Research Protocol

**Project Title:** Effect of sugammadex on the serum plasma levels of circulating oestrogens and progesterones in healthy females who take hormone contraception in the perioperative setting.

**Investigators:**

 Dr. Tamblyn Devoy – Principle Researcher, Junior Medical Officer, participant recruitment

 Dr. Natalie Smith – Research Supervisor, Clinical Associate Professor & Specialist Anaesthetist

 Clinical Anaesthetists – sample collection of participants

**Rationale/Background:**

Lab studies suggest that sugammadex can reduce plasma oestrogen and progesterone concentrations to the equivalent effect of 1 missed dose of the pill. However, there has been no investigations of this in real life patients.

**Aims/Objectives/Hypotheses:**

 Primary outcome:

* Is there a reduction in free serum oestrogen and/or progesterone after administration of sugammadex in the perioperative setting?

**Participating Sites:**

 Anaesthetic Department, The Wollongong Hospital, Illawarra Shoalhaven Local Health District

**Study Design:**

Type: prospective, controlled trial

Lead Study: The Effect of Sugammadex on Steroid Hormones: A Randomised Controlled Trial, Gunduz Gul et al. 2016

Source of participants: pre-operative patients through the Day Surgery Unit that meet eligibility criteria as detailed below.

Data Collection: 3 samples (1) pre-administration of sugammadex/before end of surgery, 2) 15mins post-administration/end of surgery , 4hrs post-administration (based on half-life of sugammadex)/end of surgery; clinical anaesthetist & health staff to collect sample; test for serum oestrogen and progesterone levels; serum tests by the Pathology Department, The Wollongong Hospital.
N.B.: end of surgery defined as when leaving OT

Sample Groups:

 “Control A”: those who do NOT receive sugammadex and are NOT on hormone contraception

 “Control B”: those receiving sugammadex who are NOT on hormone contraception.

 “Intervention”: those receiving sugammadex who ARE on hormone contraception.

Sample Size:

 Control groups: 30 participants each group (60 total)

“Intervention”: 60 (36-86) participants

Sample Size Calculation/Justification: 0.80 power (standard), 0.5 effect size (sugammadex reversal time ~half that of neostigmine – previous gold standard for reversal), Mixed Model ANOVA

Outcome Measures: significant reduction of serum oestrogen or progesterone concentration

Statistical Analysis: Research Central, Illawarra Shoalhaven Local Health District

Expected duration of study: 3-4 months

Study Outline:

 Participants: pre-menopausal women between 18-50 years old who present to the Day Surgery Unit for planned operative procedures will receive a participant information, participant consent and eligibility questionnaire to assess eligibility into study (see attachments).

Exclusion Criteria:

* Male participants
* Females <18 years old or >50 years old
* Post-menopausal women
* Incomplete/missing detail in questionnaire form

Sample Collectors: case anaesthetists who receive an instruction kit for collection of samples; and trained health staff for the final sample after their operation.

Ethical Considerations:

 Recruitment & Selection of Participants: Day Surgery Unit for planned procedures, nil change in anaesthetic protocol, inclusion/exclusion based on questionnaire provided with participation information and informed consent forms (see attachments), expected to be recruiting patients 1-2 days per week.

 Informed Consent: attempt to engage potential participants early on arrival prior to their operation/procedure to allow time to consider participation into study, and provide informed consent.(see attachments)

 Enrolment Procedure: eligible patients are consented and initial questionnaire completed, enrolled participants will be coded using the case report form using a sequential coding system. Their serum results will be extracted from patient file. This may inadvertently allow viewing of unintended results.

 Confidentiality & Privacy: data extracted and deidentified by principle researcher for statistical analysis by 3rd party (Research Centre), data will be password secured and physical forms stored with limited access to files.

 Safety: nil change in anaesthetic protocol as determined by case anaesthetist, 3x 10mL samples collected via cannula already inserted for purposes of procedure, and/or venepuncture sample if necessary.

 Data Storage & Record Retention: accessed by principle investigator and de-identified into data pool for statistical analysis by 3rd party, stored with password locked device and standard precautions, physical records will be destroyed 7 years after publication of results or as recommended by the Ethics Committee.

References:

1. Smart A, Gallagher J. Clinicians and women's learning package on Sugammadex (Bridion) and hormonal contraceptives. Australian nursing & midwifery journal. 2015;22(9):52.

