INTRAMUSCULAR KETALAR(CI-581) IN PAEDIATRIC ANAESTHESIA*

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KETAMINE HYDROCHLORIDE (CI-581), a phencyclidine derivative, is sufficiently well known now as not to require a detailed introduction.¹⁻⁴ Suffice it to say that the substance produces a state of unresponsiveness, peculiar to the drug, which has been referred to as "dissociative anaesthesia," and is characterized by analgesia with superficial sleep. One further peculiar property of the agent is its extraordinarily good tissue tolerance coupled with rapidity of effect following intramuscular injection. This property suggested to us that this might be an agent particularly suited to the needs of small children and infants in whom venipuncture is both technically difficult for the anaesthetist and upsetting to the patient. Protective reflexes are well maintained during anaesthesia, a property which might be particularly useful in situations where, for one reason or another, conventional anaesthesia would have necessitated endotracheal intubation.^{5,6}

With these thoughts in mind we embarked on this study of the intramuscular administration of Ketalar in infants and small children. In order that we might be able better to evaluate the effects of the agent, no supplementary drugs were given other than further doses of Ketalar itself when inadequate depth of anaesthesia indicated such a course. Initially, before sufficient experience had been gained, we considered the indications for intramuscular Ketalar to be those previously applied to rectal thiopental, but as experience grew indications were widened. Obviously any method which obviates the unpredictability of a rectal instillation with the inherent uncertainty of absorption and occasional partial loss of the material, has considerable advantages provided the state of anaesthesia itself is satisfactory.

Included in this review are 110 procedures in 101 patients. Seven patients were anaesthetized twice by this method and one three times.

Age and sex distribution are shown in Figure 1. No patients exceeding 12 years of age were included. Sixty-eight administrations were in males and forty-two in female children.

As far as the preoperative physical condition of the patients is concerned (Table I), the overwhelming majority were classified as good, only three were considered poor, and no patients in serious and critical condition were anaesthetized with this still experimental agent.

In eighty per cent of our patients premedication was with a belladonna derivative only (Table II). The remainder were given promethazine, meperidine, or pentobarbital, except for four patients who received no premedication at all.

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FIGURE 1. Age and sex distribution of patients.

TABLE I

Preoperative physical state of patient	Number of procedures	Per cent
Good	77	70.0
Fair	30	27.3
Poor	3	2.7
Serious or critical		
Total	110	100.0

The initial dose of Ketalar was calculated on a basis of 5 mgms/lb body weight (11 mgms/Kg), resulting in total doses as listed in Tables III and IV. In eighty-one instances the initial dose of ci-581 was entirely adequate to complete the procedure (Table V). In the remainder of cases supplemental injections were required but only exceptionally was it necessary to exceed two injections. In most instances a 5 per cent solution was used which was the only one available during the early phases of the study. In older children this involved sub-dividing the total dose and injecting half of it into each buttock. Later a 10 per cent solution

TABLE II
DISTRIBUTION OF PREMEDICATION

Premedication		Number of procedures	Per cent
None		4	3.6
Belladonna only		78	70.9
Atropine	77		
Scopolamine	1		
Promethazine with Atropine	5	6	5.5
with Scopolamine	1		
Meperidine		19	17.3
with Atropine	17		
with Scopolamine	2		
Pentobarbital			2.7
with Atropine	2		
with Belladonna	1		
Total		110	100.0

TABLE III
DISTRIBUTION OF TOTAL DOSE OF CI-581/WEIGHT

Total dose of CI-581/weight (mgm/Kg)	Number of procedures	Per cent
≤4.9		
5.0- 6.9	3	2.7
7.0- 8.9	6	5.4
9.0-10.9	28	25.5
11.0-12.9	44	40.0
≥13.0	29	26.4
Total	110	100.0

TABLE IV
DISTRIBUTION OF TOTAL DOSE OF CI-581

Total dose of CI-581 in milligrams	Number of procedures	Per cent
<50	5	4.5
50-99	21	19.1
100-149	30	27.3
150-249	41	37.3
250-499	13	11.8
≥500		
Total	110	100.0

became available which made this superfluous; the higher concentration was therefore used in twenty-two older children among the last forty cases.

A large variety of surgical procedures are included, all of a relatively minor nature (Table VI). Most prominent amongst these are neuroradiological investigations and minor ophthalmological procedures, but the large variety attests to the versatility of the method.

