RECOMMENDATIONS

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From the current study, it is recommended that:

1. Oral dexmedetomidine premedication can be used successfully for pediatric sedation.
2. Proper dose, formulation and timing of oral dexmedetomidine intake make it more effective with fewer side effects.
3. Oral dexmedetomidine alone can be not enough to preform painfull procedures.
4. Future studies should emphasize on the antrograde amnesia noticed with the dexmedetomidine with comparison to other drugs or using a larger number of patients.
5. In other studies, the combination of oral ketamine with other sedative agents should be studied.

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REFERENCES

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PROTOCOL

ORAL KETAMINE VERSUS ORAL DEXMEDETOMIDINE PREMEDICATION FOR OUT-PATIENT PAEDIATRIC DENTAL SURGERIES

الكيتامين عن طريق الفم مقابل الديكسميتوميدين عن طريق الفم ما قبل التخدير للاطفال الخاضعين لعمليات الاسنان

Protocol of a thesis submitted
to the Faculty of Medicine
University of Alexandria
In partial fulfillment of the
requirements of the degree of
Master of Anaesthesia
And Surgical Intensive Care

خطة بحث مقدمة
لكلية الطب
جامعة الإسكندرية
إيفاءً جزئياً
لشروط الحصول على درجة
الماجستير في التخدير
والعناية المركزة الجراحية

By

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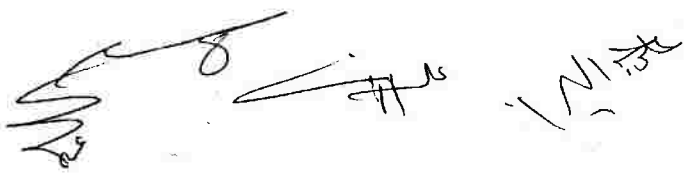

INTRODUCTION

Children undergoing surgical procedures are subjected to stressful events while preparing for surgery, such as the admission process, having blood drawn, receiving injections or having other medications administered. The children's stress continues while they are being transported, during induction and when they awaken before their parents arrive in the postanesthesia care unit. [1]

One of the challenges for paediatric anesthesiologists is to minimize distress for children in the perioperative period and to facilitate a smooth induction of anesthesia. [2]

Maladaptive behavioral responses such as general anxiety, night time crying, enuresis and separation anxiety occur up to 44% of children two weeks after surgery and about 20% of these children will continue to demonstrate negative behavior 6 months after surgery. [3]

Preoperative anxiety stimulates the sympathetic, parasympathetic and endocrine system leading to an increase in heart rate, blood pressure and cardiac excitability. [4]

Anticipation of dental procedures induces a number of physiologic changes characteristic of the anxious state. Anxiety and fear associated with dental procedures have been well documented and thought to represent a model of acute stressor. [5]

Dental treatment rendered under general anesthesia (GA) includes amalgam restorations, extractions, stainless steel crowns, composite/glass ionomer restorations, formocresol pulpotomy, fissure sealants, strip crowns and pulpectomy. Amalgam restorations and extractions constituted the most frequent dental procedure performed on child dental patients under GA. [6]

Unpremedicated children frequently object inhalational induction, and they often feel that the use of needles is one of the most worrisome aspects of the hospital stay. Children aged two to six years are especially vulnerable to this problem, Therefore, these children should be premedicated, in order to allow smooth induction, decrease anxiety and to prevent postoperative psychological and behavioral changes. [7]

various drugs have been advocated as premedication to allay anxiety and facilitate the smooth separation of children from parents. The ideal premedicant in children should be readily acceptable and should have a rapid and reliable onset with minimal side effects. [8]

Oral premedication are widely used in paedeatric aneathesia to reduce emotional trauma and ensure smooth induction.[9]

Ketamine is an arylcycloalkylamine that produces a state of sedation, anesthesia, immobility, analgesia, amnesia and dissociation from the environment. Pharmacologically, ketamine is classified as an N-methyl-d-aspartate (NMDA) receptor antagonist. It induces a state referred to as dissociative anesthesia by reducing or blocking signals to the conscious mind from other parts of the brain. [10,11]

Dexmedetomidine (Dex) has recently been added to the anesthesia. It belongs to the class of α_2 agonists and possesses the properties of sedation, analgesia and opioid sparing effect. It differs from clonidine in being 16 times more specific for α_2 receptors and with a more selective action and a shorter half-life. [12,13]

AIM OF THE WORK

The present study is designed to compare orally administered ketamine and orally administered dexmedetomidine as a sedative premedication in children undergoing out-patient dental surgery under general anesthesia as regards:

1) Sedative effect
2) Reaction to separation from the parents
3) Ease of venipuncture
4) Recovery
5) Discharge times
6) Postoperative amnesia.

