A MULTILAYER HIERARCHICAL STRUCTURE OF AN I-PAIN SYSTEM FOR THE ASSESSMENT OF POSTOPERATIVE PAIN VIA FUZZY PAIN RELIEF INDEX

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ABSTRACT
A multilayer hierarchical structure for an i-pain system is described in this paper. There are four levels which are patients’, measuring, web-based, and interpreting levels to collect massive amounts from clinical information and analyze it with both traditional and artificial intelligent methods. To support this, a novel fuzzy pain relief (FPR) index derived from the interval of each bolus of patient-controlled analgesia (PCA) is designed and documented in a large scale clinical survey. The FPR index is modeled according to a fuzzy modeling algorithm to interpret the self-titration of the drug delivery. Two hundred and fifty-five patients receiving intravenous PCA using morphine (1 mg/ml) were tested this index by off-line analysis from i-pain system. We found the FPR index modeled from a fuzzy modeling algorithm to interpret the self-titration of the drug delivery can show the patients’ dynamic pain and past efforts for overcoming pain suffering. Moreover, it could become on-line monitoring patients’ pain to be entered into a patient’s chart along with temperature, blood pressure, pulse and respiration rates when medical doctors make a visit in the ward regularly.

KEY WORDS
Fuzzy pain relief index, patient-controlled analgesia, fuzzy modeling algorithm, mean drug consumption, demand/delivery ratio, visual analog scale

1. Introduction
The need for a reliable and valid tool in pain measurement is essential for any clinical practice or trial associated with pain treatment. However, the subjective feeling of pain is extremely hard to quantify [1]. The current patient-controlled analgesia (PCA) method provides the patient with a pain-driven button that activates the pump to administer a bolus dose of analgesic at a fixed time interval (i.e., lockout time). And, the most commonly used measures of pain intensity, including visual analog scales (VASs), numerical rating scales (NRSs), and verbal rating scales (VRSs) have been shown to have adequate sensitivity to changes in pain associated with treatment across many populations and settings. However, these conventional methods have a number of limitations for measuring pain. Firstly, all these scales require intervention by other people (i.e., medical doctors or nurses) to ask the results, which not only requires too much effort and time, but also may not detect on some perceivable changes in pain that might occur just before interventions. This means that the timing to determine the patients’ pain is very difficult to synchronize with asking their VASs, NRSs, or VRSs. Secondly, they cannot indicate postoperative efforts of the patient. Although these values from clinical evaluation may be quite similar, the efforts of pressing of buttons are dramatically different. This means that VASs, NRSs, and VRSs can only show the static pain but not dynamic pain, which is related to the accumulated previous efforts. Thirdly, these methods are not practical for on-line analysis of postoperative pain intensity.

In the search for a useful adjuvant to self-reported pain intensity, the PCA device is an important means to develop a reliable, objective, continuous, and on-line index. In conventional PCA systems, consenting patients are provided with a hand-held pushbutton and are instructed to trigger the button when they require pain relief. A bolus of constant size is given an analgesic drug in response to each legitimate pushing of the button. The size of the bolus is set by the medical staff and there is a “lockout” period following each bolus administration during which time no further bolus can be delivered. Therefore, the pain pattern of patients stored inside the PCA device may differ from either analgesic drugs or surgical operations and present specific characteristics with clinical implications. Moreover, pain has recently become the “fifth vital sign” to be entered into a patient’s chart along with temperature, blood pressure, pulse and respiration rates[2]. Hence, how to model this pain pattern to be more objective and reliable in order to continuously monitor this fifth vital sign is the most important aspect of the pain measurement.

Modeling a system is very important because it is related to process characterization and design studies. In the past, it has been thought that a complicated mathematical approach could model a system more accurately. For example, pharmacokinetic and pharmacodynamic models have been applied in modeling pain. But this still has problems when ill-defined, complicated and nonlinear systems are encountered. To solve this problem fuzzy logic has been applied, as indicated by the recent survey paper for
The utilization of fuzzy technology in medicine and healthcare [3]. Fuzzy logic not only accommodates uncertainty by dealing with imprecise, qualitative terms such as low, medium and high, but also provides rules which are easy to understand and modify for discussion with experts. Using verbalization or linguistics through interaction with the human operator or domain expert, the system can be modeled [4].

