Anesthesia Control: A Personal Opinion

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Abstract

This is a short review concerning the control of anesthesia during surgical procedures, the devices deputed to give anesthesiologist a better and reliable control on the anesthetic plane and the new horizons opening in matter of safety and dedicated to patient's anesthetic problem strategies. The anesthetic control is still a matter of discussion and, in my personal opinion, many shadows still need to be dispelled. Most of them are related to a not well known anatomical knowledge of the defined fields in which anesthetic drugs act.

Many clinicians are starting just now to look at anesthesia delivery and at anesthetic drugs in an unconventional way which is compulsory for a better knowledge of pharmacodinamic-pharmacokinetic drugs changes during anesthesia. Currently, a strong general opinion is that something has to be changed when we look at anesthetic procedures especially in premature babies, neonates, toddlers and elder patients.

In the end, computer-driven anesthesia is very satisfactory and has become a pillar in the intravenous anesthetic control, the same as for volatile agents anesthetic, but Target Control Infusion and others electrical computerized devices and software dedicated to TIVA seem to be overtaken in time and in new pharmacological studies horizons. A last question has been asked to author analysis and opinion: do we have to change anesthesia or is it better to change anesthetists point of view and their therapeutic goals?

Keywords: Anesthesia control devices; Driven computer anesthesia; Anesthetic drugs pharmacodinamic-pharmacokinetic; Anesthesia delivery approach

Introduction

Many progresses have been done in anesthesia during the last three decades. Most of them have been done for the intravenous anesthesia delivery. The laringela msk and related developed devices, like Propofol, and Computer-driven anesthetics procedures, have changed the way to deliver anesthesia, the approach to a faster recovery and a shorter hospital stay and promoting a great increase in daily surgery procedures and cutting down the hospitalization costs [1-5].

What it is not under a total control by anesthesiologists is the anesthesia itself, even though very important changes in the control of its levels has certainly been done. Anesthetists still don't have a secure and reliable way to understand which is the real level of anesthesia. There is still a lack in anesthesia delivery devices availability and in monitoring the real effects of anesthetic drugs [6]. This is not totally true for the use of halogenates in gas-driven hypnosis and anesthesia level control, where new gas time and dosages delivery concepts have been added to the MAC definition.

Discussion

The most important intraoperative or perioperative risks for a patient receiving anesthesia are well defined:

A. Respiratory Depression both at induction of anesthesia and after the end of surgical procedure

B. Intra operatory awakening

C. Hemodynamic instability

D. Delayed or missed recovery from anesthesia

E. Late recurarization or missed decurarization

Even late complications can be present, including:

A. Vomiting

B. Neurological depressed or not controlled activity, especially in neonate and elder patients or after complicated procedures

C. Acute or late pulmonary damages (ALI or chronic pulmonary disease missed control)

D. Immediate or late infections due to intra operatory ventilation

During the last decades, many studies and research have been done to define a feasible clinical and instrumental way to have the greatest possible control over the hypnotic drugs and

to recognize the signs indicating the depth of the anesthetic condition. The several changes in the definition of " Anesthesia" during the last four decades show us how the research in this field has been considered as a starting point to understand what we do when we are giving anesthesia and how we do it [7-10].

In 1981 Pinsker asserted that: "Anesthesia is defined as a combination of acts tending to get a status of

A. Unconsciousness

B. Paralysis

C. Stress Response Modulation"

In 1996, Barash defined "Anesthesia" as: "A reversible clinical status, inducted from drugs depressing central nervous system, ascending and descending it , that produces a lack of response and perception to all the external stimuli".

In 1998, Glass defined Anesthesia in a different way separating, for the first time what is the lack of consciousness from what is inhibition of stimuli [11]:

"Anesthesia consists in inducing in the patient a

A) Lack of consciousness

i. Volatile or intravenous hypnotic agents

B) Inhibition of the halogenic stimulus to reach the finest cerebral neural centers with a combination of:

i. Opioids

ii. Local anesthetics

iii. Volatile agents at MAC

This conceptual change opened the way to a new point of view of what is anesthesia and what could be our targets when we give anesthesia. If we consider the changes occurred from the late 1980 in the technological developments and in the approach to study in different ways the Pharmacodinamics-pharmacokinetics of anesthetic drugs, it is compulsory for us to introduce a new concept in the anesthesia definition: "Anesthesia is a clinical therapeutic sequence of acts that must [11-20]:

A. Look at the Hypnotic components

i. Lack of consciousness

ii. Prevention of intraoperative awakening

iii. Prevention of missed awakening

B. Look at the quality of

i. Analgesia

ii. Suppression of moto neural response

iii. Suppression of somatic response

iv. Suppression of cardiovascular response

v. Suppression of neuroendocrine response

C. Modulation of all the real time variations in the body response to match the surgical necessity by the anesthesiologists

I want to focus on the (C) point because it introduces a new concept in the anesthesia delivery which is "....the immediate knowledge of variation of the anesthetic status and the immediate control and modulation of anesthesia by the anesthesiologists...."