2. Dalton J, Van Hasselt G. Sugammadex - time of onset: nine months. Anaesthesia. 2016;71(1):115-6.

3. DeAndrade DS, Berman JR, Boisen ML. Approaches to Patient Counseling Regarding Effectiveness of Oral Contraceptives. Anesthesia and analgesia. 2018;126(5):1789.

4. Williams R, Bryant H. Sugammadex advice for women of childbearing age. Anaesthesia. 2018;73(1):133-4.

5. Et T, Topal A, Erol A, Tavlan A, Kilicaslan A, Uzun ST. The Effects of Sugammadex on Progesterone Levels in Pregnant Rats. Balkan medical journal. 2015;32(2):203-7.

6. Gunduz Gul G, Ozer AB, Demirel I, Aksu A, Erhan OL. The effect of sugammadex on steroid hormones: A randomized clinical study. Journal of clinical anesthesia. 2016;34:62-7.

Research Eligibility Checklist & Participant Tracing for Data Extraction:

TITLE: Effect of sugammadex on the serum plasma levels of circulating oestrogens and progesterones in healthy females who take hormone contraception in the perioperative setting.

 [please affix patient BRADMA]

Patients approached for potential inclusion in study:

* Females >18 years old or <50 years old in Day Surgery Unit awaiting a planned procedure requiring anaesthetic management

Please tick the following when complete:

* Introduction & patient explanation of research
* Provided participant information sheet, consent form and eligibility questionnaire package
* Signed consent form
* Completed questionnaire form
* If eligible, participant involvement package provided to case anaesthetist

Exclusion criteria:

* Male participants
* Females <18 years old or >50 years old
* Post-menopausal women
* Incomplete/missing detail in questionnaire form

Please circle the appropriate categories

ELIGIBLE NOT ELIGIBLE

and

CONTROL GROUP A CONTROL GROUP B

INTERVENTION GROUP

Research Team name completing form: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Case Anaesthetist: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Anaesthetist Instructions for study participants



TITLE: Effect of sugammadex on the serum plasma levels of circulating oestrogens and progesterones in healthy females who take hormone contraception in the perioperative setting.

Thank you for your assistance in completing this project. Whilst under sedation, patients will need 3 samples of venous blood for analysis in the Pathology Department. Please ensure sample times and/or order number is clearly marked on each sample.

 [please affix patient BRADMA]

Is this patient receiving sugammadex as a part of the anaesthetic protocol?

Yes / No

Please take the following samples and record the details below.

Sample 1: at induction (prior to sugammadex administration/end of surgery\*)

 Time: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

What time did the patient receive sugammadex, if given?

Time: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Sample 2: 15 minutes after administration of sugammadex/end of surgery

Time: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Sample 3: 4 hours after administration of sugammadex/end of surgery

Time: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

\*Note: end of surgery defined as when leaving OT

Case Report Form

Study ID:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  |  |  |  |


TITLE: Effect of sugammadex on the serum plasma levels of circulating oestrogens and progesterones in healthy females who take hormone contraception in the perioperative setting.

 [please affix patient BRADMA]

Group: Control A Control B Intervention

Questionnaire Data:

|  |  |
| --- | --- |
| Age:  |  |
| Self-stated menopause: | Yes / No |
| On hormone contraceptive: | Yes / No |
| Last menstrual period: |  |
| **If Yes;**  |
| Contraceptive type (+strength if known):  |  |
| Timing of contraceptive:  |  |
| **If ORAL contraceptive;** |
| Been taking regular in past week: | Yes / No |
| Any missed doses in past week: | Yes / No |
| Currently active or inactive tablet: | Active / Inactive  |
| **If NON-ORAL contraceptive;**  |
| What device:  |  |
| When inserted: |  |

Sugammadex & Serum Data:

|  |  |
| --- | --- |
| Sugammadex administration time:  |  |
| Sample 1 time: |  |
| Sample 2 time: |  |
| Sample 3 time: |  |

Case Report Form

Study ID:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  |  |  |  |


TITLE: Effect of sugammadex on the serum plasma levels of circulating oestrogens and progesterones in healthy females who take hormone contraception in the perioperative setting.

Progesterone levels:

|  |  |
| --- | --- |
| Sample 1 Level |  |
| Sample 2 Level |  |
| Sample 3 Level |  |

Oestrogen levels:

|  |  |
| --- | --- |
| Sample 1 Level |  |
| Sample 2 Level |  |
| Sample 3 Level |  |