The physiological effects of remifentanil on hemodynamic stability during elective surgery

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Abstract

The general anaesthesia inductions may cause hemodynamics disturbance. These responses are often suppressed by administration of remifentanil. In this study the aim is to assess the effects of infusion Remifentanil on hemodynamic stability during general anesthesia. This prospective study we collects 50 healthy patients aged between 20 to 65 years scheduled for elective surgery in Baghdad teaching hospital with ASA, (I. II). All these patients received 1mcg/kg/min remifentanil by continuous infusion over 30 minutes. The recording of mean arterial, heart rate, respiratory rate and peripheral oxygen saturation 10, 5 minutes pre induction, throughout infusion and at 5, 10, 15 Minutes after induction. The results showed decreases in heart rate and blood pressure values during infusion of Remifentanil and the value started to increase after the infusion is stopped. The respiratory rate and SPO2 (peripheral O2 saturation) values reminded in the same limits during and after infusion of Remifentanil with no major changes. Remifentanil infusion affectively attenuate the hemodynamic response of the heart rate and blood pressure and there was significant decrease in them during infusion with no significant effect on respiratory rate and peripheral oxygen saturation.

Keywords: *remifentanil; hemodynamics instability; general anesthesia; peripheral oxygen saturation; blood pressure.*

التاثيرات الفسلجية لعقار الرميفنتانيل على استقرارية الدورة الدموية خلال العمليات الجراحية

م.د. محمد عبدالحميد يونس

الخلاصة

قد تسبب تعرض المريض الى التخدير العام اضطراب في ديناميكا الدم. غالبًا ما يتم قمع هذه الاستجابات عن طريق إعطاء الريميفنتانيل. الهدف في هذه الدراسة هو تقييم آثار التسريب ريميفنتانيل على استقرار الدورة الدموية أثناء التخدير العام. هذه الدراسة المرتقبة قمنا بجمع 50 مريضاً أصحاء تتراوح أعمارهم بين 20 إلى 65 سنة من المقرر أن يخضعوا لعملية جراحية اختيارية في مستشفى بغداد التعليمي مع ASA، (I. II)). تلقى جميع هؤلاء المرضى 1 ميكروغرام / كغ / دقيقة ريميفنتانيل بالتسريب المستمر على مدى 30 دقيقة. تسجيل متوسط الشريان ، معدل ضربات القلب ، معدل التنفس والتشبع بالأكسجين المحيطي 10 ، 5 دقائق قبل

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التحريض ، طوال فترة التسريب وبعد 5 ، 10 ، 15 دقيقة بعد التحريض ، وأظهرت النتائج انخفاضًا في معدل ضربات القلب وقيم ضغط الدم أثناء تسريب الريميفنتانيل وبدأت القيمة في الزيادة بعد توقف التسريب. يتم تذكير قيم معدل التنفس و SPO2 (تشبع الأكسجين المحيطي) بنفس الحدود أثناء وبعد تسريب الريميفنتانيل بدون تغييرات كبيرة. يخفف تسريب الريميفنتانيل بشكل فعال من استجابة الدورة الدموية لمعدل ضربات القلب وضغط الدم ، وكان هناك انخفاض معنوي فيها أثناء التسريب مع عدم وجود تأثير معنوي على معدل التنفس وتشبع الأكسجين المحيطي.

الكلمات المفتاحية : *الريميفنتانيل ، عدم استقرار الدورة الدموية ، التخدير العام ، نسبة التشبع بالاوكسجين ، ضغط الدم .*

Introduction

Remifentanil this is derivative of fentanyl, which is an ultra- short acting, it is a selective μ-opioid receptors agonist. The aims of General anesthesia(GA) are to provide the patient with a condition by which the unpleasant or noxious interventions can be easily tolerated; usually associated with surgery and interventions. General anesthesia is a reversible condition induced by drugs that includes specific behavioral and physiological effects associated with stability of the, cardiovascular, respiratory, autonomic and thermoregulation systems. [1،2]

The most common management technique used in anesthesia care is balanced general anesthesia, which was required administration a combination of different agents to produce an optimal anesthetic state. This approach were developed by several Anaesthesiologists to avoid alone reliance on ether for the maintaining general anesthesia. So it was proven that balanced general anesthesia using each drug with less than if the drug administration occurs as a sole, this method was believed to augment likelihood of desired effects in drugs and reduce the likelihood of its adverse effects. [3، 4]

