Series 2 – dexmedetomidine, tramadol, fentanyl, intellectually disabled patients:

Read the following published scientific articles and answer the questions at the end:

Abstract

We get a substantial number of sedation-related articles annually, usually research studies on newer drugs and the side effects of the drugs. There are also studies that compare the efficacy and safety of drugs. These studies are first published in abstract form. The idea in this CPD article is to look at some of the studies that are important for us as sedation practitioners and give a short discussion. It is meant to update our knowledge and skills.

Article 1: Postoperative respiratory and analgesic effects of dexmedetomidine or morphine for adeno-tonsillectomy in children with obstructive sleep apnoea [1]

The above study is a randomized double-blind study of 60 children, aged 2-13 years, recruited to receive either intravenous dexmedetomidine 1µg.kg(-1) or morphine 100µg.kg(-1) with start of anaesthesia.

Conclusion

Dexmedetomidine (Precedex®) produced less respiratory depression than morphine, but less effective analgesia.

Discussion

This is an interesting article as dexmedetomidine is nowadays seen as one of the "revolutionary" drugs in sedation practice. It is attractive as the drug is both a sedative and analgesic, very popular for use with MRI scans. This article then shows, at this dose, that the drug does not cause significant respiratory depression, but analgesia is not better than morphine; something that one may expect. But note that some clinicians in the world give up to 3*µ*g.kg of dexmeditomidine intravenously! We will hear more about the use of this drug in future [2].

Some clinicians believe this should be an ideal drug for Obstructive Sleep Apnoea, however the first decision is really whether the patient is an ASA 1 or 11 for sedation outside the operating room.

Article 2: Analgesic effect of oral tramadol on transrectal ultrasound-guided needle biopsy of the prostate in a randomized double-blind study [3].

This is a randomized double-blind study of 121 Japanese patients scheduled for prostate biopsy. They received a single oral dose of 100 mg Tramadol mixed with 20ml of sugar syrup or placebo, 30 minutes before the procedure. Pain severity was measured by verbal rating scale (VRS) and visual analog scales (VAS).

Conclusion

The oral administration of a single dose of 100 mg Tramadol 30 minutes before a transrectal needle biopsy of the prostate was safe, but not effective to reduce the pain severity.

Discussion

The above conclusion is to be expected. Tramadol is a weak opioid and certainly not a drug that will provide anxiolysis and analgesia given orally for such a procedure.
Opiates are not sedative agents.

Tramadol is also probably not the best drug to use as a single analgesic agent in such a low dose for this procedure. Patients are usually anxious and it would be advisable to add a sedative agent e.g. oral midazolam. Maybe using Tramacet® (a combination of tramadol and paracetamol) would have been a better option.

If we look at the WHO step ladder on the management of pain then one of the first drugs to consider for pain is a non-steroidal anti-inflammatory agent. The use of tramadol as an intravenous analgesic during conscious sedation is gaining in popularity. Post-operative analgesic affect could last for 8 hours which makes this an attractive drug. The drug has an excellent haemodynamic profile and can be used safely in the elderly.

Tramadol can be used with propofol.
The drug should not be used when patients are on psychotropic drugs.

Article 3: Dental sedation for patients with intellectual disability: a prospective study of manual control versus Bispectral Index-guided target-controlled infusion of propofol[4]

The aim of this study was to investigate the effectiveness of propofol sedation by using the Bispectral Index (BIS)-guided target-controlled infusion (TCI) in dental patients with intellectual disability.

Forty ASA physical status 1 and 2 patients with intellectual disability were selected for this study. One group had sedation with a manually controlled infusion of propofol without a BIS index monitor. The BIS-TCI group had sedation by BIS-guided TCI of propofol. The required dose of propofol for sedation, recovery time for the eyelash reflex, and spontaneous eye opening times were recorded.

Conclusion

BIS-TCI significantly reduced the dose of propofol needed for sedation and shortened the recovery times for eyelash reflex and spontaneous eye opening. Propofol sedation using BIS-guided TCI is a useful and safe method in the management of patients with intellectual disability.

Discussion

The above results are not surprising. One just expects TCI controlled sedation infusions to be more accurate. The issue regarding the BIS monitor is more complicated. This monitor is mainly used during general anaesthesia to determine the level of consciousness (LOC).

The BIS measures cortical activity and monitors the EEG waveforms. It does provide an objective measure of the hypnotic effects of sedative drugs on the brain [5]. The value of the BIS during sedation is still debated. However this is and can be a valuable monitor of the LOC during sedation, especially when doing smaller children.

There is controversy as to the value of using the BIS with certain drugs e.g. ketamine. It is also believed that the BIS monitor is too expensive to routinely use during sedation for sedation outside the operating theater. The main issue that concerns us as sedation practitioners, is whether the BIS monitor has been validated as an accurate tool for the LOC during sedation.

One of my postgraduate students for a Masters degree in sedation is currently doing a study comparing the BIS and the Wilson sedation scale to find if there is a correlation between the two scales and LOC. Preliminary results show that there is an interesting correlation, meaning that the Wilson sedation scale may be an accurate tool in evaluating sedation levels accurately.

Although international sedation guidelines do not expect of sedation practitioners to routinely use the BIS the monitor will become a very important tool for safety of patients during sedation.

Article 4: A comparison of fentanyl with tramadol during propofol-based deep sedation for pediatric upper endoscopy[6].

The aim of this study was to evaluate the efficacy and safety of tramadol with that of fentanyl in eighty pediatric patients aged 1-16 years undergoing upper gastrointestinal endoscopy (UGIE). Propofol 1mg·kg(-1), was used for baseline anesthesia, additional propofol, 0.5-1mg·kg(-1) , was administered when needed. The children were randomly assigned to receive either 2μg·kg(-1) fentanyl (group F, n=40) or 2mg·kg(-1) tramadol (group T, n=40).

Conclusion

Tramadol in pediatric patients undergoing UGIE provided sedation as efficient as fentanyl with a better hemodynamic and respiratory stability and provided a superior safety and tolerance in younger children.

Discussion

Paediatric upper endoscopy sedation is one of the most challenging experiences for a sedation practitioner. The stimulation can be intense and effective analgesia is needed. I am surprised that the tramadol and the baseline propofol infusion (which is very low for what the authors claim to be a propofol-based deep sedation) were as effective as the fentanyl and propofol in the other group.

Timing of the procedure after drug administration is extremely important, as it takes longer to reach a peak effect with tramadol than with fentanyl. Fentanyl, a phenylpiperidine, will also produce more intense analgesia.

I am not surprised by the better respiratory stability with tramadol, as the drug is known for that! I use intravenous tramadol more or less for all my adult sedation cases for “background” analgesia (and post-operative analgesia), and find this tramadol is an extremely useful drug with less respiratory depression and better post-operative analgesia.

When I read about the use of fentanyl for UGIE I am always reminded of the cases we did in Nairobi, it was one of the worst laryngospasms I have seen when the registrar used a combination of fentanyl and propofol for an UGIE. The other cases we did with

remifentanil and propofol and this worked extremely well showing the intense analgesia we need.

The combination of ketamine/propofol (ketofol) I find very useful for upper endoscopy procedures.

References

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