THE USE OF TRIFLUOROETHYL VINYL ETHER (FLUOROMAR®*) IN ANAESTHESIA FOR DENTISTRY**

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THE quest for an agent which will completely fulfil the requirements of patient, surgeon, and anaesthetist will never end. Pharmacologists and chemists are constantly studying and testing chemicals in the hope of discovering a drug which is safe and simple to administer to patients of all ages, is pleasant to the individual and permits a rapid uncomplicated recovery. Krantz (1) and his co-workers had for some time been examining the anaesthetic possibilities of certain hydrocarbons and ethers. In 1947, he reported his laboratory studies of ethyl vinyl ether (Vinamar®), an agent which has since been proven to have definite merits for induction and maintenance of anaesthesia in children (2). The chemical properties designated Vinamar as a hybrid of diethyl and divinyl ethers, exhibiting many of the good features of both agents. Vinamar possesses excellent analgesic properties and, together with nitrous oxide and oxygen, becomes a useful tool for anaesthesia of the ambulatory patient.

TABLE I
(SADOVE, BALAGOT AND LINDE)(5)

Property	Diethyl ether "Ether"	Divinyl ether "Vinethene"	Ethyl-vinyl ether "Vinamar"	Trifluoroethyl vinyl ether "Fluoromar"
Boiling point	34 6° C	28 4° C	35 5° C.	42 7° C.
Vapour pressure mm of Hg				
at 20° C	442	553	428	295
at 40° C	921	1145		670
Gas density (Air = 1)	2 6	2 4	2 5	4 4
Lower flammability limit				
In O ₂	2 0%	1 9%	2 2%	*4 0%
Air	1 9%	1 7%		4 2%
75% O ₂ -25% N ₂ O				4 0%
Minimum spark ignition energy, millijoules for				
3% of vapour in dry O ₂	0 39		high	—
4%	0 05		0 13	—
6%	0 01		0 02	0 30
8%	0 01		0 01	0 08
Solubility in water ml/100 ml	8 0	0 7	0 8	0 4
Oil/H ₂ O ratio at 37 5° C	3 2	41	45	91
Blood concentration for surgical anaesthesia (mgm %)	50-150	30-40	ca 25	17-38

*dry gas mixture

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In 1953, Lu *et al.* (3) reported a study of fluorinated hydrocarbons and ethers; they concluded that the partially fluorinated ethyl vinyl ether may be useful as an anaesthetic. Later, on April 10, 1953, following extensive investigations in animals, Krantz (4) submitted Dr. M. Sadove to an open-drop administration of Fluoromar®. The results were gratifying and encouraging for further studies. In Canada, this new ether was employed for the first time (by the author) on February 8, 1954. The subsequent administrations constituted a study of the agent primarily in paediatric anaesthesia. However, a number of adults also received this ether. Of the 178 cases in which Fluoromar was given, 158 were for dental procedures. The observations were based on the value of this fluorinated ether as an analgesic and a supplement to nitrous oxide and oxygen anaesthesia compared to other volatile agents—in particular, trichloroethylene.

Properties (Table I)

The formula of Trifluoroethyl vinyl ether is similar to that of ethyl vinyl ether but three hydrogen molecules are replaced by three fluorine molecules ($\text{CF}_3\text{CH}_2\text{—O—CH}_2\text{=CH}_2$) (4). It is an unsaturated fluorinated ether. The compound has a specific gravity of 1.13 at 25°C. and is volatile, colourless, with a markedly less pungent odour than that of ethyl vinyl ether. This latter property alone was most acceptable to both young and old alike. Because its boiling

cc /Kg RESPIRATORY ARREST

minus cc /Kg INDUCTION

FIGURE 1 Safety margin for ethers (Krantz *et al.*)

point is 42.7°C., compared to 28.4 of divinyl ether and 87°C. of trichloroethylene, it can be used in open drop techniques for children. Kriantz has demonstrated that the margin of safety is somewhat comparable to that of diethyl ether (Fig. 1).

Fluoromar is quite stable in closed absorption systems (6, 7) but is sensitive to light. Therefore, 0.1 per cent phenyl-alpha-naphthylamine is added as an inhibitor, retarding decomposition to the toxic trifluoroethanol and acetaldehyde (6).