PATIENTS

This study will be carried out on 80 ASA I and II patients aged between 4 and 6 years admitted to Department of paediatric dentistry,Alexandria Main University Hospital, scheduled for elective out-patient dental surgery under general anesthesia.

Sample size is statistically approved by the biostatistics department of the High Institute Of Public Health,Alexandria University.

Exclusion criteria

Patients suffering from:

- Cardiac disease.
- Neuromuscular disease.
- Pulmonary disease (e.g. asthma).
- Anticipated difficult airway.
- Any condition with increased risk of regurgitation and aspiration of gastric contents.
- Patients suffering from pharyngeal pathology e.g. abscess and haematoma.
- known allergy or hypersensitivity reaction to any of the study drugs.

METHODS

After approval of Medical Ethics Committee of the Faculty of Medicine and taking an informed written consent from the parents, every patient will be subjected to a careful pre-anesthetic assesement including:

Pre-operative evaluation:

- History of medical illness and drugs.
- Complete physical examination.
- Routine laboratory investigation: Complete blood count, bleeding time, clotting time, prothrombin time, partial thromboplastin time and International normalized ratio .

Pre-medication

- Children will be randomly allocated to one of the two equal study groups using computer-generated random numbers.
  - I. Group K :will receive 5 mg/kg oral ketamine[14]
  - II. Group D: will receive oral dexmedetomidine 3 μg/kg .[15]

    Both oral premedications will be duliuted in 3 ml of apple juice to be given thirty minutes before induction of anaesthesia.
- Children will be given premedication in the preoperative holding area in the presence of one parent.
- Emla cream will be applied to the place of possiable venipuncture.

Monitoring:

- All patients in the operating theater will be connected to multichannel monitor (Trakmon-Kontron-Limited- England) for display of:
    - Non invasive blood pressure.
    - HR and lead II ECG
    - Oxygen saturation.

Anesthesia:

- On arrival to operating room, an intravenous cannula will be inserted.
- All patients will be subjected to the same anesthetic protocol

a) **Induction:**

Atropine (0.02mg/kg IV) followed by propofol (2-3 mg/kg IV) Endotracheal intubation will be facilitated by atracurium (0.5mg/kg IV).

Intra-operative analgesia will be maintained by ketorolac (0.5mg/kg IV)

b) **Maintenance:**

Anesthesia will be maintained by isoflurane (1-2%) in 100% oxygen. Ventilation will be mechanically controlled. Atracurium increments will be given as required.

c) **Recovery:**

At the end of the procedure isoflurane will be discontinued . Neuromuscular block will be antagonized by neostigmine

(0.04mg/kg IV) and atropine (0.02mg /kg IV). Children will be extubated after return of protective reflexes.

d) **Discharge:**

Children will be discharged home on meeting discharge criteria.[16]

MEASUREMENTS:

1)Demographic data:

Age, sex and weight

2)Duration of surgery in minutes.

3)Vital signs

- Heart rate (beats/min).
- Mean arterial blood pressure (mmHg).
- Oxygen saturation percentage (SaO_2%).

Will be recorded at the following times:

- Base line (before sedation).
- Before induction of general anesthesia (30 min after sedation).
- During the procedure: Every 15 min.
- Post-operative: Every 30 min till discharge

4) Assessment of sedation

will be recorded after admission to OR (30 min after sedation) using sedative score: [17]

1	Sleeping, no response to patting the shoulder.
2	Sleeping, no response to call. Responds to patting on the shoulder.
3	Eyes closed, dull reaction. Responds to verbal stimulus.
4	Eyes open and closed by turns, dull reaction. Responds to verbal
5	Eyes open, dull reaction. Responds to verbal stimulus.
6	Normal reaction.
7	Irritable with body movement.

5)Assessment of ease of Separation and venipuncture

Will be graded according to Ease of Induction Score System: [18]

1	Excellent	Patient unafraid, cooperative or asleep.
2	Good	Slight fear and/or crying, quiet with reassurance.
3	Fair	Moderate fear and crying, not quiet with reassurance.
4	Poor	Crying, need for restraint.