TABLE V
DISTRIBUTION OF TOTAL NUMBER OF DOSES OF CI-581

Number of dose of CI-581	Number of procedures	Per cent
1	81	73.6
2	25	22.7
3	3	2.7
4	1	1.0
≥5		
Total	110	100.0

TABLE VI
DISTRIBUTION OF OPERATIVE PROCEDURES

Operative procedures		Number of procedures	Total
Neurosurgery			
Ventriculogram		8	
Pneumoencephalogram	29		
with refraction or fundoscopy	2		
with skin biopsy	1		
with subdural tap	1	33	
Myelogram		2	
Carotid Angiogram		1	
Removal Subdural—Perit. Shunt		1	45
Ophthalmology			
EUA ± refraction, tonometry, fundoscopy, gonioscopy	19		
with conjunctival scraping	1		
with removal cyst eye	1	21	
Probing Tear Duct	6		
with EUA eyes	1	7	
Cryocyclodiathermy		2	
Fundoscopy and fitting contact lenses		1	
Change Eye Prosthesis		1	
Removal Granulation Tissue		1	
Removal Sutures Eye		1	34
ENT			
Myringotomy with insertion Silastic tubes		6	6
Plastic*			
Excision Skin Tags		1	
Removal Sutures	4		
Removal Wires	2	6	7
Orthopaedic			
Closed Reduction CDH	1		
with Adductor Tenotomy	1	2	
Subcutaneous Tenotomy Foot		1	
Removal Sutures; POP		3	
Manipulation Arthrogryposis & POP		1	7
Therapeutic radiology			
Liver Scan		1	
Bone Radiation		2	
Radiation Keloids & Removal Sutures		1	4
Dental			
Extraction	1		
with fillings	1	2	2

TABLE VI (continued)

Operative procedures		Number of procedures	Total
Urology			
Cystoscopy			
with Ureteral Dilatation	1		
with Retrograde Pyelogram	1		
with Gonadal Biopsy	1	3	3
Miscellaneous			
Application Protective Face Mask		1	
Oesophageal Dilatation		1	2

*Since the conclusion of this series several burns dressings have been done also.

In the overwhelming number of cases the quality of anaesthesia was assessed as excellent or good by both the anaesthetist and surgeon (Table VII); only in a little over 4 per cent were conditions judged fair or poor.

Blood pressure, pulse-rate and respiration were monitored and recorded throughout each operation (Tables VIII, IX, X, and XI). Because of the youth of the patients, it was not possible frequently to record baseline vital signs; hence the relatively large number of instances in which changes from controls could not be determined. However, it is abundantly clear that in all parameters increases far outweigh decreases and "no changes." In other words the drug tends to spare both circulation and respiration.

After the operation, all patients were admitted to the Recovery Room where the wake-up time following the last injection of Ketalar was recorded and was related to the kind of premedication each patient had received (Table XII). Not only does this reveal the relatively lengthy sleep time after Ketalar, but also that premedication with more than a belladonna drug tends to delay awakening even further.

Patient stay in the Recovery Room was even more prolonged (Figure 2). Comparing inpatients with outpatients, their respective length of stay is comparable, and a patient's imminent discharge from hospital did not prolong substantially the period of post-anaesthetic observation required.

Adverse reactions are shown in Table XIII. The relatively high incidence of increased salivary secretions is noteworthy. Less infrequent were manifestations of increased neuromuscular activity such as clonus, increased muscle tone, tremors, fasciculations, and even convulsions. Increases in temperature were also seen. The cases of ventilatory insufficiency include those patients in whom there was either a decrease or no change in respiratory rate and refer to total ventilation rather than rate alone. The one case of cardiorespiratory arrest will be discussed in detail further on.

DISCUSSION

Our experience with the intramuscular administration of Ketalar indicates that this is a satisfactory and safe anaesthetic for minor procedures in infants and children which, in the majority of cases, gives excellent operating conditions.

TABLE VII
EVALUATION OF ANAESTHESIA BY THE ANAESTHESIOLOGIST AND SURGEON

Evaluator	Evaluation	Number of procedures	Per cent
Anaesthesiologist	Excellent	90	82.6
	Good	13	11.9
	Fair	4	3.7
	Poor	2	1.8
	NS ^a	1	
Surgeon	Excellent	88	80.7
	Good	16	14.7
	Fair	3	2.8
	Poor	2	1.8
	NS	1	
Total		110	100.0

^aNot specified; Case No. 124.

TABLE VIII
DISTRIBUTION OF MAXIMUM PER CENT CHANGE IN
SYSTOLIC BLOOD PRESSURE

Maximum per cent change in systolic blood pressure	Number of procedures	Per cent
Decrease	4	12.1
No change	5	15.2
Per cent increase		
1-9	5	15.2
10-24	10	30.3
25-49	7	21.2
50-74	2	6.0
75-99		
≥100		
NS ^a	77	
Total	110	100.0

^aNot Specified.