In a few words, anesthetists can and must know in real time, which is the level of anesthesia and how to change it, if needed, closing a loop, considering the most of covariates data in their knowledge. Tachycardia and hypertension are not considered enough to define deep anesthesia, especially when a combination of volatile agents and opioid drugs is in use.

Even EEG response is not reliable, in many of its forms, since we still don't know very well the anesthetic mechanism defining the anesthetic status; this is more understandable when we consider the neural species variability and the not well known function of premature, neonatal, and elderly brain. SEMG (Surface electromiography can give a good panoramic of the decurarizazion (an increase of 30% from the basal value is acceptable) but doesn't give us any other data.

The BIS analysis (Bi-spectral Index) is not totally adequate to give a satisfactory indication about the depth of anesthesia since it is a number, and in 2018 it is not acceptable to indicate a condition with numbers; we need and must analyze the decadence or increase of the slope curves obtained analyzing specific data with a Fast Fourier Analysis FFA..

Starting from this point of view many electrical devices have been proposed to control the anesthetic deep:

A) Midalatency Auditory Evoked Potentials (AEP)

B) Electroencephalography Spectral Entropy.

i. State entropy

ii. Response entropy

C) A.-Line ARX Index (AAI)

D) Patient State Index (PSI)

E) EEG Based SNAP Index

F) 2007 NeuMonD

-AEP – anterior/posterior signal

-EEG-Latero-Lateral signal (this device has been never commercialized) And last but not least:

G) Train of Four (TOF)

(That is not a new technology since it was used in Liverpool in 1979 by Ali et others, as an indication of the power of muscles action and currently it is to indicate the muscular activity using an acceleration value)

H) Time to Peak effect. (t-Peak) (TCI devices)

I) Automatic Gas Control. (F-i-AGC) (used to control and better define the action time of volatile agents)

l) CONOX (Fresenius)

It is evident that a so high number of devices to control the anesthetic levels and its numerous covariables shows the importance of the problem and the difficulties to define an accurate and uniform way to control anesthesia [21-26].

A change was needed and this change came from the late 1989 early 1990, when the problem was studied from a different point of view i.e. not considering the results of anesthesia looking at clinical data, but trying to understand how to give the exact amount of drug to patients in order to reach a better defined effects.

It was evident that a second order pharmacodinamic-pharmacokietic model was not enough therefore Shafer and Varvel (TCI Model) and Kern (CACI)Model) developed a different mathematical algorithm to create a theoretical third compartment, a depth compartment, to equilibrate the drugs action at Bio-phase. With the term Bio-phase we identify the receptoral activity and its clinical real time anesthetic drug consumption.

It is a combination of

A. Pharmacodinamic phase : relationship between dose of drug administered and plasmatic concentration

B. Pharmacokinetic Phase : relationship between drug administered dosage, plasmatic concentration, and clinical effect

This is a TIVA model

The Bio-phase or Site Effect is defined as the relationship between plasmatic therapeutical concentration and clinical effects. It is defined with an elimination constant value called "K0" that gives the exact theoretical amount of drugs acting in real time on the receptor

This is a TCI Model

It is not the aim of this communication to deeply treath TCI device or the way of using it, but it was compulsory to me to define in a short way the TCI concepts, because in my opinion, this is an absolute way to look after anesthesia (when we talk of intravenous anesthesia).

Not more." which exact quantity of drug do I have to administer to a patient to get the desired effects?" but "……if I want to have a specific, targeted, controlled effect when I administer an anesthetic drug with a bolus followed by a continuous effect, which are the changes that this drug undergoes until it chains the receptors and which is the distribution volume of the drug that has to be mantained from the device to avoid the so called No Valley anesthesia, Intraoperative Awakening, drug overload? "

In order to do this, the TCI considers In real time:

A. Distribution volume of the drug

B. Metabolism of the drug

C. Clearance of the drug

D. Receptor interaction at bio-phase (even if bio-phase is not anatomically defined)

The TCI t-Peak Time considers the time in which the drug reaches the desired Target concentration. My simple consideration is that in the beginning, when I was in Glasgow with Gavin Kenny, who is the inventor of TCI, it was very difficult for anesthesiologists to accept this new point of considering drugs as they were using them.

A retraining of the drug effects was needed because it was compulsory to learn the different actions of drugs at different distribution volumes! In the case of volatile agents, a similar option can now be considered; as I said before, the Automatic gas Control (F-i-AGC) gives us the opportunity to decode and target before starting the volatile agent to the patient the time that the gas has to be administered to reach the desired effect.