6) Assessment of recovery:[19]

will be assessed as base line then postoperative every 10 min till baseline score regained, using "Vancouver sedative recovery scale for children". Recovery time from discontinuation of anesthesia till regaining baseline score will be recorded.

	Parameter	Finding	Points
(A)	Awake-asleep	Awake and alert.	4
		Awake but drowsy.	3
		Asleep but easily aroused.	2
		Asleep and difficult to arouse.	1
		Asleep and unable to arouse.	0
(B)	Response to stimuli	Responds fully to stimuli.	2
		Delayed response to stimuli.	1
		Absent response to stimuli.	0
(C)	Facial expression	Alert.	1
		Flat.	0
(D)	Appearance of eyes	Bright eyes.	1
		Dull eyes; glazed.	0
(E)	Feeling how looks at you	Looks "at you"	1
		Looks "through you"	0
(F)	Visual stimulus	Recognition of stimulus.	1
		Limited or no recognition of stimulus.	0
(G)	Eye movement	Purposeful and spontaneous.	1
		Little or no spontaneous or purposeful.	0
(H)	Activity	Spontaneous & varied central activity.	4
		Spontaneous & varied peripheral activity.	3
		Central activity in response to stimuli.	2
		Peripheral activity in response to stimuli.	1
		No movement.	0
(I)	Tremor or ataxia	Absence of tremor or ataxia.	1
		Ataxia or tremor on being moved.	0
(J)	Spontaneous movement	Coordinated spontaneous movement.	2
		Weak/coarse spontaneous movement.	1
		No purposeful spontaneous movement.	0
(K)	Hand movements	Age-appropriate manual dexterity.	2
		Awkward or clumsy hand movement.	1
		No fine hand movement.	0

7) Discharge time: [20]

Discharge time from discontinuation of anesthesia until the patient is discharged to home, using" The Short-Stay Surgery Discharge Score" will be recorded (A score of 10-12 was needed for discharge).

Parameter	Finding	Points
Temperature	Severe chills and/or increased perspiration.	0
	Oral temperature > 38°C or < 36°C.	1
	Oral temperature 36-38°C.	2
Circulation	Blood pressure and heart rate changed more than 20 % from preoperative values.	0
	Standing blood pressure < supine blood pressure. Pulse increases >10 beats/min when standing.	1
	Standing blood pressure about the same as supine. Pulse increase < 10 beats/min when standing.	2
Activity	Unable to ambulate, sleepy.	0
	Out of bed with assistance.	1
	Out of bed without assistance and able to states discharge instructions.	2
Pain	Needs pain medicine administered IM.	0
	Needs pain medicine administered PO.	1
	Free of pain.	2
Bleeding	Large amount of surgical bleeding.	0
	Moderate amount of surgical bleeding.	1
	No surgical bleeding and no hematoma.	2
Intake Output	No PO fluids; unable to void.	0
	PO ice chips, sips fluids; voids into urinal.	1
	PO fluids without nausea or vomiting for 1 hour; voids quantity sufficient in bathroom.	2

8) Assessment of amnesia: [21]

The anterograde amnesia will be assessed after 24 hours by a recall questionnaire of the parents, which will include the questions about events which takes place after the administration of sedative.

RESULTS

The results obtained from this study will be tabulated and statistically analyzed using the standard statistical methods with the aid of different ways of presentation: numerical, mathematical and graphical.

DISCUSSION

The results of the study will be discussed in details and compared with any available and published data.

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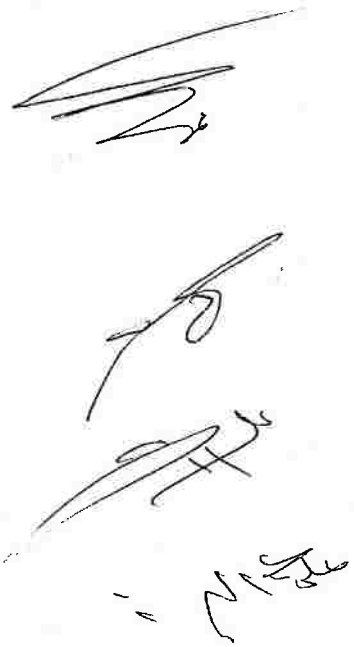

ARABIC SUMMARY

الملخص العربى

من الواضح أن عدم وجود القدر الكافى من التهدئه قبل العمليات الجراحيه فى الاطفال ينتج عنه شعور هؤلاء الاطفال و عائلاتهم بالقلق خلال الفتره المحيطه بالعمليه و أن زياده التوتر و القلق أثناء مرحله الأدخال التخديرى من الممكن أن يؤدى لزياده الضلالات أثناء الأفاقه.

