



Local Anesthetic Efficacy of Tramadol Hydrochloride with Adrenaline in the Extraction of Maxillary Teeth

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Abstract

Aims: To access the local anaesthetic effect of tramadol hydrochloride with adrenaline and its applicability in the extraction of maxillary teeth. **Methodology:** 100 patients were selected from the outpatient department (OPD) of oral and maxillofacial surgery, who needed extraction of any maxillary teeth and were under ASA – I category, and Using software SPSS Version 16 statistical analysis was done. **Results:** Tramadol hydrochloride 50mg with adrenaline 0.0225mg exhibits a local anaesthetic effect that enables successful and painless extraction of maxillary teeth. **Conclusion:** Tramadol hydrochloride does exhibit local anaesthetic effect and can be used as an alternative to conventional anaesthetics however due to certain unusual reasons this it cannot be proposed as a first-line agent.

Keywords: Tramadol hydrochloride Local Anesthesia Extraction.

Introduction

All humans on the earth are scared of the term 'pain', which is an unpleasant feeling, even in a lower threshold makes life uncomfortable. During a surgical procedure, many cells are damaged, which evoke the path of inflammation, releasing numerous chemical mediators which would evoke the pain. As it is said "the pain of the mind is worse than pain in the body", its management requires dampening both mental and physical pain, therefore,

making patients comfortable. Dealing with this kind of pain would differ from prescribing analgesics or anaesthetics rely on the intensity and availability.¹

Local anaesthetic agents are known to occult impulse conduction by restraining the voltage gradient sodium channels in a concentration-dependent manner, they are also capable of conducting nerves without affecting resting membrane potential. It is postulated that

tramadol, a synthetic opioid in the aminocyclohexanol group, has the same local anaesthetic effect as that of lidocaine following intradermal injection.²

Skeletally this drug is related to codeine and morphine and acts mainly on the central nervous system; it is six thousand times less potent than morphine and ten times less potent than codeine. It was first discovered in the year around the 1970s and was accepted by the FDA (Food and Drug Administration) in 1995 to relieve and treat severe to moderate pain. Tramadol hydrochloride exhibits low affinity for μ -opioid and κ -opioid receptors, acting as a weak agonist and it acts upon monoamine receptors by blocking the reuptake of norepinephrine and serotonin (5-HT) which is required to ward off the pain stimulus transmitted in the spinal cord.³ This unique pharmacological profile of tramadol hydrochloride makes it more advantageous than common opioid agents, as it exerts fewer incidences of side effects & abuse potential.⁴

Clinical and laboratory studies have also shown that tramadol hydrochloride has local anaesthetic effect on peripheral nerves in addition to its systemic effects. In a study, in 2010 it was found that 5% tramadol hydrochloride plus adrenalin could provide safe and effective local anaesthesia during circumcision procedures and post-operative periods in children.⁵ However, the local anaesthetic effect of tramadol hydrochloride in oral and maxillofacial surgery has not been studied much, so in this study, the local anaesthetic effect of tramadol hydrochloride with adrenaline and its applicability in the extraction of maxillary teeth is evaluated.

Methods

The study was conducted in the Department of Oral and Maxillofacial Surgery, INSTITUTE OF DENTAL SCIENCES AND SUM HOSPITAL Bhubaneswar, after obtaining ethical committee clearance [Annexure -1]. The purpose of the study was explained to all the patients included in the study and written informed consent was obtained. [Annexure -2].

100 patients were selected from the outpatient department (OPD) of oral and maxillofacial surgery, who needed extraction of any maxillary teeth and were under the ASA – I category.

Study design: In this study, a sample size of 100 patients was taken. Each subject was randomly assigned and the parameters taken for consideration to evaluate the efficacy of tramadol hydrochloride with adrenalin were

- *Latency* i.e. – After injection of the anaesthetic solution, to the time of first anaesthetic effect (objective sign)
- *Duration of anaesthesia* i.e. – the time from an initial patient perception of the anaesthetic effect to the moment in which the effect began to fade.
- Visual analogue scale [VAS]- 10 cm
- Vomiting
- Paresthesia.
- Soft tissue changes.

Inclusion criteria: The subjects were in good health (ASA-I) and were not taking any medications that would alter their perception of pain; with any maxillary teeth indicated for extraction and orthodontic extraction.