TABLE IX
DISTRIBUTION OF MAXIMUM PER CENT CHANGE IN
DIASTOLIC BLOOD PRESSURE

Maximum per cent change in diastolic blood pressure	Number of procedures	Per cent
Decrease	2	10.5
No change	1	5.3
Per cent increase		
1-9	2	10.5
10-24	5	26.4
25-49	4	21.0
50-74	4	21.0
75-99		
≥100	1	5.3
NS ^a	91	
Total	110	100.0

^aNot specified.

TABLE X
DISTRIBUTION OF MAXIMUM PER CENT CHANGE IN
PULSE-RATE

Maximum per cent change in pulse-rate	Number of procedures	Per cent
Per cent decrease		
1- 9	2	2.3
10-24	2	2.3
No change	2	2.3
Per cent increase		
1- 9	8	9.3
10-24	26	30.3
25-49	32	37.2
50-74	14	16.3
NS ^a	24	
Total	110	100.0

^aNot specified.

TABLE XI
DISTRIBUTION OF MAXIMUM PER CENT CHANGE IN
RESPIRATORY RATE

Maximum per cent change in respiratory rate	Number of procedures	Per cent
Per cent decrease		
1- 9		
10-24	1	2.2
No change	2	4.3
Per cent increase		
1- 9	1	2.2
10-24	6	13.1
25-49	27	58.7
50-74	5	10.9
75-99	1	2.2
>100	3	6.4
NS ^a	64	
Total	110	100.0

^aNot specified.

Induction is fast and supplemental doses, if required, may be administered at any time. Our findings agree with those in the literature that changes in vital signs are minimal and as a rule fluctuate in the direction of increase rather than depression of vital functions. This method is much superior to rectal thiopental because doses can be accurately calculated, absorption is more predictable and fast, and no part of the pre-calculated dose is lost. It has in common with rectal thiopental, however, the prolonged sleep and need for a considerable period of postoperative observation which makes the agent less than ideal for outpatient work. This sleep time is further prolonged by premedication, but belladonna drugs in adequate amounts are absolutely essential to control otherwise bothersome secretions. Endotracheal intubation has never been required despite the many changes

TABLE XII
DISTRIBUTION TIME OF AWAKENING BY PREMEDICATION

Minutes	Without premedication or belladonna drug only		With premedication		Total procedures	Per cent
	Number of procedures	Per cent	Promethazine	Pentobarbital		
<60	13	16.25	2		1	10.7
60-119	43	53.75	1	2	8	39.3
120-179	22	27.5	1	1	7	32.2
180-239	2	2.5			1	3.6
240-299			1		1	7.1
>299			1		1	7.1
Total	80*	100.00			28*	100.00

*Two cases are not included. Patient No. 45 was not truly asleep and Patient No. 124 had diazepam to control post-arrest convulsion (see Special cases).

FIGURE 2. Length of patient stay in the recovery room.

of position inherent in neuro-radiological procedures. Central nervous system and musculo-skeletal manifestations such as clonus, tremors, convulsions, increase in muscle tone, and nystagmus do occur and body temperature elevations have been seen. Post-anaesthetic nausea and vomiting are not problems. Occasional coughing has been noted. This usually has been associated with the incision of the ear-drum during myringotomy. The incidence of hallucinations, unpleasant dreams, etc. has not been great, probably due to the fact that we have dealt with small children who in many instances would not have been able to communicate these manifestations to the observers. The nurses on the paediatric ward have remarked that many of the children behaved a little strangely after return but this has always been transitory and has not been a great problem. Where hallucinations have occurred and it has been possible to document them, it was always in older children.

TABLE XIII
DISTRIBUTION OF ADVERSE REACTIONS

Adverse reaction	Total occurrence
Headache	1
Ventilatory insufficiency	3
Hypertension	1
Apprehension	1
Clonus, tremors, and fasciculation	6
Cough	5
Dizzy	1
Dreams—pleasant	2
Erythema and/or rash	9
Generalized convulsion	2
Hallucination	2
Increased muscle tone w/wo movement	2
Increased temperature	5
Increased secretions	19
Nystagmus	4
Prolonged recovery	1
Purposeless movement	1
Vomiting	2
Nausea	1
Tachycardia	1
Dyspnea	1
Cardio-respiratory arrest	1

Special cases

Case No. 14: This was a 3½-year-old epileptic who, for his own protection, required the fitting of a face mask because of an uncontrollable number of attacks provoked by the slightest stimulus. There is no doubt that the application of a plaster of paris mold would have caused an epileptic seizure, but the procedure was easily accomplished under CI-581, obviating the necessity for endotracheal intubation in a case in which a face mask could not have been applied for maintenance of anaesthesia.

Case No. 26 and 27: This 2½-year-old girl required Cobalt radiation to tibia and femur for metastatic retinoblastoma. Use of CI-581 made it possible for the radiation to be carried out with the anaesthetist observing the patient through an observation window only, without the inherent risks of inhalation anaesthesia by remote control.