Since 2004 there was not a pediatric dedicated TCI system. The first application has been experimentally done from the author in Glasgow in 1996. TCI was delivered for the use in adults or in patients weighting >30kg. In 2004 Absalom, Lal, Kenny registered a system called "Pdfusor2 for the use in patients weighting <30 kg.

The Pd-Pk parameters of the software were studied from others authors ,as Kataria and Minto, for the use of Ketamune or alfentanyl, but it is singular that in the last 15 years the Pediatric use of TCI has not been well studied and we still do not have dedicated devices to give computer - driven anesthesia to neonates and toddlers. My opinion is that, nowadays ,we are in the same situation of the late 1980s. The peculiarity of anatomy, physiology, pathology diagnosis, weight, eight and organ immaturity or transitory dysfunctions are the basis to propose a different approach to anesthetic procedures.

The research in the field of premature receptor for pain, depression of central nervous system and consequences of anesthesia on the noble organ, requires a precise and specific approach, especially in the pharmacodinamic-pharmacokinetic field regarding anesthetic drugs pathways to perform anesthesia from premature age to 30kg of weight.

A revolutionary change is required in the pharmacological approach.

This change can come from the past.

We must consider what has been already done and studied to explain the changes happening in the field of a very rapid cell growth biochemistry. The Kleiber laws, consider the therapeutic adaptations to cellular growth: there has been a great interest in the study of the rapid cells development and growth characteristics, especially in the research of cancer

cells metabolic functioning; a consideration is necessary as consequence of this observation: only another type of rapid growth exists in biology and is the neonatal and pediatric growth as established from the Tanner-Whitehose Percentile Growth.

Kleiber laws define a non-linear relationship between the SIZE of the patient and the organ function.

At the basis of this relationship is the metabolic power related to the body mass of the patient:

$$K_L = \frac{\text{metabolic Power}}{\text{mass}} \longrightarrow P = (a) \times (w)^b$$

Where:

P= Pharmacokinetic parameter to be adopted

W=Body mass in Kg

A= Allometric coefficient   :

i.   BMR (basal metabolic rate)

ii.   SIZE -weight

 -height

B= allometric exponent:

i.   Drug Clearance

ii.   V/D distribution Volume o Half-time (1/2)

We consider this law and the laws related to it as:

A)   Maturation functional process : MF

$$MF = \frac{PMA^{Hill}}{TM_{50}^{Hill} + PMA^{Hill}}$$

B)   The Hill equation quantifies the receptor-agonist relationship; it is a quantitative receptor Model expression of the Ligand number related to the Binding number giving us a receptorial ligand concentration at equilibrium as mass action of a drug.

C) The De Castillo-Katz law that defines how many receptors are able to develop an action :

$$AR \underset{K_2^{II}}{\overset{K_1^{I}}{\rightleftarrows}} AR^*$$
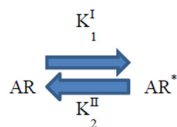
Where AR are active complex and AR* are inactive complex.

We have a slope curve defined as "EC slope curve" that gives us in real time the drug concentration at the effect site. Many others allometric laws are required to define a new pd-pk model , and at the moment a dedicated manuscript that describes new pharamacological relationship concepts is on the way to be submitted for publication.

Conclusion

A huge number of covariate values need to be recognized and inserted in a new software to create a new pd-pk pharmacological model to give a correct anesthesia to young patients and old patients; allometric laws must be strictly related one to the other in order to obrain this dedicated pd-pk model.

A new anesthetic approach is compulsory; the evidence of the great differences that are at the basis of neonate and toddlers anatomic and functional developmental pathways, needs to to be undertaken from the new pd-pk concepts; new theoretic distribution volume has to be defined and mathematically fixed to perform computer- driven anesthesia in this kind of patients, but in my personal opinion the pharmacological concepts we are rarely used to work with are not enough precise and adequate to get this result.

The conceptual equation regulating a thricompartimental theoretical deep equilibrium at bio-phase model is correct by itself, but in neonates, toddlers and elderly patients a quantistic biomolecular pd-pk pharmacological approach is compulsory. A change in anesthetic approach must give to anesthetists the chance not only to recognize a correct anesthesia delivery from the analysis of the clinical drug effect reported data, but give them the skills and the devices to deliver a personal and dedicated anesthesia for each patient requirements starting from a predefined targeted point break.

References

1. Milella L (2000) Advances in Pediatric Cardiovascular Anesthesia, Round Table: The State of the Art in Anesthesia. 9th Congress of Latin American Society of Cardiology and Cardiac Surgery Miami, USA.

2. Milella L (2014) Anaesthesia protocols in paediatric cardiac surgery: the use of sugammadex Patients and surgical Procedures, Italy, (2nd edn.), pp. 31-43.

