POSTOPERATIVE ANTEROGRADE AMNESIA

BY
RONALD P. GRUBER AND DAVID R. REED

SUMMARY

The problems of defining and estimating pre- and postoperative amnesia are discussed. The extent of postoperative (anterograde) amnesia in patients receiving pre-operative medication (consisting of atropine, pethidine and pentobarbitone) followed by general anaesthesia (consisting of thiopentone, halothane and nitrous oxide) was ascertained. Two control groups were employed; one received spinal anaesthesia following pre-operative medication, and the other received no medication and did not undergo surgery. Various age groups were compared and various memory tests were employed. Results indicate that postoperative amnesia is primarily related to the general anaesthetic and not to the pre-operative medication.

In some studies designed to elucidate the extent of pre- and postoperative amnesia, the role that pre-operative medications play in producing the amnesia is referred to. For instance, Feldman (1963) asked patients if they remembered the injection before they went to sleep. An appreciable percentage replied in the negative; amnesia was more frequent in those patients receiving hyoscine in their premedication. But it is not to be concluded that amnesia is solely due to the pre-operative medication. It may be due in part to a retrograde amnesia induced by the general anaesthetic. Jarvik (1964) refers to retrograde amnesia as an "impairment of retention" and has demonstrated it with the use of thiopentone. Patients were given a picture memory test either immediately before thiopentone anaesthesia or 10 minutes before the anaesthetic. Results in patients given immediate anaesthesia showed that 24 hours later they forgot 46 per cent of pictures, whereas patients given anaesthesia 10 minutes after the pictures forgot only 21 per cent.

Feldman went on to ascertain the extent of amnesia occurring after operation and correlated this with the presence of hyoscine. But, as is the case with pre-operative amnesia, the postoperative amnesia may be related to both the hyoscine and the general anaesthetic, both of which may tend to produce anterograde amnesia. Jarvik (1964) attributes anterograde amnesia to an "impairment of registration" (meaning neural registration of events), and has clearly demonstrated it with the use of hyoscine.

Another difficulty when studying amnesia lies in estimating its duration. Lambrechts and Parkhouse (1961) asked patients what time they thought they awoke following the operation. Forty per cent of patients under 60 years of age who received atropine and a sedative claimed to be awake less than 15 minutes after the operation and 33 per cent claimed to be awake 15 minutes to 2 hours following the operation. However, it must be admitted that the patient's estimation of the time of his awakening is subjective, on the one hand, and it does not exclude the possibility that he remembers events occurring prior to the stated time of awakening, had these events been specifically tested for.

The study of pre- and postoperative amnesia, therefore, necessitates a classification of amnesia into retrograde and anterograde types as caused by pre-operative medication, general anaesthesia or both. A schematic representation is shown in figure 1. As seen, drugs given before anaesthesia can produce retrograde amnesia for the premedication period and can produce anterograde...
amnesia for the postmedication period (preanaesthetic period); similarly, general anaesthesia can produce retrograde amnesia for the preanaesthetic period (after premedication has been given) and anterograde amnesia for the postanaesthetic period. Finally, the anterograde amnesia induced by pre-operative drugs may extend into the postanaesthetic period.

It was the purpose of this study to ascertain the extent of postoperative anterograde amnesia which may be due to pre-operative medication and/or general anaesthesia. Various stimuli were presented to the patient in the postoperative period and these were tested for 24 hours later. It was also intended to show whether the extent of amnesia is related to the age of the patient and the type of memory test given—whether auditory, visual or tactile.

SUBJECTS AND METHODS

The subjects were adult male and female patients undergoing minor surgical procedures ranging from herniorrhaphy to haemorrhoidectomy. They were divided into two groups, one receiving general anaesthesia (GA) and the second receiving spinal anaesthesia (S). A third group consisting of non-surgical patients acted as control (C). All groups were divided into subgroups, of fifteen patients each, according to age as follows: 10-40, 40-60, and 60-80 years. There were 135 patients in all. Each patient in group GA was given premedication according to body weight as follows: atropine 0.4 mg/70 kg, pentobarbitone 100 mg/70 kg and pethidine 75 mg/70 kg. Then patients received halothane and nitrous oxide for general anaesthesia after induction with thiopentone. The mean duration of operation for patients in groups GA and S was 1½ hours. Thus the extent of amnesia in each group could be compared to others without concern that the duration of anaesthesia would influence the duration of amnesia.

