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Paediatric Total Intravenous Anaesthesia (TIVA) using single pump propofol-remifentanil

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Abstract:
Total intravenous anaesthesia (TIVA) using a mixture of propofol and remifentanil in the same syringe is slowly becoming an accepted practice in paediatric anaesthesia. Based on recent study, the safety profile of the propofol and remifentanil mixture has a comparable complication rate as any other anaesthetic techniques, with no specific complication related to mixing of these two drugs [1] . This article provides a comprehensive overview of essential aspects for healthcare providers to ensure patient safety and effective anaesthesia. The text addresses methods for administering a remifentanil-propofol single syringe TIVA to children aged 1 to 16 years. It covers patient selection, required equipment, and precautions for ensuring safe TIVA practices.
Key Word*: Paediatric anaesthesia; Paediatric sedation TIVA, Single pump TIVA.*

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I. Introduction

Propofol based TIVA has been widely used for adults for many years and the application in paediatrics is becoming increasingly common[2] .The mixing of propofol and remifentanil in the same syringe, although not licensed, has been shown to have the same safety profile as any other anaesthetic technique[1].With the increasing use of TIVA in paediatric anaesthesia[3], this article provides guidelines for safely administering anaesthesia using this mixture for both General anaesthesia and sedation.

Indications:

This mixture is mainly used in cases lasting less than an hour. Separate infusion pumps with drug specific target-controlled infusion (TCI) programs of propofol and remifentanil are recommended for longer procedures due to varying pharmacokinetics following prolonged infusion. Separate pumps are also recommended for procedures requiring precise titration of medications (e.g. neurosurgery), procedures not reliant on remifentanil for analgesia and procedures where patient movement must be avoided (e.g., middle ear surgery).

Contra-indications:

Similar to the contraindications of TIVA based anaesthesia in children which includes:

- Significant cardiac dysfunction
- Shock
- Drug allergy
- Lack of equipment
- Increased risk of propofol related infusion syndrome
- Mitochondrial disease

II. Checklist of Required Equipments

1. Giving set with appropriate safety features

It is essential to ensure that there is a luer-lock connector at each end, an anti-siphon valve on the drug delivery line, and an anti-reflux valve on the fluid administration line.

2. TIVA Infusion Pump

Infusion pump capable of TCI program (e.g. Alaris PK infusion pump)

Recommended TCI program: Propofol 1% Paedfusor model, for children aged 1-16 years and weighing 5-61 kg. Adolescents over 61 kilograms may benefit from the Marsh 1% model due to their adult-like metabolism.

Please note that only the target plasma concentration (Cpt) and the calculated plasma concentration (Cp) are displayed. When adjusting the Cpt, there will be a delay of at least 30 to 60 seconds before the Cp displayed can be considered as the equivalent to effect site concentration (Ce).

3. Depth of anaesthesia monitor

Processed electroencephalography (pEEG) monitor e.g. BIS for children >1 yr of age

III. Safety of drug administration

Using 1% propofol is recommended, as it causes less pain at the infusion site compared to 2% propofol.

Due to the possibility of drug degradation and to reduce human error we recommend preparing the mixture shortly before it is required.

The standard procedure for using TIVA is consistent with the guidelines published by The Association of Anaesthetists under Safe Practice of Total Intravenous Anaesthesia 2018[4] .

Salient safety points include:

- Always keep intravenous (IV) cannula visible.
- Use of anti-reflux valves
- Use multi-lumen extension set
- Maintain minimal dead space volume in the administration line.
- Flush dead space at the end of case
- Appropriate clinical monitoring: pEEG, heart rate, blood pressure
- Pumps programmed correctly (patient demographics / drug concentration / syringe type)
- Pressure alarm to be set appropriately

Safety Precaution: Using a 22g cannula can cause the TIVA pump to stop during delivery of the induction dose due to pressure alarm limits. To avoid this from occurring, the pressure limit can be adjusted prior to delivering the induction bolus. If this is performed, we would strongly recommend reducing the pressure alarm limit back to the prior setting after induction to promptly notice cannula failure and reducing the risk of awareness

IV. TIVA for General Anaesthesia

Drug preparation

PR5 (propofol 1% + remifentanil 5 micrograms/ml) is considered to be the optimum ratio of propofol and remifentanil for short procedures under general anaesthesia taking into consideration the pharmacokinetic and pharmacodynamic properties of both drugs.

To achieve the appropriate mixture for general anaesthesia remifentanil is mixed with 1% propofol to reach a concentration of 5 micrograms/ml of remifentanil within the propofol.