Exclusion criteria

- Younger than 14 years old.
- Patient with compromised medical status.
- Allergy or hypersensitivity to the drugs used in this study.
- Pregnant or lactating women.
- Patients who refused to be involved in the study.

Execution: A special questionnaire was added to record relevant history and to record the above-mentioned parameters [Annexure- 3]. Each patient received an initial dose of 1 injection (mixture of tramadol HCl 50 mg and adrenalin 0.0225 mg diluted to 1.8 ml by distilled water) using a 25G needle, 25 mm. The

study drug was prepared by an autonomous investigator in the Department of Pharmaceuticals science, who was not involved in the surgical procedure. [Drug Preparation-Annexure 4]. Drug preparation was done taking tramadol HCL of 50mg/ml and adrenaline of 0.0225mg (0.8ml). Since adrenaline is supplied as 1mg/ml, but the requirement of adrenaline is 0.0225mg in 0.8ml. The adrenaline is diluted with sterile water using a dilution factor.

Dilution factor: Concentration required/ Concentration given

On calculating the dilution factor was 1:35.5, where the solution should be diluted up to 35.5ml with sterile water i.e., taking 1ml of adrenaline it was diluted up to 35.5ml with sterile water. The concentration of newly prepared solution is $0.0281\text{mg/ml} = 0.0225\text{mg}/0.8\text{ml}$, this solution will be 'stock solution'. So, 0.8ml of stock solution of adrenaline was taken to make 1.8ml of dental cartridge and 0.4ml of stock solution to make 0.9ml of the dental cartridge.

The supra-periosteal infiltration technique was used to anaesthetize the teeth, solution deposited in buccal aspect is - 1.6 ml and palatal aspect -0.2ml. Mucoperiosteal flap was elevated 3 minutes after administration of the anaesthetic solution by the operator. The patient was asked to acknowledge the investigator about the degree of pain at any time during extraction by moving or raising the left hand. The amount of pain was estimated with a 10-cm VAS (visual analogue scale).

The Visual analogue scale consisted of an interval scale ranging from 0 (no pain or discomfort) to 10 (maximum pain). The national initiative on pain control (NIPC) has provided certain diagnostic tools in grading the severity and quality of pain felt by patients. Different pain assessment scales like Wong-Baker FACES pain rating scale, Visual Analog Scale (VAS), verbal pain intensity scale and descriptor differential scale.³⁵ In the present study the visual Analog scale, a unidimensional measure of pain intensity has been used in

patients. The pain visual analogue scale is a continuous scale comprised of horizontal (HVAS) or vertical (VAS) lines, usually 10cm (100 mm) in length, anchored by two verbal descriptors, one for each symptom extreme. Score interpretations of the visual analogue scale have been recommended as – no pain (0-3), mild pain (4-5), moderate pain (6-7), severe pain (8-10).³⁶ The mean of the VAS scores during the extraction was calculated and recorded. During the extraction, when the Visual analogue scale exceeds 3 points, an additional 0.9 ml of the same drug was injected into the site of extraction. The amount of solution infiltrated, in addition to the duration of extraction, which represents the interval from the gingival separation to the completion of tooth extraction were recorded. During the extraction procedure, all emergency backups such as oxygen, epinephrine, avil, anti-emetics, steroids, etc were maintained chair side to counter any adverse events. Nausea and vomiting were recorded using a 3-point ordinal scale (0, none; 1, nausea; 2, vomiting). Patients were reviewed after 24 hours and 48 hours and information about adverse effects were recorded like paresthesia, tissue irritation, etc.