Patients in group GA were presented with various stimuli at a pre-designated time following the onset of verbalization in the recovery room. Verbalization was said to occur at zero time when the patient was first able to give a verbal answer to a question (no matter how dysphasic the answer may have been). Fifteen minutes later the patient was given (1) a visual (picture) stimulus, (2) a painful stimulus (squeezing the tendon of one limb), and (3) two auditory stimuli (a buzzer and an answer-provoking question). Sixty minutes after zero time, another, but different, series of stimuli was given, and 120 minutes after zero time, a third series was given. No patient received medication during this time.

The patients in the spinal (S) group underwent the same pre-anaesthetic medication procedure as group GA except that (1) they received a 1 per cent amethocaine subarachnoid block and (2) zero time began 15 minutes after patients entered the recovery room. Thereby, zero time was approximately 1½ hours after the induction of anaesthesia for both groups. Finally, group C consisted of non-surgical patients receiving no medication. They also underwent the same series of memory tests but without spinal or general anaesthesia. For these patients zero time was arbitrarily selected.
Twenty-four hours after the various stimuli were presented, the patients in all groups were questioned to ascertain the extent of their amnesia. No patient received any medication in the 6 hours preceding questioning. In order to avoid suggesting to the patients that they did have amnesia and to avoid denial of amnesia by the patients, they were asked to recollect all events in the postoperative period. Then the patients were instructed that they were about to be shown several stimuli, only some of which had been presented during their recovery from anaesthesia. They were asked to confirm or deny recognition of the stimulus by answering "yes", "no", or "not sure". "Not sure" was considered a "no" when scoring the results. Then the total of twelve stimuli that had been presented in the immediate postoperative period were presented in a random fashion along with four other stimuli not previously presented. The four new stimuli were included to ascertain the extent of false recognition answers.

Surprisingly, none of the patients gave a false recognition to more than one of the four previously unseen stimuli, and only a few did so to one. This is probably because patients were permitted to give a "not sure" answer. Therefore, it was concluded that this type of recognition test eliminates most but not all false recognition answers; none of the patients was eliminated from the study.

There is possibly one other objection to the use of this type of recognition test. It is that it does not exclude the factor of retroactive inhibition which theoretically may account for a decrement in recall for the first of two or more presented stimuli (or tasks). This phenomenon is classically seen when testing for the immediate recall of numbers. The first of several presented numbers is not recalled as often as the second; and the second is not recalled as often as the third, etc. In this experiment, then, it might be argued that stimuli presented at 15 minutes after zero time are not recalled as well as those presented at 60 minutes and 120 minutes after zero time because of (at least in part) the phenomenon of retroactive inhibition. Two comments will negate this argument. (1) The effects of retroactive inhibition and any other factors which prevent an exact measure of the degree of recall or amnesia should be evident in both experimental and control groups. Thus the score difference between these two groups should not be related to these factors. And it is precisely this difference that was determined. (2) Retroactive inhibition was in fact demonstrated not to exist. As will be demonstrated, the control groups showed no statistically significant difference between the recall scores for stimuli presented at various times after zero time. The chief advantages of this type of recognition test are its ease of applicability and replicability.

RESULTS

All patients were allotted a score consisting of the percentage of stimuli recalled for each time of stimulus presentation (15, 60, 120 minutes). Subgroups of each group were combined for this analysis. Then the mean score of each group (GA, S and C) was plotted as a function of the time of stimulus presentation (fig. 2). The results in

Memory scores at various postoperative time intervals of patients receiving general anaesthesia (GA) and spinal anaesthesia (S) as compared to controls (C).

group GA demonstrated inferior performance (greater degree of amnesia) compared with those from both groups S and C (P<0.001, analysis of variance). In group S the results proved to be only slightly inferior to those of group C and the difference is not statistically significant at the 5 per cent level.

The results obtained in the subgroups of each main group were compared to determine the
The effect of age on recall. The results in the subgroups of the general anaesthetic group are illustrated in figure 3. It will be seen that older patients showed poorer performances; these differences are not, however, statistically significant at the 5 per cent level. A similar difference between the results in the subgroups of the spinal and control groups was noted but is not illustrated.

![Memory scores at various time intervals of patients in various age groups undergoing general anaesthesia.](image)

Groups GA, S and C were also scored by noting the percentage of patients from each group who responded to each of the four stimuli. This was also plotted as a function of the time of stimulus presentation (minutes after zero time). Group GA is an illustrated example (fig. 4). As seen, the question stimulus was recalled by the largest percentage of patients (P<0.025, analysis of variance), followed next by the visual and other auditory stimulus which were recalled by approximately the same percentage of patients. The painful stimulus was recalled by the significantly smallest percentage of patients (P<0.025). In other words, of the four stimuli, the question proved to be the most sensitive test of memory. A similar difference between stimuli is noted but not shown for both groups C and S.