The present study had two primary goals. The first was to build a multilayer hierarchical structure of i-pain system which is able to collect the post-operative records of PCA device and patients’ basic information uploaded to web-server PC using standard web-based TCP/IP. The web-server acts as a database for multimodal electronic patient record information, storing and intelligent analyzing patient data. Under this i-pain system, the second goal of this paper was to propose a novel fuzzy pain relief (FPR) index derived from the interval of each bolus of PCA using fuzzy modeling algorithm. We wish to know how the rule-base of FPR index is generated from experts (i.e., anaesthetists) and how this rule-base is related to FPR index perturbed by different generated rule-bases. We also examine the relationship of FPR index in comparison with conventional parameters, standard mean drug consumption (MDC), demand/delivery ratio (D/D ratio), and clinical observation pain using the visual analog scale (VAS) measured at rest and during movements.

2. A multilayer hierarchical structure of i-pain system

A multilayer hierarchical structure of i-pain (where i means information and intelligence) system for data collection and interpretation includes the four levels of patients, measuring, web-based and interpreting levels, as shown in Fig. 1.

2.1. Level 1: Patients (i.e., Patient level)

This study was approved by the Shin Kong Wu Ho-Su Memorial Hospital Ethics Committee. Two hundred and fifty-five patients with American Society of Anesthesiologist physical status 1, 2 or 3 for upper and lower abdominal, spinal, and extremity procedures using analgesic dosage of morphine (1 mg/ml) alone were screened from the i-pain database and entered into this study. Patients were excluded from the study if they were morbidly obese, unable to understand the use of the PCA or had a history of allergy to morphine. According to routine clinical practice, patients were instructed on the correct use of the PCA pump and given standardized PCA education by a PCA team nurse.

2.2 Level 2: Measuring patients’ demand and inputting patients’ basic information (i.e., Measuring level)

PCA has become an established procedure for clinical pain relief. A number of studies have shown the advantages of PCA over regularly scheduled and as-required administration of analgesics. That is why a significant improvement in satisfaction score was seen after the introduction of an acute pain service [5]. The PCA machine provides a system where the patient operates a hand-held button interfaced to a microprocessor that drives an infusion pump delivering intravenous analgesic. Furthermore, the pain demand and delivery of patients stored inside the PCA device may represent different degrees of pain relief. Hence, the second level is a measuring level that involves an instrument device (i.e., Abbott AIM Plus pump), which collects all the patient demands and deliver a bolus to patient when they require pain relief. The collecting information has two modules, which provide basic information input and items, and data retrieving from the PCA machine. A basic module provides the information inputs and items, such as the patient height, weight and age, doctor’s and nurse’s name, drug’s name, dosage and concentration, …, etc. Also, the clinical observation pain using the visual analog scale (VAS) was measured at rest and during movements via medical visit by anaesthetists or nurse anaesthetists as shown in Fig. 1. The data retrieving module from the PCA machine provides the number of demands and delivery, the bolus volume, the continuous infusion volume, and the total drug consumption for each day. Then, the patients’ basic information and post-operative records of PCA device are transmitted to personal computer (PC) to create a comprehensive file in PC-based i-pain system.

2.3. Level 3: Constructing a web-based i-pain system for collecting large scale of clinical data (i.e., Web-based level)

With the large scale clinical data input from a PCA device via a RS232 communication port, we constructed a comprehensive web-based i-pain platform to encompass the high-throughput data acquisition. Hence, level 3 is a web-based level that involves all data files which are merged off-line and uploaded to a web-server PC using standard TCP/IP. The web-based i-pain system acts as a database for multimodal electronic patient record information and storing for conventional data analysis (e.g., the MDC, D/D ratio, and VAS) and further intelligent analysis (e.g., the FPR index as shown in Fig. 1).

2.4. Level 4: Data mining of the pain database (i.e., Interpreting level)

In order to encompass the high-throughput data analysis to yield evidence-based medical information, the data mining of the database is like an interpreting level that involves interpreting patients’ pain intensity to obtain pattern of delivery, and then interpreting the pain pattern to fuzzy pain relief (FPR) index. Also, the conventional patients’ MDC, D/D ratio, and VAS are also calculated and measured. In order to show the change of all these values, our clinical analysis data are divided into six periods after the start of PCA: period 1 (0-4 h), period 2 (4-8 h), period 3 (8-12 h),
period 4 (12-16 h), period 5 (16-20 h), and period 6 (20-24 h).

2.4.1 Fuzzy pain relief index using the fuzzy modeling algorithm

Fig. 2 shows the conventional PCA and the PCA+FPR structure for the modeling of acute pain for the assessment of postoperative pain via a PCA device. The current PCA method as shown in Fig. 2 (a) provides the patient with a pain-driven button that activates the pump to administer a bolus dose of analgesic at a fixed time interval (i.e., lockout time). In contrast, the proposed PCA+FPR structure in Fig. 2 (b) to interpret the pain intensity derived from the button-pressing profile more accurately and easily reflects the real pain and the patients’ efforts to reduce the pain. According to a previous study of cancer pain relief [6], adequate relief was defined not by asking patients what degree of relief they perceived as acceptable, but by their no longer requiring additional opioid doses as rescue medication. Therefore, a more reliable, objective, continuous, and online monitor of dynamic pain like the vital signs would be possible from this PCA+FPR structure.