3. Absalom A, Kenny G (2005) Paedfusor, pharmacokinetic data set. British Journal of Anaesthesia 95(1): 1-110

4. Absalom A, Amutike D, Lal A, White M, Kenny GN (2003) Accuracy of the Paedfusor in children undergoing cardiac surgery or catheterization. Br J Anaesth 91(4): 507-513.

5. Plaud B, Meretoja O, Hofmockel R, Raft J, Stoddart PA, et al. (2009) Reversal of rocuronium-induced neuromuscular blockade with sugammadex in pediatric and adult surgical patients. Anesthesiology 110(2): 284-294.

6. Marlow N (2014) Anesthesia and long-term outcomes after neonatal intensive care. Paediatric Anesth 24(1): 60-67.

7. Milella L (2014) Anaesthesia protocols in paediatric diagnostic and interventional cath lab procedures: the use of sugammadex-patients and emodinamic procedures. (2nd edn), Italy, pp. 44-55.

8. Ficarella MT, De Renzo V, Natale C, Milella L (2015) Anaesthesia protocols in paediatric video thoraco laparoscopic surgical procedures: the use of rocuronium bromide and sugammadex. (3rd edn), Italy, pp. 41-54.

9. Milella L, Da Cruz E, Gajraj RJ, Corno AF (1997) Computerized anaesthesia and normothermic perfusion in paediatric cardiac surgery. The second world congress of pediatric cardiology and cardiac surgery honolulu.

10. Allegaert K, Verbesselt R, Naulaers G, van den Anker JN, Rayyan M, (2008) Developmental pharmacology: neonates are not just small adults. Acta Clini Belgian 63(1): 16-24.

11. Fuchs Buder T (2010) Neuromuscolar Monitoring in Clinical Practice and Research. Springer.

12. Kluger MT, Bullock MF (2002) Recovery room incidents: a review of 419 reports from the Anaesthetic Incident Monitoring Study (AIMS). Anaesthesia 57(11): 1060-1066.

13. SchiffJH, Welker A, Fohr B, Henn Beilharz A, Bothner U (2014) Major incidents and complications in otherwise healthy patients undergoing elective procedures: results based on 1.37 million anaesthetic procedures. Br J Anaesth 113(1): 109-121.

14. Curreri G, Ancona MA, Sciascia M (1996) Myorelaxants in pediatric anesthesia. Minerva Anestesiol. 62(4): 125-130.

15. Shaginian AK, Mikhel'son VA, Agavelian EG (2008) Myoplegia with rocuronium bromide in children. Anesteziol Reanimatol (1): 29-32.

16. Allegaert K, van de Velde M, van den Anker J (2014) Neonatal clinical pharmacology. Pediatric Anesth 24(1): 30-38.

17. McPherson C, Grunau RE (2014) Neonatal pain control and neurologic effects of Anesthetics and sedatives in preterinfants. Clinic Perinatol 41(1): 209-227.

18. Meretoja OA (2010) Neuromuscolar block and current treatment strategies for its reversal in children. Pediatric Anesth 20(7): 591-604.

19. Kotake Y, Ochiai R, Suzuki T, Ogawa S, Takagi S (2013) Reversal with sugammadex in the absence of monitoring did not preclude residual neuromuscolar block.Anesth Analgesia 117(2): 645-651.

20. (2015) 69th Italian National Anaesthesia Society Congress (SIAARTI): SARNePi (Italian Society of Paediatric and Neonatal Anesthesia and ICU) at SIAARTI: Paediatric Anaesthesia: Paediatric TIVA-TCI: Tips and Pricks Bologna, Italy;

21. Bosenberg A, Flick RP (2013) Regional Anesth in neonates and infants. Clin Perinatol 40(3): 525-538.

22. Chambers D, Paulden M, Paton F, Heirs M, Duffy S (2010) Sugammadex for the reversal of muscle relaxation in general anaesthesia: a systematic review and economic assessment Health Technol Assess l 14(39): 1-211.

23. Milella L, Mele D (1998) TCI: preliminary experience in paediatric cardiac anaesthesia, Pratica Anestesiologica, Italy.

24. Milella L (1999) TCI in Paediatric Cardiac Anaesthesia, 5th Course in Cardiothoracic Anaesthesia, Italy.

25. Milella L, Calabrese G (2000) TCI in Pediatric Cardiac Anesthesia: a better choice for early extubation? 9th Congress of Latin American Society of Cardiology and Cardiac Surgery, USA, pp. 23-28.

26. (2005) TCI in Paediatric Cardiac Anesthesia: 59 cases, Minerva Anestesiologica.

27. (2017) Teaching Project for analgesic and sedation therapeutics in pediatric patient in ICU Italian project AS-TIP, SARNEePI (Italia Society for Neonatal and Pediatric Anesthesia and ICU) S.I.A.A.R.T.I. (Italian Society of Anesthesia and ICU).