Finally, the average time between completion of surgery and onset of verbalization (zero time) was recorded for subgroups of group GA. For patients aged 10-40 it was 9.7 minutes; for those 40-60 it was 12.3 minutes; and for those 60-80 it was 14.0 minutes. The only statistically significant difference occurred between patients aged 10-40 and those aged 60-80. All patients in group S were able to verbalize immediately after completion of surgery.

**DISCUSSION**

The results indicate that, as expected, patients undergoing general anaesthesia have a significantly greater degree of postoperative amnesia than those receiving spinal anaesthesia when compared to the control group. These same patients have a 20 and 55 per cent recall for various stimuli given 15 minutes and 2 hours respectively after the onset of verbalization (fig. 2). Correcting for the control group’s performance (69 per cent at 15 minutes and 78 per cent at 2 hours), this is in effect 28 per cent recall at 15 minutes and 72 per cent at 2 hours. Taking into account that the onset of verbalization occurred on the average at 12 minutes after surgery, these values change to 28 per cent recall at 27 minutes and 78 per cent recall at 2 hours and 12 minutes following the completion of surgery.

The above analysis is based upon the combined results from four test stimuli. If only the most sensitive test for amnesia is considered, i.e. questioning, the results change to 52 per cent recall at 15 minutes and 75 per cent recall at 2 hours after onset of verbalization (fig. 4). Correcting for control group again (results not shown), the results become 55 and 78 per cent respectively. These results are similar to those of Lambrechts and Parkhouse (1961) who found that 74 per cent
of patients receiving atropine and a sedative, before operation, thought they were awake within 2 hours after completion of the operation. However, as shall be seen, these results will not, unlike those in the study of Lambrechts and Parkhouse, be attributed to the pre-operative medication.

Patients receiving spinal anaesthesia (and pre-operative medication) demonstrated 53 per cent recall and 84 per cent recall at 15 minutes and 2 hours respectively (fig. 2). Correcting for controls, these figures become 77 and 100 per cent at 15 minutes and 2 hours respectively. But, as mentioned, these figures are not significantly different from those obtained in the control group. Therefore, the postoperative anterograde amnesia must be attributed to the general anaesthetic and not to the pre-operative medication. In this case the combination of nitrous oxide, thiopentone and halothane is the causative agent. It would not be unreasonable to assume that other agents used in general anaesthesia have a similar effect. In fact, Lambrechts and Parkhouse (1961) have demonstrated that nitrous oxide is followed by less postoperative amnesia than is trichloroethylene-air anaesthesia. Furthermore, it is not to be assumed that other pre-operative medications such as hyoscine do not produce more anterograde amnesia than the combination of atropine, pethidine and pentobarbitone, or that they do not produce as much anterograde amnesia as the anaesthetic agents with which they are used. Lambrechts and Parkhouse (1961) have also demonstrated that the combination of hyoscine and papaveretum produces more amnesia after operation than does atropine combined with a sedative. In the case of atropine, however, it is quite clear from this study that this drug does not contribute to the production of postoperative amnesia.

The lack of a significant difference between subgroups is at first surprising, since other studies have demonstrated that amnesia is greater in older patients. However, in this study memory tests were not given until the “onset of verbalization” which was significantly delayed in the older age group. Finally, the differences in amnesia for the various stimuli need little comment except that tests of memory or amnesia are known to vary with the quality of the test stimuli employed.

REFERENCES

AMNESIE ANTEROGRADE POSTOPERATOIRE

SOMMAIRE
Les problèmes de définition et d’estimation de l’amnésie pré- et postopératoire sont discutés. Le degré d’amnésie (anterograde) postopératoire chez des patients recevant une prémédication (composée d’atropine, pethidine et pentobarbitone), suivie d’une anesthésie générale (composée de thiopentone, halothane et protoxyde d’azote) a été déterminé. Deux groupes de contrôle ont été utilisés: un recevait une anesthésie duraire après prémédication, le second ne recevait pas de médication et ne subissait pas d’opération. Les divers groupes d’âge ont été comparés et divers tests de mémoire ont été appliqués. Les résultats montrent que l’amnésie postopératoire est primairement due à l’anesthésie générale et pas à la médication préopératoire.

ÜBER DIE POSTOPERATIVE ANTEROGRADE AMNESIE

ZUSAMMENFASSUNG