal route.

These 159 records were statistically analyzed.
Curvilinear regression of dose of procaine (mg/kg/min) plotted against age in boys. Significance of log log slope: $F=19.33$; $F_{0.01}$ for 1 and 78 degrees of freedom $= 6.96$; $r=-0.481$; $p<0.001$.

Curvilinear regression of dose of procaine (mg/kg/min) plotted against age in girls. Significance of log log slope: $F=47.15$; $F_{0.01}$ for 1 and 79 degrees of freedom $= 6.96$; $r=-0.614$; $p<0.001$.

Double log regression of procaine on gallamine showing the positive correlation of procaine and gallamine. Significance of log log slope: $F=24.87$; $F_{0.01}$ for 1 and 78 degrees of freedom $= 6.96$; $r=0.494$; $p<0.001$. 
Regression of gallamine on age showing that younger children need larger mg/kg/min doses for adequate relaxation. Significance of slope: $F=28.4; F_{0.01}$ for 1 and 79 degrees of freedom $= 6.98; r=0.518; p<0.001$.

Regression of procaine adjusted to a mean gallamine and plotted against age. The correlation between procaine and age is independent of gallamine. Significance of slope: $F=9.84; F_{0.01}$ for 1 and 78 degrees of freedom $= 6.96; r=-0.337; p<0.01$.

Regression of procaine on gallamine adjusted to mean age. It can be seen that the correlation between procaine and gallamine is independent of age. Significance of slope: $F=8.8; F_{0.01}$ for 1 and 78 degrees of freedom $= 6.96; r=0.321; p<0.01$.

Regression of gallamine adjusted to a mean procaine, on age: it shows a significant correlation between gallamine and age independent of procaine. Significance of slope: $F=4.25; F_{0.05}$ for 1 and 78 degrees of freedom $= 3.96; r=-0.2288; p<0.05$. 
The data have been tested for linearity and in some cases they fitted a linear regression only after a double log transformation, that is, for instance, log of procaine × 100 used in a given case plotted against the log dose of gallamine injected in this same patient × 1000 (fig. 2).

These data were then submitted to an analysis of variance to test the significance of the slope and to calculate the correlation coefficient r.

In figures 1A and 1B the antilogs of the regressions were afterwards calculated to fit the original raw data.

In all the other cases no log transformation was needed and the original values were analyzed.

Now, since all the substances were administered together it was not possible to assess the action of procaine independently of gallamine and vice versa. This problem was solved by eliminating each of the correlated variables at a time by adjusting the experimental values to the mean of the respective variable (age, gallamine and procaine). In this way the influence of age on dosage of procaine could be calculated independently of gallamine (fig. 5) and so on.

Only significant correlations have been considered and their values as well as the significance of the slopes may be found in the legend of each figure.

RESULTS

The quantity of procaine, expressed as mg/kg/min necessary to obtain a satisfactory light level of anaesthesia diminishes with increasing age, as is shown in figures 1A (boys) and 1B (girls). No difference could be detected when double log slopes of girls versus boys were analyzed.

The curvilinear regression shown in these figures can be used to find out the approximate dose of procaine for a given case in relation to age.

It was also found unexpectedly that when higher doses of procaine were injected, higher doses of gallamine were required. This is shown in figure 2, where a double log regression of procaine on gallamine may be seen. Now gallamine dosage is also related to age in the same way as procaine dosage (fig. 3), but plotting procaine against gallamine adjusted to mean age, in order to eliminate this influence, it can be seen that the correlation of procaine dosage and gallamine dosage is independent of age (fig. 4.)

When the dosage of procaine is adjusted to a mean dosage of gallamine and plotted against age, a significant slope still exists as can be seen in figure 5.

The same happens when gallamine dosage is adjusted to a mean procaine dosage and plotted against age as is shown in figure 6.

Therefore the influence of age on the dosage of procaine seems independent of the influence of gallamine.

DISCUSSION

The results described seem to demonstrate that young children need higher doses of procaine than the older ones, to achieve the same level of anaesthesia.

This fact is probably attributable to the higher levels of cholinesterase known to exist in young children (Hutchinson and Widdowson, 1952), since this enzyme is responsible for the hydrolysis of procaine.

The results reported here show also that more gallamine is needed when higher doses of procaine are injected. This could be explained by the fact that procaine occupies cholinesterase leaving then a larger quantity of free acetylcholine at the neuromuscular junction, which then displaces gallamine.

If the present statement is true this would also confirm that acetylcholine can be hydrolyzed by the plasma pseudocholinesterase (Hazard, Nicaud and Lafitte, 1949) (procainesterase), particularly when as in the present case, the concentration of acetylcholine is high (Wylie and Churchill-Davidson, 1960).

Young children need higher doses of gallamine than the older ones. Knowing that higher levels of cholinesterase are present in younger children it could be assumed that acetylcholine is also present in higher amounts. This could explain the need for more gallamine.

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REFERENCES


SOMMAIRE
La dose de procaïne en mg/kg/min. nécessaire pour obtenir une profondeur satisfaisante d'anesthésie légère chez des enfants de 18 à 168 mois, décroît avec l'âge. Il n'y a pas de différence entre les deux sexes dans leur besoin en procaïne. Lorsqu'on injecte des doses importantes de procaïne, de plus grandes quantités de gallamine sont requises pour maintenir un relâchement satisfaisant. Des doses plus importantes de gallamine sont nécessaires chez les jeunes enfants que chez les plus âgés. Une régression curviligne a été construite qui permet de trouver facilement la dose de procaïne en mg/kg/min. en rapport au sexe et à l'âge.

ZUSAMMENFASSUNG

BOOK REVIEW

It may not be coincidence that the two books planned to provide undergraduates with an outline of anaesthesia are by authors no longer actually engaged in the subject. The author of the volume under review was formally a consultant on the staff of St. Thomas's Hospital but now holds an important post in medical administration. Perhaps it is that those whose career evolves along such unusual paths are able to take a more detached view of the place of anaesthesia in the world of medicine than are the practising specialists. It may be easier for them to see that there is always likely to be a demand for anaesthesia from those who have not got highly specialized training and that it is still incumbent upon every doctor to loose upon the public to be able to care for the unconscious patient and to render a patient unconscious in dire emergency or in situations where no better qualified person is present.

This little “paper-back” has been produced with an eye on the economic situation of the average undergraduate. There are, therefore, no illustrations. On the whole, despite the advantage of economy, the reviewer regrets such an omission. There are points which can be better elucidated with a simple diagram than with a page of involved explanation. Nevertheless, this book is surprisingly readable; perhaps the use of a number of colloquialisms, such as “a flying start” and “the small print stuff”, help. The teaching throughout is based on common sense and a considerable experience in the instruction of students in elementary anaesthetic principles. Some points are open to criticism such as the “little qualified” advocacy of thiopentone for casualty anaesthesia and pethidine for the premedication of elderly subjects.

Although local analgesia is covered in the penultimate chapter the description of those techniques, such as pudendal block and finger block, which are likely to be of use to the general practitioner could have received a little more detailed description and emphasis.

The final chapter is a brief coverage of the more interesting activities of the anaesthetist and is obviously directed towards recruitment.

The author claims to have been able to do no more than “nibble round the edges of the subject”. Nevertheless, he has provided a very reasonably priced book for the undergraduate which, if read carefully, will give him a basis for his practice of anaesthesia and from which he will gather a number of sound tips which may be life saving.

Cecil Gray