Results

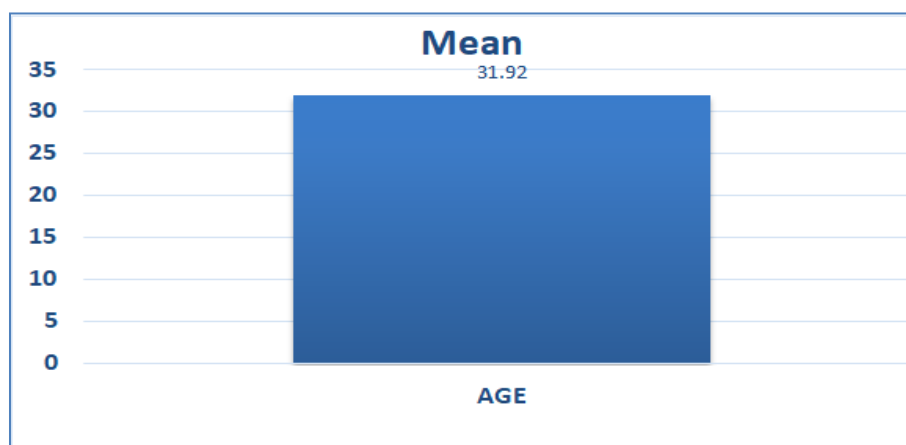
In this descriptive study, 100 subjects underwent extraction of maxillary teeth using tramadol with adrenalin, and the applicability of the drug was evaluated with the following parameters: the need for 1st and 2nd injection, visual analogue scale, latency, duration, male and female predilection and complications. Using software SPSS Version 16 statistical analysis was done. All the patients were evaluated with a VAS scale after 1st injection and 2nd injection if needed. The Mean age predilection is 31.92 (with SD 13.40), the mean volume of 1st injection is 1.8 (with SD .00) and the mean volume for 2nd injection is .90(with SD .00), the mean latency is 5.01 (with SD 1.88) and the mean duration is 2634.60 (with SD 1075.19). (Table -1). Out of 100 patients, the sex ratio was, 65% were female and 35% were male (Table -2).

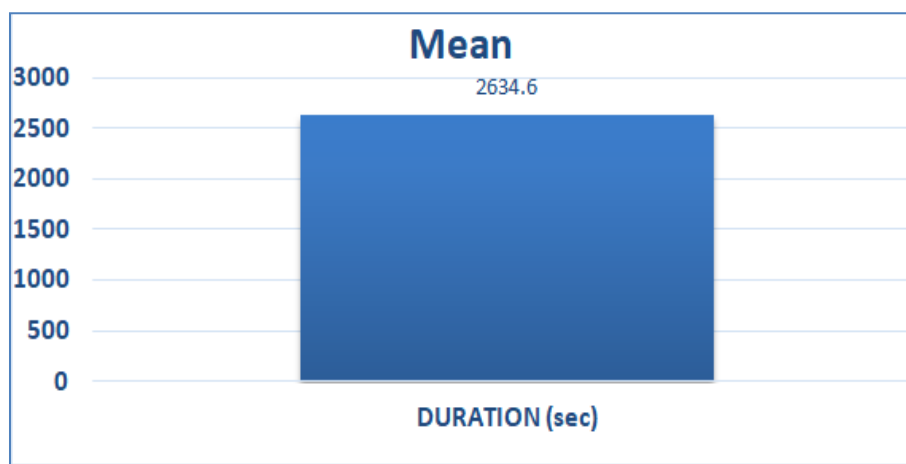
Table 1: Mean and standard deviations of age, the volume of 1st and 2nd injection, latency, duration

Parameters	Mean	SD
Age	31.92	13.40
Volume of 1 st Injection (ml)	1.80	0.00
Volume of 2 nd Injection (ml)	0.90	0.00
Latency	5.01	1.88
Duration	2634.60	1075.19

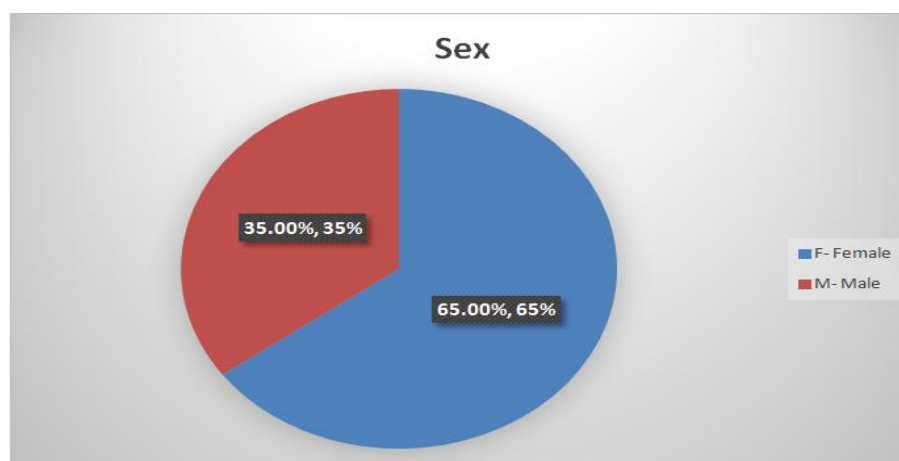
Table 2: Mean values of male and female predilection