2.4.1.1 Definition and calculation of pain intensity and pain pattern

To obtain the different pain intensity from the patient’s button-pressing profile, the big pain (BP), small pain (SP) and zero pain (ZP) levels of pain intensity were defined as follows:

(a) BP: at least two buttons have been pushed during 4 lockout intervals
(b) SP: one button has been pushed during 4 lockout intervals
(c) ZP: no button has been pushed during 4 lockout intervals

Since the 4 lockout intervals act as a data window segment obtained by breaking the data sequence into equal lengths, the segments of data may overlap or they may be disjoint. However, if the segments are made to overlap, more segments can be taken from the same sequence. In this study, an overlap of 75% has been recommended for a data sequence with ten lockout intervals. Hence, the individual pain pattern within four consecutive lockout intervals can be calculated, as shown in the example of Fig. 3.

2.4.1.2 Fuzzy pain relief index derived from pain pattern according to fuzzy modeling algorithm

Model rules, membership functions, fuzzy inference engine and defuzzification are the essential elements in the fuzzy modeling algorithm. To perform fuzzy inference and describe this fuzzy modeling system, we chose the three inputs of BP, SP and ZP, with the single output of FPR index. In order to fuzzify the inputs and output, the BP, SP and ZP value was divided into the following nine levels: zero (Z), between zero and small (ZS), small (S), between small and medium (SM), medium (M), between medium and plus (M+), between medium plus and big (MB), big (B), between big and big plus (BB), and big plus (B’). And, the FPR index was divided into eleven levels which were the zero (Z), between zero and small (ZS), small (S), between small and medium (SM), medium (M), between medium and medium plus (MM+), medium plus (M’), between medium plus and big (MB’), big (B), between big and big plus (BB’), and big plus (B’). There is no any negative fuzzy set because of the non-feasible nature for pain intensity. Here we use eleven levels instead of nine levels because this will increase the resolution of FPR index. Moreover, in order to perturb the anaesthetists’ rule-base, the 20, 36 and 60 rules have been tested in simulation to see what effect it has on the FPR index. Finally, 36 rules were chosen and developed to model the FPR index instead of the total rules of our system for 729 (i.e., 9×9×9). Since the rules have been decided, it is easy to use our previous studies in the control of depth of anaesthesia [7,8] to produce a three-input and one-output look-up table for interpreting the FPR index. As the output fuzzy set of the model is defuzzified, it can be shown the FPR index after being scaled from normalized values to real values. In this study, the real values of FPR index were chosen between 0–10. These values were aimed at providing a sensitive pain intensity similar to the VAS value in order to compare the pain intensity.

2.4.2 Mean drug consumption

Dosage was calculated by summing the total volume of opioid administered during each period and expressing the dose as milliliters per hour.

2.4.3 Demand/delivery ratio

Demand was the mean number of times every period that the patient made a request by pushing the PCA button. In addition, delivery was the number of successfully completed demands, i.e., demands that were met by administration of the drug. Hence, the D/D ratio is the ratio of demands to completed deliveries. A low ratio suggests that the patient’s demands were frequently met by delivery of the drug, whereas a high ratio suggests that the patient made frequent demands during the lockout interval when the drug was not delivered.

2.4.4 Visual analog scale score

The visual analog scale is a 10 cm line with the endpoints labeled ‘no pain’ and ‘maximum pain’ [9]. The patient marks the line at the distance corresponding to the intensity of present pain. The routine protocol for analgesia assessment was evaluated two or three times every day by a specially trained nurse with no knowledge of the treatment. Each patient rated pain on a VAS graded from 0 (i.e., no pain) to 10 cm (i.e., maximum pain) during rest (i.e., for rest pain) and movement (i.e., for most pain).

2.4.5 Statistical analysis

Kruskal-Wallis test was used to assess for statistically significant differences in the median FPR index across perturbing the anaesthetists’ rule-base (i.e., 20, 36, and 60 rules) [10]. P < 0.05 was considered statistically significant. Moreover, the Pearson product-moment correlation
coefficient was used to assess the relationship of two indexes (i.e., FPR vs. MDC, D/D ratio, or VAS).