Management

The majority of patients selected for this study were children requiring exodontia or operative dentistry (8, 9). Some procedures were short extractions, while others were difficult and long. The average dental filling operation took one and one-quarter hours (Table II). The remaining twenty cases were not

TABLE II
DURATION OF ANAESTHESIA

Time	No. of patients
Less than 5 minutes	8
5-15 minutes	69
15-30 minutes	45
30-60 minutes	26
1-1½ hours	14
1½-1¾ hours	6
1¾-1¾ hours	7
1¾-2 hours	3

dental but did offer an opportunity for observing other clinical phenomena. In other instances student volunteers were subjects for analgesia tests, with various types of "inhalers." The ages of the patients ranged from 6 weeks to 60 years (Table III).

TABLE III
AGE DISTRIBUTION

Age	No. of patients
6 weeks- 1 year	6
1- 5 years	40
5-10 years	66
10-15 years	23
15-20 years	5
20-25 years	12
25-35 years	5
35-45 years	9
45-55 years	6
55-60 years	3

Because of the desirability of having rapid recoveries with early (if not immediate) ambulation, premedication was kept to a minimum. The usual premedicant was a barbiturate, seconal or nembutal, administered to the patient 1-1½ hours before operation. Occasionally, additional codeine with acetylsalicylic acid was given to adults to potentiate the barbiturate. Patients who were

hospitalized were given a combination of barbiturate, morphine, and scopolamine or barbiturate with nisentil or demerol. Very few were in this last category. Approximately 85 per cent of the cases received barbiturate alone. This offered an excellent opportunity of noting the presence or absence of excessive secretions or cardiac irregularities.

Many individuals, especially children, object to an induction with any agent having a strange odour. Therefore they were first rendered unconscious with high flow nitrous oxide and air. The face mask or nasal inhaler was usually off the face at this point. As soon as hyperventilation was noted (and before evidence of cyanosis), 20 per cent oxygen was added along with Fluoromar. Fluoromar was usually administered from the Heidbrink Trimar vaporizer, and the initial setting was at #9 or #10 for 2 to 3 minutes; then, as the breathing became quiet, this setting was immediately changed to #5 or #6. Below this, the concentration of Fluoromar was insufficient to maintain an even plane of anaesthesia. The technique just described was adequate for all dental extractions.

Operative dentistry for fillings was managed in much the same manner except that following the nitrous oxide-oxygen-Fluoromar sequence, a minimal dose of succinylcholine was given intravenously. A nasotracheal tube was then inserted by direct vision or blindly, and anaesthesia maintained by the high flow technique of 80:20 nitrous oxide, oxygen and Fluoromar. Spontaneous breathing returned within a matter of 2 or 3 minutes; during this time artificial respiration is instituted. Periodic inflation of the chest assured better alveolar gas exchange.

The anaesthetic equipment employed was of the standard unmodified types. Vinethene, ether, and trichloroethylene vaporizers had individual differences, but, with experience, the appropriate settings were achieved without difficulty.

Observations

Trifluoroethyl vinyl ether was found to be a most interesting and unusual ether. Generally speaking, the agent appeared to fulfil the role of a potent safe supplement to nitrous oxide-oxygen anaesthesia. There were several striking clinical observations noted in this study:

1. Fluoromar did not have the irritating effects on both respiratory and salivary systems as compared to trichloroethylene, diethyl ether and divinyl ether.

2. The agent was most acceptable to the patients and operating personnel. Children reacted favourably to the pleasant odour and did not exhibit evidence of lingering objectionable odours after operation, as they do with diethyl ether. This fact alone seemed to reduce the incidence of nausea, vomiting, coughing and increased salivation.

3. The onset of analgesia and anaesthesia with nitrous oxide-oxygen-Fluoromar sequence was smooth and without evidence of breath-holding, laryngospasm or excitement.

4. Although the agent seems to be very potent, it has a margin of safety greater than that of divinyl ether, cyclopropane, and chloroform and ethyl chloride. It is somewhat comparable to diethyl ether.