Case No. 57: This three-month-old baby had developed convulsions following a cephalo-haematoma which had occurred at birth. After premedication with atropine 0.2 mgms intramuscularly, anaesthesia was induced with 60 mgms 5 per cent Ketalar intramuscularly which failed to provide adequate anaesthesia. Twenty-two minutes later another 10 mgms were administered followed after 8 minutes by a further 30 mgms and 27 minutes later by another 30 mgms. Fifteen minutes after the first injection the child developed opisthotonos and while he became drowsy, he was aroused by any stimulus, even by touch, so that the procedure had to be abandoned.

Fifteen days later the patient was brought back. After the same premedication for another attempt at the operation, his body stiffened and he again developed opisthotonos on induction with nitrous oxide-oxygen and halothane. At the same

time there appeared a peculiar generalized pink skin discolouration. Induction could not be accomplished and attempts with this method were discontinued after approximately 1½ minutes. He then was just given oxygen by mask, was allowed to settle down and 12 minutes later was given thiopental 40 per cent rectally. An unknown amount of this was lost and was replaced. He became drowsy and sufficiently quiet to permit the pneumoencephalogram to be carried out.

It is of interest that while this child could not be anaesthetized with Ketalar, he reacted abnormally also to conventional anaesthetics.

Case No. 124: Cardiorespiratory arrest occurred in a two-month-old baby undergoing lumbar pneumoencephalography immediately after injection of 20 ml of air into the subarachnoid space. The usual resuscitative measures were instituted, some of the air was withdrawn and the patient made an uneventful recovery. Later studies revealed the presence of an aqueduct stenosis, which would explain the episode as due to a sudden increase in fourth ventricular pressure from the air which had no ready avenue of escape. It is felt that this occurrence was entirely unrelated to the use of Ketalar and would have occurred under any type of anaesthesia.

Multiple administrations

Review of those patients who were anaesthetized twice or more by this method failed to reveal any very major discrepancies which might have pointed to irreproducibility of results, bearing in mind the variable rate of absorption of any drug administered by any route other than the intravenous one.

SUMMARY AND CONCLUSIONS

Before a new anaesthetic agent can be recommended for general use it must prove its usefulness in definite clinical situations. Preferably, it should have advantages vis-a-vis established agents and techniques which outweigh its possible disadvantages. If it does not fulfil these criteria it becomes just another item on the shelf which unnecessarily complicates an already complicated situation.

On the basis of our experiences with intramuscular Ketalar in infants and children and that reported in the literature, CI-581 seems to fulfil these requirements. This is not to mean that it is an ideal agent and that it cannot be improved upon. However, its minimal cardiorespiratory depressant effect together with the retention of many protective reflexes allows one to anaesthetize these little patients for diagnostic and minor operative procedures without the necessity for endotracheal intubation and to do this more satisfactorily and predictably than with rectally administered barbiturates. In view of these advantages, the adverse reactions which we have observed and described and which are also well documented in the literature assume a significance of lesser magnitude.

Ketalar is a step in the development of new anaesthetics and it is probable that it points towards a development of anaesthesia in the future, which combines general analgesia with sedation. No doubt, drugs will be developed which will fulfil these requirements more perfectly than Ketalar, thus making it possible to widen considerably the indications for this technique.

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RÉSUMÉ

Dans cet article, nous faisons part de nos expériences avec le Kétalar (CI-581) donné par voie intramusculaire à des enfants et à des nourrissons pour pratiquer des examens diagnostiques et de la chirurgie mineure. Chez 101 malades, nous avons analysé 110 anesthésies. La dose initiale de Kétalar était calculée sur la base de 5 mgms/livre; à tout considérer, cette dose, d'après l'anesthésiste et le chirurgien, a produit un état de bon à excellent. La qualité extraordinaire a été les effets stimulants du médicament sur la tension artérielle, la fréquence cardiaque et la respiration. En injection intramusculaire, l'induction est rapide. D'autre part, nous avons observé que, après la dernière injection de Kétalar, le réveil était plutôt tardif, entraînant un séjour prolongé inhabituel du malade dans la salle de réveil postopératoire. Les réactions indésirables ont été peu nombreuses et, à notre avis, elles sont compensées par les avantages décisifs de cet agent sur son prédécesseur: le thiopental rectal et à cause du fait que, avec cet agent, il n'y a pas lieu de faire d'intubation endotrachéale.

À la lumière de nos expériences avec le Kétalar intramusculaire chez les enfants et les nourrissons nous sommes d'avis qu'il s'agit d'un agent utile dans les situations mentionnées et qui peut ouvrir la voie à de nouvelles applications en anesthésie.

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