+Model
BJANE-728; No. of Pages 9
ARTICLE IN PRESS

Rev Bras Anestesiol. 2016;xxx(xx):xxx–xxx

Sociedade Brasileira de Anestesiologia

REVISTA BRASILEIRA DE ANESTESIOLOGIA

Publicação Oficial da Sociedade Brasileira de Anestesiologia
www.sba.com.br

SCIENTIFIC ARTICLE

Regulation of hypnosis in Propofol anesthesia administration based on non-linear control strategy

Muhammad Ilyas[a], **Ali Khaqan**[a], **Jamshed Iqbal**[b,*], **Raja Ali Riaz**[a]

[a] *Department of Electrical Engineering, COMSATS Institute of Information Technology, Chak Shahzad, Pakistan*
[b] *Department of Electrical Engineering, National University of Computer and Emerging Sciences (FAST-NU), Islamabad, Pakistan*

Received 28 May 2015; accepted 17 August 2015

KEYWORDS
Closed-loop anesthesia;
Modern control;
Biocontrol;
Pharmacodynamics;
Pharmacokinetics

Abstract Continuous adjustment of Propofol in manual delivery of anesthesia for conducting a surgical procedure overburdens the workload of an anesthetist who is working in a multi-tasking scenario. Going beyond manual administration and Target Controlled Infusion, closed-loop control of Propofol infusion has the potential to offer several benefits in terms of handling perturbations and reducing the effect of inter-patient variability. This paper proposes a closed-loop automated drug administration approach to control Depth Of Hypnosis in anesthesia. In contrast with most of the existing research on anesthesia control which makes use of linear control strategies or their improved variants, the novelty of the present research lies in applying robust control strategy i.e. Sliding Mode Control to accurately control drug infusion. Based on the derived patient's model, the designed controller uses measurements from EEG to regulate DOH on Bispectral Index by controlling infusion rate of Propofol. The performance of the controller is investigated and characterized with real dataset of 8 patients undergoing surgery. Results of this *in silico* study indicate that for all the patients, with 0% overshoot observed, the steady state error lies in between ± 5. Clinically, this implies that in all the cases, without any overdose, the controller maintains the desired DOH level for smooth conduction of surgical procedures.

* Corresponding author.
E-mail: jamshed.iqbal@nu.edu.pk (J. Iqbal).

http://dx.doi.org/10.1016/j.bjane.2015.08.011

PALAVRAS-CHAVE
Anestesia de circuito fechado;
Controle moderno;
Biocontrole;
Farmacodinâmica;
Farmacocinética

Controle da hipnose na administração de propofol com base na estratégia de controle não linear

Resumo O ajuste contínuo de propofol na administração manual de anestesia para a realização de um procedimento cirúrgico onera a carga de trabalho de anestesistas que trabalham em ambiente multitarefa. Indo além da administração manual e da infusão alvo-controlada (IAC), o controle de circuito fechado da infusão de propofol tem o potencial de oferecer vários benefícios em termos de manejo das perturbações e reduzir o efeito da variabilidade interpaciente. Este artigo propõe uma abordagem para a administração automatizada de drogas em circuito fechado para controlar a profundidade da hipnose (PDH) em anestesia. Em contraste com a maioria das pesquisas existentes sobre o controle da anestesia que usam estratégias de controle linear ou de suas variantes melhoradas, a novidade da presente pesquisa reside na aplicação de uma estratégia de controle robusto; isto é, o Controle por Modos Deslizantes (CMD) para controlar com precisão a infusão da droga. Com base no modelo derivado do paciente, o controlador projetado usa as medições do EEG para regular a PDH no Bispectral Index (BIS), controlando a taxa de infusão de propofol. O desempenho do controlador é investigado e caracterizado com um conjunto de dados reais de oito pacientes submetidos à cirurgia. Os resultados deste estudo in silico indicam que, para todos os pacientes, com 0% de excesso observado, o erro de estado estacionário fica entre ± 5. Clinicamente, isso implica que em todos os casos, sem qualquer sobredosagem, o controlador mantém o nível desejado de PDH para a condução tranquila dos procedimentos cirúrgicos.

Introduction

Thanks to technological advancements, the benefits offered by modern medicine have totally transformed the concept of clinical surgery. Nowadays, surgical procedures can be performed with much ease and comfort. This incredible milestone has been achieved only through the research outcomes in modern anesthesia. Prior to the discovery of anesthesia, surgery has to be conducted extremely fast. Historically, trivial techniques like application of cold, compression of nerve or reduction in cerebral perfusion were employed to keep patient unconscious.[1] Undoubtedly, invention of inhalation gases in 1840 by Hickman was a pivotal step toward discovery of anesthesia to finally permit conduction of invasive surgeries. The first procedure of anesthesia, based on diethyl ether, was performed in 1842 by C.W. Long. This new revolutionary concept was later on termed as anesthesia meaning lack of esthesia i.e. sense.

Anesthesia is intensively used particularly in medical domain in many applications including surgical operation with incision, dental surgery and intensive care.[2] The primary objective of anesthesia is to offer painless feelings to a patient under operation by driving him/her into unconscious state without memory. The overall functional scenario of anesthesia can be categorized into three temporal phase in sequence: induction, maintenance and emergence. During the first phase, the objective is to bring a patient to a reference Depth of Hypnosis (DOH). It is then necessary to administer the anesthetic drug in order to maintain an adequate DOH. For induction and maintenance of anesthesia, commonly used intravenously administered anesthetic drug is Propofol.[3] During emergence phase in post-surgery activities, vaporizer and other infusion devices are turned off so as to enable patients to awake fast.

During general anesthesia, Propofol is usually used together with fast acting opioids e.g. remifentanil to have a synergistic effect.[4] Under-dosing of anesthetic drugs may lead to insufficient analgesia or awareness. On the other hand, it is dangerous for patients to have excessive amount of drug. Thus careful management of the intravenous drug delivery is the key factor behind successful anesthesia practice. It is desirous to access the depth of anesthesia together with automatic and interactive drug administration with little human intervention so as to adjust drug dosage accordingly for balancing the anesthetic state, autonomic function and response to noxious stimuli.

The procedures to administer intravenous drug delivery have been evolved from simple manual delivery and computer-assisted automated Target Controlled Infusion (TCI) to more sophisticated Closed-Loop ANesthesia (CLAN). Traditionally, hypnotic drug delivery rates in intravenous anesthesia are manually controlled by an anesthetist. Doses are principally decided based on patient demographics, qualitatively measured signs (e.g. presence of certain reflexes, movement) and quantitatively measured signals (e.g. oxygen saturation, blood pressure, heart rate). The dosage scheme is then tuned by hit and trial to optimize anesthesia and to evade toxicity. TCI, also known as Computer Assisted Continuous Infusion (CACI),[5] relies on population-based pharmacokinetic (PK) and pharmacodynamic (PD) models[6] for calculating an adequate infusion profile to achieve the reference drug concentration set by the anesthesiologist. Given the past and present infusion rates, these models can predict the time evolution