5. The transition from light to deeper planes and back to lighter levels of anaesthesia was accomplished smoothly and without untoward effects on the subject. The respiratory pattern resembled that of cyclopropane but the eye signs paralleled those of ethyl vinyl ether. It was obvious that the patients were never in deep surgical anaesthesia and yet their breathing was quiet and unlaboured. In the beginning, this confused the anaesthetist; what appeared to be deep anaesthesia, as judged by the respirations, would often be light, and the patient would move his head, legs, or arms. This rarely delayed the operation, for a slight increase in Fluoromar concentration eliminated these movements.

6. Better management was attained when the Fluoromar concentration in the inhaled mixture was initially high, and then tapered off to a minimal level. When vaporization was gradually increased, there was more evidence of excitement, retching, and salivation.

7. In the concentrations of Fluoromar employed for dental surgery, there were no untoward cardiovascular complications. As in the case of other commonly used anaesthetics, overdosage for a long period produced bradycardia in two cases. This was obviated by "flushing" the patients with oxygen and reducing the quantity of inhaled agent. There was no evidence of hypotension in this series.

8. The administration of opiates before operation and the use of thiopental for induction, diminished significantly the quantity of Fluoromar required for smooth maintenance of anaesthesia.

9. Where no relaxant was given prior to intubation, it was necessary to maintain Fluoromar at a high concentration for an average of five minutes. The time allowed for introducing the laryngoscope and endotracheal tube was indeed limited, but of no great concern.

10. In the group of subjects observed, there was no evidence of convulsions, "running" movements, or other central nervous system disturbances.

11. In all instances, the recoveries were amazingly rapid. Even more remarkable was the quick mental orientation with absence of throbbing headaches and epigastric pains commonly seen with trichloroethylene and nitrous oxide.

12. The type of anaesthetic machine employed was unimportant. However, vaporizers with short bottles and some form of wick were preferred. Heat of vaporization presented no problem because of the low concentrations of the agent used.

13. Fluoromar can be administered by any of the inhalers such as the Cyprane, Duke, Trilite, and the Goldman vinethene inhaler. The Emotril type of apparatus is better suited for this purpose since it maintains a more consistent concentration over a longer period of time as observed clinically. Therefore there would seem to be a possibility for its use in dental analgesia. The main difficulty is that Fluoromar does not remain in the blood stream for long (5) and the analgesic effects disappear rapidly. Trichloroethylene is much better from this standpoint.

14. Lastly, although the jaws did not relax completely, mouth props were inserted without too much difficulty.

15. Complications are listed in Table IV.

TABLE IV
COMPLICATIONS

	No of cases
1. Breath-holding—mild	3
—severe	0
2 Prolonged induction	1
3 Laryngospasm—mild	1
—severe	0
4 Vomiting—during induction	1
—during maintenance	9
—during recovery	4
5. Retching—during anaesthesia	2
—during recovery	1
6. Stridor during operation	2
7. Increased secretions	4
8 Excessive sweating	1
9 Bradycardia	2
10 Inadequate anaesthesia	4

SUMMARY

1. The pharmacologic properties of trifluoroethyl vinyl ether (Fluoromar®) are outlined.
2. Favourable clinical observations of Fluoromar in dentistry indicate its use as an adjuvant to nitrous oxide-oxygen analgesia and anaesthesia.
3. Statistical data are presented.

RESUMÉ

Depuis les travaux de Krantz, publiés en 1947, on connaît les propriétés analgésiques de l'éther-vinyle (Vinamar®) qui en font un agent surtout utile en anesthésie pédiatrique et chez le patient ambulant. Plus tard, en 1953, Lu et ses collaborateurs, puis Krantz, font paraître une étude sur l'éther éthyl-vinyle fluoré (Fluoromar®). L'auteur du présent travail est le premier à l'employer au Canada, le 8 février 1954. Il en étudie la valeur et comme analgésique et comme complément de l'anesthésie protoxyde d'azote-oxygène. Il le compare à d'autres agents volatils, en particulier, le trichloréthylène.