		N	%
Sex	F	65	65.0%
	M	35	35%

**Graph 1: Bar diagram showing mean age group****Graph 2: Bar diagram showing mean latency of the solution**



Graph 3: Bar diagram showing mean duration in seconds



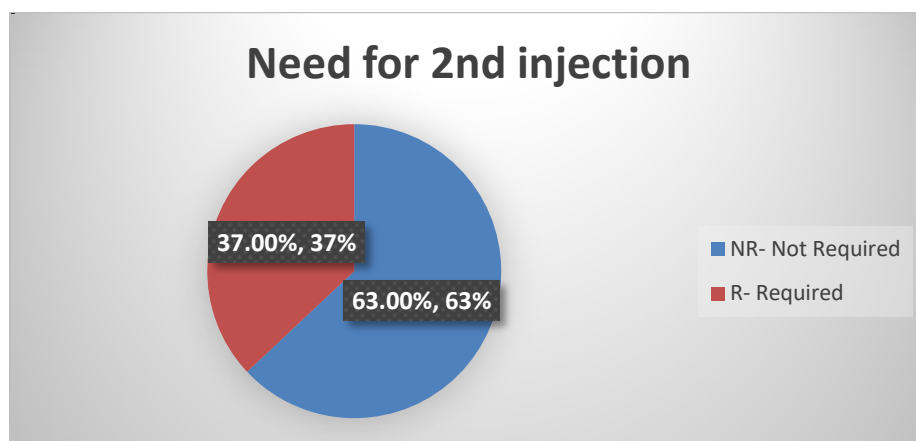
Graph 4: Pie diagram showing a male and female predilection

Out of 100 subjects, 37% needed 2nd injection whereas 63% did not need 2nd injection. Complications like nausea and vomiting were noted down using an ordinal scale marked with 3 points- (0 none; 1 nausea; 2 vomitings) out of which 92% showed '0' on ordinary scale, 7% showed '1' on the ordinary scale and 1% showed '2' in ordinal scale. Paresthesia and other complications like tissue irritation were not seen. (Table -3)

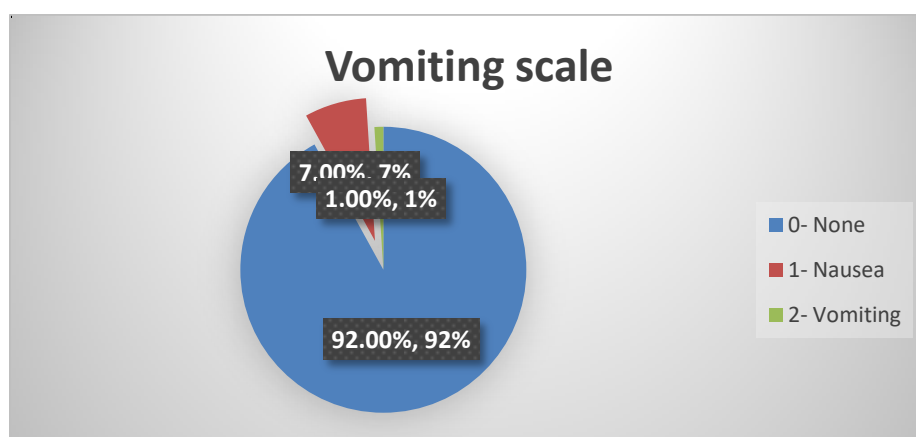
Table 3: Percentages of need for the second injection, complications (vomiting scale, paraesthesia, others

		N	Percentage (%)
Need for Second Injection	NR	63	63.0
	R	37	37.0
Vomiting Scale	0	92	92.0
	1	7	7.0
	2	1	1.0
Parasthesia	NIL	100	100
Others	NIL	100	100

