Target Controlled Infusion American Style

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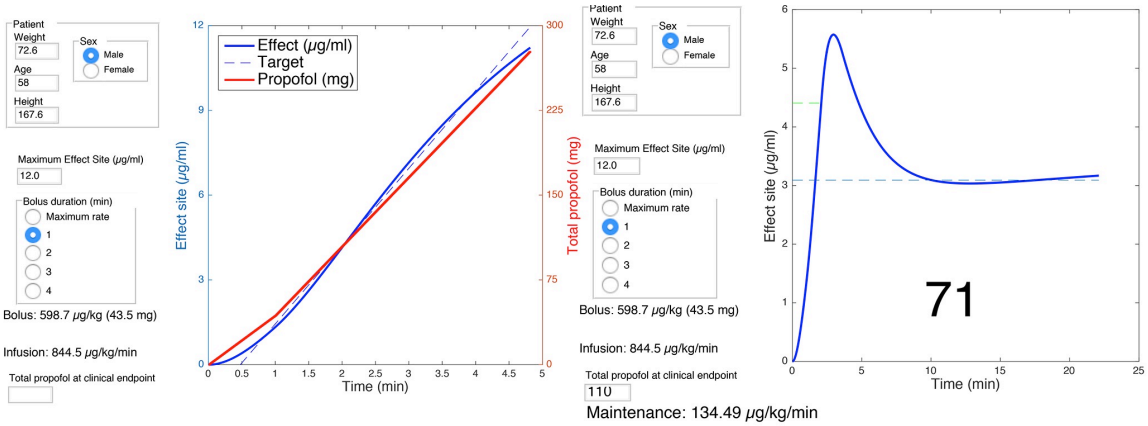
Target controlled infusion is a mature technology, although the regulatory obstacles for FDA approval have not yet been met[1]. Target controlled infusions systems use published pharmacokinetic models to calculate infusion rates at regular intervals. While it is possible to perform the calculations to achieve stable effect site concentrations using small boluses delivered by a PCA pump [2], this is not practical for most clinicians. A system that permits titration to a clinical endpoint and subsequent transition to a stable effect site concentration corresponding to that endpoint that can be achieved using an FDA-approved pump is described.

The Alaris Medley 8100 pump is used as the predicate device. This pump is capable of delivering a bolus over an integer number of minutes (or at the maximum rate of 999 ml/hr) followed by an infusion. This represents three degrees of freedom. For each bolus duration, the optimum bolus size and infusion rate to achieve an increase in effect site from zero to a specified maximum at a constant rate of increase is determined for the specified patient using constrained linear minimization. These rates are entered into the pump, and the volume totalizer zeroed. When the clinical endpoint is observed, the total propofol given at that point is entered, and the propofol infusion is paused for a specified time and resumed at a specified rate. All entries to the pump are made manually by the clinician, and the total propofol dose is depicted prior to induction. In addition to providing a predictable titration schedule, the system estimates the effect site concentration at the time of the clinical transition. The system is written in Matlab 2015b, and can be accessed remotely via a web interface. The regulatory status of the system has not yet been determined.

1. Dryden PE. Target-Controlled Infusions: Paths to Approval. Anesth Analg. 2015;
2. Mandel JE, Lichtenstein GR, Metz DC, Ginsberg GG, Kochman ML. A prospective, randomized, comparative trial evaluating respiratory depression during patient-controlled versus anesthesiologist-administered propofol-remifentanil sedation for elective colonoscopy. Gastrointest Endosc. 2010;72:112-7.


Patient
Weight
72.6
Age
58
Height
167.6
Sex
Male
Female
Maximum Effect Site (μg/ml)
12.0
Bolus duration (min)
Maximum rate
1
2
3
4
Bolus: 598.7 μg/kg (43.5 mg)
Infusion: 844.5 μg/kg/min
Total propofol at clinical endpoint
Effect (μg/ml)
Target
Propofol (mg)
Effect site (μg/ml)
Total propofol (mg)
Time (min)
110
Maintenance: 134.49 μg/kg/min
71