Numerous methods exist of achieving this concentration. We recommend reconstituting 1 mg remifentanil in 20mls 0.9% sodium chloride thus making 50mcg/ml of remifentanil. Use this solution to make 5 micrograms/ml in 1% propofol to a desired volume depending on expected length of case.

Propofol 1%	*Remifentanil 50mcg/ml*	*Total volume*
18mls	2mls	20mls
27mls	3mls	30mls
36mls	4mls	40mls
45mls	5mls	50mls

Induction

A period of effective pre-oxygenation prior to a TIVA induction is important as the longer bolus time may cause patients to desaturate prior to airway manipulation.

During induction care should be taken to avoid dislodgement of the IV line, this can include securing the IV cannula thoroughly and gently holding the limb during induction. 1-2mls of IV lidocaine 1% can also be considered pre-induction to reduce discomfort during initial infusion.
The administration of a remifentanil bolus may occasionally result in chest wall rigidity. As the induction bolus progresses, propofol will deepen anaesthesia, resulting in the cessation of rigidity.

Pump settings
As a guide, the pump should initially be programmed to a Cpt of 5-6mcg/ml. For patients less than 3 yrs, the Cpt may be set as high as 7mcg/ml to deliver an adequate bolus dose. If the patient is not sufficiently anaesthetised, airway manipulation should be halted. The Cpt should be increased by approximately 1 mcg/ml, and sufficient time should be allowed for equilibrium before continuing. Once the patient is deeply anaesthetised, the Cpt can be reduced to achieve the desired level of anaesthesia.
Similar to a maintenance of anaesthetic using a volatile gas, the use of neuromuscular blocking agents is not always necessary with TIVA. When neuromuscular blocking drugs are used, the use of pEEG is strongly recommended to reduce the risk of awareness.

Maintenance
The typical target concentrations (Cpt) recommended for this technique are as follows

LMA	Spontaneous ventilation	2.5mcg/ml-4mcg/ml
LMA	Controlled Ventilation	2.5mcg/ml-4mcg/ml
ETT	Spontaneous Ventilation	3.5mcg/ml-6mcg/ml
ETT	Controlled Ventilation	3.5mcg/ml-6mcg/ml

Please note that the Cp should be titrated individually for each patient based on pEEG, HR, BP and surgical stimulation.

Emergence
Emergence of anaesthetic is guided by patient demographics and clinical narrative as per general anaesthesia with a volatile anaesthetic. Of particular importance is to ensure all IV cannula are flushed prior to leaving theatre with appropriate documentation in the anaesthetic record and verbal handover to the recovery staff. Failure to perform this can result in patient apnoea in recovery secondary to an unintentional remifentanil bolus located in the deadspace of the cannula.

V. TIVA for Sedation

TIVA benefits micro laryngoscopy and GI endoscopy by providing separate routes for oxygenation and anaesthesia, even with a partially obstructed airway. This method achieves adequate depth without relying on inhaled volatile gasses such as sevoflurane.

Drug preparation:

We recommend using **PR2.5** (propofol 1% + remifentanil 2.5 micrograms/ml) for less stimulating surgical procedures such as endoscopy or dental extractions where advanced airway management is not anticipated. In order to provide adequate analgesia/anaesthesia but to reduce the risk of remifentanil induced apnoea/hypoventilation the remifentanil dose is reduced.

As discussed above, numerous methods exist for achieving PR2.5. Again, we recommend reconstituting 1 mg remifentanil in 20mls 0.9% sodium chloride thus making 50mcg/ml of remifentanil. The table below suggests appropriate ratios to produce PR2.5.

Propofol 1%	Remifentanil 50mcg/ml	Total volume
19mls	1mls	20mls
28.5mls	1.5mls	30mls
38mls	2mls	40mls
47.5mls	2.5mls	50mls

Safety Precaution: The propofol-remifentanil mixture carries a risk of apnoea and may require basic airway maneuvers. It is recommended to have the face mask readily available and to consult with your assistant regarding the appropriate size of the endotracheal tube (ETT) in case any changes to the airway management plan become necessary during the procedure

VI. Conclusion

In conclusion, this review has covered safety, patient selection, and practical strategies to help healthcare providers optimize the use of the propofol-remifentanil mixture in paediatric anaesthesia. PR5 is suggested for cases requiring a general anaesthesia lasting less than 60 minutes and PR2.5 is recommended for sedation where spontaneous patient ventilation is encouraged.

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