N: Number; NR: Not required; R: Required



Graph 5: pie diagram showing the need for the second injection

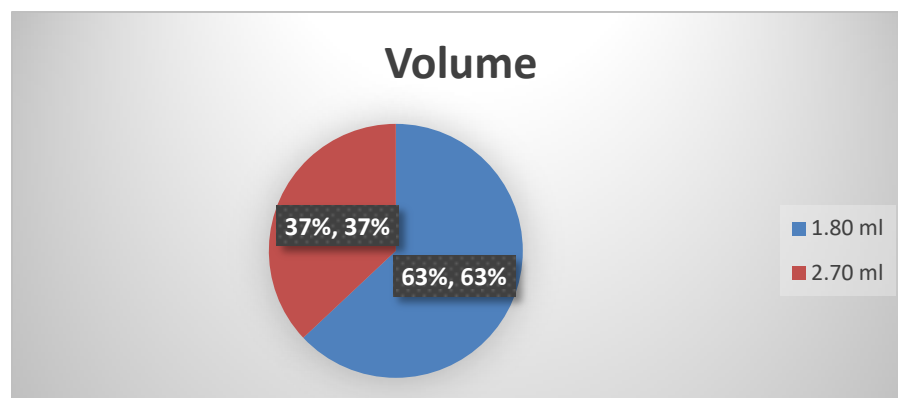


Graph 6: Pie diagram showing the vomiting scale

Out of 100 patients, 63% received a single dose of 1.8 ml of the prepared solution whereas 37 % received an additional dose of 0.9 ml i.e., total 2.70 ml maximum dose. The mean volume of solution was 2.1330 (with SD - .43671). (Table -4)

Table 4: Percentage of the volume of solution after 1st and 2nd injections

Volume	N	Percentage (%)
1.80 mL	63	63.0
2.70 mL	37	37.0



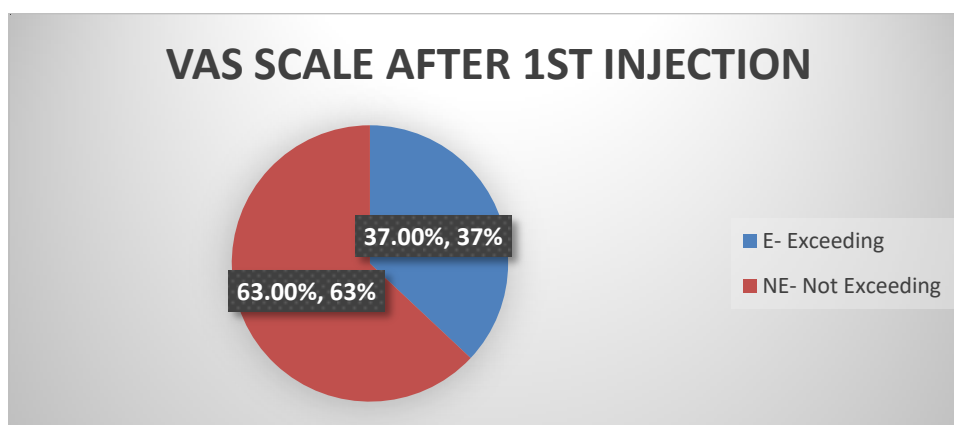
Graph 7: Pie diagram showing total volume of the solution deposited

In 63% of patients who underwent extraction, the VAS score did not exceed 3 after 1st injection whereas in 37% of patients the VAS score exceeded 3 for which 2nd injection was given. After the 2nd injection, 37% of the patients showed \leq a 3 VAS score. (Table -5)

Table 5: Percentages of VAS score after 1st and 2nd injections

		N	Percentage (%)
VAS Scale after 1 st injection (E/NE)	E	37	37.0%
	NE	63	63.0%
VAS Scale after 2nd injection (E/NE)	NE	37	37.0%

N: Number; E: Exceeding; NE: Not Exceeding



Graph 8: Pie diagram showing VAS scale

Discussion

The international association for the study of Pain (IASP) has described the pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.” Their published taxonomy includes several specific pain terms including allodynia, analgesia, anesthesia Dolorosa, causalgia, central pain, dysesthesia, hyperalgesia, hyperesthesia, hyperpathia, and hypoalgesia.⁶⁻⁹