3. Results

Two hundred and fifty-five patients (i.e., 146 female and 109 male), with upper and lower abdominal, spinal, and extremity procedures using analgesic dosage of morphine (1 mg/ml) alone were entered into the study. The mean age was 56.7(15.4) years, mean height was 154.8(12.8) cm, and mean weight was 58.7(9.9) kg. In addition, the mean lockout time was 8.0(2.0) min, and mean PCA using time was 5.2 (2.5) days. In order to perturb the anaesthetists’ rule-base, the 20, 36, and 60 rules have been tested in simulation to see what effect it has on the FPR index. Since the rules have been decided, combining all rules produces a three-input and one-output look-up table of 729 possible values (i.e., 9×9×9) for interpreting the FPR index. Fig. 4 is the comparison of FPR index at different rule-base of 20, 36, and 60 rules from the left top corner to the right bottom corner of the look-up table. The FPR values in look-up table of rule-base of 36 and 60 rules are smoother than the rule-base of 20 rules. Although the continuity of rule-base of 60 is very smooth in the low FPR index, there is a sharp corner of the look-up table. The FPR values in look-up table of rule-base of 36 and 60 rules are smoother than the rule-base of 20 rules. Although the continuity of rule-base of 60 is very smooth in the low FPR index, there is a sharp discontinuity at FPR index between 8–9. Hence, in terms of smooth and continuity of FPR index, the overall performance of rule-base of 36 is better as shown in Fig. 4. However, there were no significant differences ($P > 0.05$) using Kruskal-Wallis test for these three rule-bases in terms of FPR values at each interval.

Fig. 5 is the comparison of FPR index, MDC, D/D ratio, and VAS score at most pain and rest pain during 6 intervals. This figure was selected from two patients of i-pain system in order to demonstrate that the FPR index was dramatically different although the MDC, D/D ratio, and VAS score at most pain and rest pain were quite similar. Moreover, the Pearson product-moment correlation coefficients of FPR index with MDC, D/D ratio and VAS score at most pain and rest pain were 0.629, 0.277, 0.002 and 0.001, respectively. This result indicates that FPR index has some relationship with MDC but it has very weak relationship with D/D ratio and VAS. That is because D/D ratio and VAS are not entirely determined by the nociceptive stimuli but rather as a result of both sensory-discriminative and emotional-cognitive components of patient's suffering. Although the FPR index has strong relationship with MDC, it is because FPR index was derived from four deliveries as shown in Fig. 3. However, in terms of dynamic phenomena to show the pain, the FPR index is much better than MDC which can only show the past cumulative pain effect. In order to show that FPR index can demonstrate the dynamic pain, we calculate the FPR index for 1, 10, 100, and 200 patients as shown in Fig. 6. This result indicates that FPR index can show the dynamic pain but it will be smoothed out when averaged many patients together. The dynamic phenomena of FPR index is the most beneficial to clinical assessment of pain management because the medical doctor want to know this patient’s dynamic pain and past efforts for overcoming pain suffering during medical visiting of this patient. Then, he (or she) can judge what kinds of setting of PCA parameters (e.g., lockout interval, drug type, and dosage amount) will be suitable to this patient.

4. Conclusion

For this paper, we built up a multilayer hierarchical structure of i-pain system to collect the patients daily medical information into major server since 2003. At present, a total of 8 medical centers have joined to share the i-pain system in Taiwan. Cumulative evidence from our preliminary results has yielded fruitful implication that in turn can provide an immediate feedback for daily practice [11]. With the large scale of clinical data input, we have successfully constructed a comprehensive platform to encompass the high-throughput data acquisition and systemic analysis to yield a series of evidence-based medical evaluation for modern acute pain service. We also found the FPR index modeled from a fuzzy modeling algorithm to interpret the self-titration of the drug delivery can show the patients’ dynamic pain and past efforts for overcoming pain suffering. Moreover, it could become online monitoring patients’ pain to be entered into a patient’s chart along with temperature, blood pressure, pulse and respiration rates when medical doctors make a visit in the ward.

References


Fig. 1 A multilayer hierarchical structure of i-pain system

Fig. 2 Block diagram modeling the proposed pain system to interpret the pain measurement (a) Conventional PCA system; (b) PCA+FPR system

Fig. 3 Data sequence with ten lockout intervals broken into segments with four lockout intervals each and obtained seven 75% overlapping segments (Star indicates a button has been pushed in the lockout interval)

Fig. 4 The comparison of FPR index at different rule-base of 20, 36, and 60 rules from the left top corner to the right bottom corner of the look-up table. (X axis: the number of the left top corner to the right bottom corner of the look-up table; Y axis: the FPR index)
Fig. 5 The comparison of FPR index, MDC, D/D ratio, and VAS score at most pain and rest pain at different dosages during 6 intervals selected from two patients of i-pain system (r is the Pearson product-moment correlation coefficients).
Fig. 6 The comparison of FPR index under 1, 10, 100, and 200 patients.