ان القلق المرتبط بعمليات الاسنان يمثل حاله من التوتر و توقع الخطر، و أن توقعها يحفز مجموعه من التغيرات الفسيولوجيه المميزه لحاله القلق.

ان أدويه ما قبل التخدير فى الاطفال عاده ما تكون فى صوره ادويه مساعده للتخفيف من التوتر و الخوف المصاحب للعمليات الجراحيه ، كما يسهل فصل الابناء عن الاباء و يحقق السهوله فى الإدخال التخديرى.

ان أفضل عقار للتهدئه قبل التخدير و طريقه أعطاءه لا يزال محل خلاف.

هدف البحث

كان الهدف من هذا البحث دراسة و مقارنه عقارالكيتامين و عقار الديكسميتوميدين عن طريق الفم فى الاطفال للتهدئه قبل عمليات الاسنان الصغرى تحت تأثير التخدير الكلى من حيث التأثير على العلامات الحيويه، درجه التهدئه، سهوله الانفصال بين الطفل و ابويه ، سهوله ادخال قسطره وريديه طرفيه ، التأثير على الفتره الزمنيه اللازمه للأفاقه من التخديرو الخروج للمنزل، و كذلك قدره العقار على أحداث فقدان للذاكره.

أجريت هذه الدراسة على ثمانين طفلا سليما ، تتراوح أعمارهم بين اربع و ست سنوات و كانوا بالوضع الصحى الاول او الثاني حسب تصنيف الجمعيه الامريكيه للتخدير، و الذى حدّد لهم سلفاً جراحات أسنان صغرى تحت تأثير التخدير الكلى.

وقد تم تقسيم المرضى إلى مجموعتين متساويتين حسب نوع العقار المستخدم كدواء مهدء قبل العملية:

المجموعة K: تم إعطائهم شراب عقارالكيتامين عن طريق الفم ، ثلاثون دقيقه قبل دخول حجره العمليات.

المجموعة D: تم إعطائهم شراب عقار الديكسميتوميدين عن طريق الفم ، ثلاثون دقيقه قبل دخول حجره العمليات.

تم تقييم كل المرضى قبل العمليات الجراحية عن طريق التعرّف علي التاريخ المرضي، الفحص السريري الكامل، تقييم الممرات الهوائية، و الإختبارات المعمليّة الروتينية. عند وصول المرضي إلي غرفة العمليات تم توصيلهم بأجهزة المراقبة القياسية و التي تشتمل علي؛ رسم القلب، قياس ضغط الدمّ، و قياس نسبة تشبع الدمّ بالأكسيجين،ثم تركيب قسطره وريديه طرفيه. جميع المرضي الذين شاركوا في هذه الدراسة تم إخضاعهم لنفس نظام التخدير.

القياسات

لكل المرضى المشتركين فى هذه الدراسة تم قياس معدل ضربات القلب و متوسط ضغط الدم الشريانى و نسبة تشبع الدم الشريانى بالأكسجين باستمرار مع تسجيلها قبل العملية الجراحية وكل ١٥ دقيقه أثناء العمليه وبعد العملية كل ٣٠ دقيقه. كذلك تم قياس درجه التهدئه قبل العملية الجراحية باستخدام مقياس التهدئه،و تم قياس سهوله الحصول علي وريد بعد استخدام الدواء بنصف ساعه باستخدام مقياس سرعه الادخال التخديرى و سرعه دخول القسطره الوريديه، كما تم قياس نسبه وعى الطفل بعد العمليه بالمقارنه لقبل استخدام الدواء باستخدام مقياس التعافى التخديرى، و قياس الوقت اللازم للإفاقة الكاملة و أمكانيه الخروج الى المنزل، كما تم التحقق من قدره العقارعلى أحداث فقدان للذاكره عن طريق اسئله مباشره للاهل و الطفل.