Propriétés

Le Fluoromar® est un éther fluoré non saturé, volatile, incolore, avec une odeur moins pénétrante que celle de l'éther éthyl-vinyle; son point d'ébullition à 42.7°C. permet de l'employer en goutte à goutte chez les enfants. Il est stable en circuit fermé, mais se décompose au contact de la lumière en acetaldéhyde et en trifluoréthanol, produit très toxique.

Emploi

Les observations de l'auteur portent sur 178 cas dont 158 de chirurgie dentaire. La majorité des patients sont des enfants; toutefois, l'âge de ceux à qui il fut administré varie de 6 semaines à 60 ans. Dans 85 pour cent des cas, on emploie seulement un barbiturique comme prémédication, 1-1½ hrs avant l'opération; quelquefois on lui associe de la codéine, de l'A.A.S., de la morphine-scopolamine,

du nisentil ou encore du démerol. L'induction se fait au protoxyde d'azote à l'air libre; dès le début de l'hyperventilation, on ajoute de l'oxygène à une concentration de 20 pour cent en même temps que le Fluoromar®. On administre cet agent au moyen d'un vaporisateur Heidbrink Trimar® que l'on fixe à #9-10 pendant les 2-3 premières minutes, pour les extractions dentaires. On diminue ensuite à #5-6 comme dose d'entretien. Pour les obturations dentaires, une intubation nasotrachéale est pratiquée. L'induction se fait telle que décrite plus haut; au moment de l'intubation, quelques mgms de succinylcholine sont administrés par voie intraveineuse. L'anesthésie se maintient ensuite en semi-fermé avec du protoxyde d'azote et oxygène 4:1 et le Fluoromar®.

Conclusions

Le Fluoromar® s'est avéré un complément puissant, et sûr à la fois, de l'anesthésie au protoxyde d'azote-oxygène. Comme caractéristiques propres, soulignons les suivantes:

1. Le Fluoromar® est dépourvu d'effets irritants sur les voies respiratoires et salivaires.

2. Son odeur se tolère assez facilement aussi bien par les patients que par le personnel qui l'administre; absence d'odeurs désagréables et persistantes dans la période post-opératoire, comme avec l'éther diéthylique. Ce fait seul semble être responsable de la diminution dans l'incidence des nausées, vomissements, de la toux et de l'augmentation de la salivation.

3. L'établissement de l'analgésie et de l'anesthésie se fait sans incidents, v.g., Laryngospasme ou agitation.

4. Sa marge de sécurité se compare à celle de l'éther diéthylique; elle dépasse celle de l'éther divinyle, du cyclopropane, du chloroforme et du chlorure d'éthyle.

5. Le passage de plans légers à des plans plus profonds et inversement se fait sans incidents même si l'anesthésie est maintenue superficielle, la respiration des patients est calme et se fait sans difficultés.

6. On obtient un meilleur contrôle de l'anesthésie en employant des concentrations plus élevées de Fluoromar® au début pour diminuer ensuite graduellement.

7. L'auteur n'a pas noté de complications cardio-vasculaires; le surdosage peut entraîner de la bradycardie qui disparaît en oxygénant abondamment le patient.

8. L'emploi d'opiacés en prémédication et de pentothal pour l'induction contribuent à diminuer la quantité de Fluoromar® requise pour une anesthésie adéquate.

9. Si on ne donne pas de curare avant l'intubation, il faut maintenir les concentrations élevées de Fluoromar® pendant environ 5 minutes.

10. Pas de convulsions ni autres signes d'atteinte du système nerveux central n'ont été notés.

11. Le réveil est très rapide; le patient peut reprendre aussitôt son activité mentale sans accuser de ces violentes céphalées ou douleurs épigastriques qui se produisent si souvent avec le trichloréthylène et protoxyde d'azote.

12. On préfère des vaporisateurs à petites bouteilles.

13. On peut administrer le Fluoromar® au moyen de n'importe lequel des inhalateurs suivants: Cyprane, Duke, Trilite ou le M.I.E. Le type Emotril semble le mieux adapté, car il peut maintenir une concentration plus uniforme pendant une plus longue période de temps. La plus grande difficulté vient de ce que le Fluoromar® s'élimine rapidement et que l'analgésie est de très courte durée.

14. L'introduction d'un ouvre-bouche peut se faire assez facilement

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