The most commonly used local anaesthetic for dental surgery is 2 per cent lignocaine with 1:80000 adrenaline. The 1:200,000 or 1:100,000 solutions gives a sufficient duration of action for the majority of minor surgical procedures in dentistry.¹⁰⁻¹² Adrenaline is combined with the LA to enhance its anaesthetic efficiency, mainly duration and it also gives a bloodless operative site and decreases the absorption rate of local

anaesthetics by reducing the plasma concentration.¹³⁻¹⁷

Tramadol hydrochloride is a synthetic opioid analgesic drug, which indicates both opioid and non-opioid properties. This drug is structurally alike to codeine, morphine and acts in particular on the central nervous system. It was first observed in the 1970s and later recognized by Food and Drug management (FDA) in the year 1995 for management and treatment of mild to extreme pain situations. Tramadol hydrochloride acts on μ -opioid and κ -opioid receptors with much less affinity, with a susceptible agonist effect, and it impacts monoamine receptor structures utilizing interfering nor-epinephrine and serotonin (5-HT) reuptake, which is accountable for blocking of pain transmission within the spinal cord. This particular pharmacological action of tramadol hydrochloride makes it more beneficial than other regular opioids, in terms of side effects and abuse potential.¹⁸⁻²¹

Tramadol hydrochloride is essentially metabolized inside the liver via cytochrome isoenzymes P450 2D6, and P450 2B6 and P450 3A4, to O-desmethyl tramadol (M1) and N-desmethyltrama-dol (M2) respectively, having the primary segment-1 metabolites. Further, these are metabolized to 3 secondary metabolites, particularly N, N- di desmethyl tramadol, N, N, O-tri-desmethyl tramadol and N, O-desmethyl tramadol. All metabolites are sooner or later related to glucuronic acid and sulfate earlier than excretion in urine.¹⁹⁻²³ The course of elimination includes the kidneys. About 30% of the dose is passed out in the urine as an unchanged drug, even as 60% of the dose is passed out as metabolites. The remaining drug is expelled within the faeces, consequently, biliary excretion is minimal.²⁴

The latency of an anaesthetic drug depends on various factors, such as the anaesthetic technique employed and the intrinsic properties of the drug substance used. Latency is directly proportional to the corresponding pKa value - smaller pKa values related to shorter latency. Likewise, tramadol Hydrochloride has a pKa = 9.41 whereas 2 per cent lignocaine has a pKa = 7.9.²⁵ In a study, it has been shown that 5 per cent Tramadol Hydrochloride has a local anaesthetic effect similar to that of 2 per cent prilocaine when used intradermally for excision of soft tissue lesions (Yahya A. et al 2013).⁵ Other studies have supported that tramadol hydrochloride has a local anaesthetic activity similar to, but weaker than, that of lidocaine.

Like previous studies, tramadol Hydrochloride has a local anaesthetic effect, but in the present study minor Oral surgical procedures (teeth extractions) are involved, whereas the other studies evaluated only soft tissue surgery.²⁶⁻²⁹

The supra-periosteal infiltration of tramadol hydrochloride gave a positive result because the presence of adrenaline in combination with tramadol hydrochloride produces vasoconstriction and confines the tramadol hydrochloride locally to produce its effects on the nerve accurately. However, owing to certain limitations like increased incidence of

postoperative nausea and the need for preparation of the drug, it cannot be recommended as a first-line agent.³⁰

Conclusion

The statistical analysis of this descriptive study on extraction of maxillary teeth with tramadol HCl(50 mg) and adrenalin(0.0225 mg) showed that the mean value of age predilection is 31.92 (with SD= 13.40), the mean volume of 1st injection is 1.8ml (with SD= .00) and the mean volume for 2nd injection is .90 ml (with SD= .00). With the mean latency of 5.01 min (with SD= 1.88) and the mean duration is 2634.60 sec (with SD= 1075.19). Thus, the conclusion which was drawn from this study was that tramadol hydrochloride 50mg with adrenaline 0.0225mg exhibits a local anaesthetic effect that enables successful and painless extraction of maxillary teeth by a subperiosteal infiltration technique and can be used as an alternative to local anaesthetic in oral surgery, when for some unusual reasons a patient cannot receive a conventional local anaesthetic. However, this study had some limitations like increased incidence of postoperative nausea. need for preparation of the drug and it cannot be recommended as a first line agent.

Ethical Approval: Approved by Institutional ethical committee

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