نتائج البحث

- لا توجد فروق ذات دلالة إحصائية بين المجموعتين المشتركتين فى هذه الدراسة من حيث السن والنوع ووزن الجسم، وقت العملية.
- لا توجد فروق ذات دلالة إحصائية بين المجموعتين المشتركتين فى هذه الدراسة من حيث العلامات الحيويه.
- يوجد فروق ذات دلالة احصائية بين معدل ضربات القلب بين المجموعتين عند ٣٠ دقيقه بعد اعطاء العقار و في لدقيقه ٠ و ٣٠ ما بعد العمليه.
- يوجد فروق ذات دلاله احصائيه بين متوسط ضغط الدم الشرياني بين المجموعتين عند ٣٠ دقيقه بعد اعطاء العقار و في الدقيقه ٣٠,٠و٦٠ بعد العمليه.

- لا توجد فروق ذات دلاله احصائيه ما بين المجموعتين فيما يتعلق بنسبه تشبع الاكسجين بالدم علي مدار الدراسه.
- درجه التهدئه كانت أفضل فى المجموعه D مع وجود فارق ذو دلالة إحصائية بين المجموعتين.
- سهوله انفصال الطفل عن والديه و تركيب قسطره وريديه طرفيه كانت افضل فى المجموعه D مع وجود فارق ذو دلاله احصائيه بين المجموعتين.
- لا توجد فروق ذات دلالة إحصائية بين المجموعتين المشتركتين فى هذه الدراسة من حيث الوقت اللازم للنهوض من التخدير و لأمكانيه الخروج الى المنزل.
- قدره العقارعلى أحداث فقدان للذاكره تحقق بنسبه أكبر فى المجموعه D مع وجود فارق ذو دلالة إحصائية بين المجموعتين.

نستخلص من هذا البحث:

١. عقارى الكيتامين و الديكسميتوميدين عن طريق الفم ممكن استخدامهم لتهدئه الاطفال قبل العمليات الجراحيه بنجاح.
٢. اعطاء عقار الديكسميتوميدين عن طريق الفم وحده قبل العمليه الجراحيه كافى لتهدئه الطفل بصوره مرضيه و لا يحتاج بجانبه الي اى محاولات تعديل اخرى لتهدئه الطفل سلوكيا.
٣. أعطاء عقار الكيتامين عن طريق الفم وحده بجرعه ٥ مجم/كجم غير كافي لتهدئه الطفل تماما.

التوصيات

١. أستخدام عقار الديكسميتوميدين عن طريق الفم قبل التخدير فى الأطفال بالجرعه و الوقت الامثل لتفادى اي اعراض جانبيه للعقار.
٢. عقار الديكسميتوميدين وحده غير كافي للقيام بعمليات مؤلمه نسبيا كما يجب ضروره دراسه تاثيره في فقدن الذاكره .
٣. ضرورة دراسة أستخدام عقار الكيتامين قبل التخدير فى الاطفال مع أدويه مهدئه أخرى.

الملخص العربى

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الكيتامين عن طريق الفم مقابل الديكسميتوميدين عن طريق الفم ما قبل التخدير للاطفال الخاضغين لعمليات الاسنان

مقدمة من

منار محمود علوى
بكالوريوس الطب والجراحة - جامعة الإسكندرية، ٢٠٠٨

للحصول على درجة

الماجستير

فى

التخدير والعناية المركزة الجراحية

لجنة المناقشة والحكم على الرسالة	موافقون
أ. د./ سلوى شعبان شعراوى أستاذ التخدير والعناية المركزة الجراحية كلية الطب جامعة الإسكندرية	.....
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د./ علا محيى الدين زناتى استاذ مساعد التخدير والعناية المركزة الجراحية كلية الطب جامعة الإسكندرية	.....

الكيتامين عن طريق الفم مقابل الديكسميتوميدين عن طريق الفم ما قبل التخدير للاطفال الخاضغين لعمليات الاسنان

رسالة علمية

مقدمة إلى كلية الطب– جامعة الإسكندرية

إستيفاء للدراسات المقررة للحصول على درجة

الماجستير

فى

التخدير والعناية المركزة الجراحية

مقدمة من

منار محمود علوى

بكالوريوس الطب والجراحة - جامعة الإسكندرية، ٢٠٠٨
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