Remifentanil is an analgesic drug having selective opioid agonist. Because of it is unique structure due to presence of ester-linkage Remifentanil's ester structure renders it more susceptible to hydrolyzed by nonspecific plasma and tissue esterase to inactive metabolites. This unique pathway of metabolism lead to short action, accurate and rapidly treating effect due to its rapid onset and short duration, negligible accumulation, and rapid return of recovery after discontinuation of its administration, No clinically significant changes in intraocular or intracranial pressure, cerebral blood flow, cerebrovascular carbon dioxide reactivity, or brain function were seen in remifentanil users. capacity. Combined with vaporizing or injectable anesthetics, Remifentanil exhibits the normal hypnotic sparing effects of opioids. [5]

So this study aimed to assess some effects of remifentanil on the haemodynamic parameters [(heart rate (HR), mean arterial pressure (MAP)] and peripheral oxygen saturation and respiratory rate (RR), with a dose of 1mcg/kg/min over 30 minutes of infusion. Remifentanil could have a variety of potential uses in addition to those that are related to surgery. Remifentanil, for instance, may be helpful by bolus injection for analgesia during brief, excruciating techniques for diagnosis or

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treatment, like lumbar wound, central venous catheter, or puncture Dress modifications. Continuous use of it could potentially be beneficial. For the cognizant patients in the intensive care unit, infusion Patients on mechanical ventilation receive sedation and analgesia. Remifentanil may be helpful in the treatment of persistent pain. as a diagnostic instrument in the outpatient clinic to identify whether a person suffering from complicated chronic pain opioid analgesics are effective in treating the condition.

Patients and methods

This study was done in Baghdad teaching hospital and carried out on a period between 3-December to 2- June in the 2021-2022 on fifty patient, aged 20-65years scheduled for elective surgery with general anaesthesia they were 36 females and 14 males. All patients were physical fit belonging to ASA I or ASA II presenting for elective surgeries. All patients have surgeries that took time more than 30 minutes and with oral endotracheal intubation. All patients received a dose of 1mcg/kg/min infusion of Remifentanil over 30 minutes, throughout the surgery the patient were continuously monitored, and the reading of blood pressure, pulse rate, respiratory rate, peripheral oxygen saturation, before the induction of remifentanil by 10, 5 minutes and throughout the infusion of 1mcg/kg/min of remifentanil the values were recorded after 1 minute from the start of infusion and every 5 minutes for the left of 30 minutes of infusion, Then we took record of the values for 5, 10, 15 minutes after the stop of the infusion. If the heart rate decreased less than 50 beats per minute for more than 1 minute, 0.5 mg of atropine sulphate was administered intravenously. If systolic blood pressure (SBP) was less than 80 mmHg or the mean arterial pressure was less than 60 mmHg for more than 2 minutes the hypotension was corrected by intravenous administration of vasopressor (ephedrine 5-10mg). The Statistical Analysis System- SAS (2012) program was used to detect the effect of difference factors in study parameters. Least significant difference LSD test (Analysis of Variation-ANOVA) was used to significant compare between means.

Results

Table (1): The Effect of Remifentanil on H.R Comparison between difference groups in HR. There are significant changes in heart rate during the infusion of remifentanil.

Group	No	Mean ± SE of HR
Before	100	108.51 ±1.75 a
Intra-induction	350	84.63 ±0.96 b
After	150	79.08 ±1.07 c
LSD value	--	3.773 **
P-value	--	0.0001
Means having with the different letters in same column differed significantly. ($P \leq 0.01$).**		

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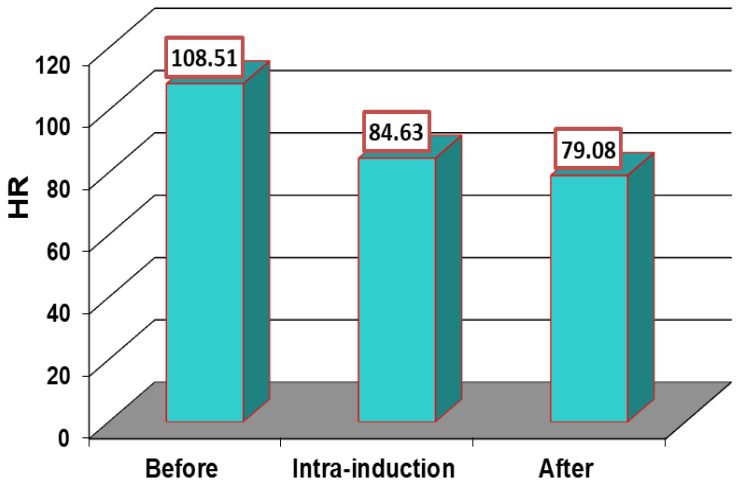

Fig. (1): Comparison between difference groups in HR.

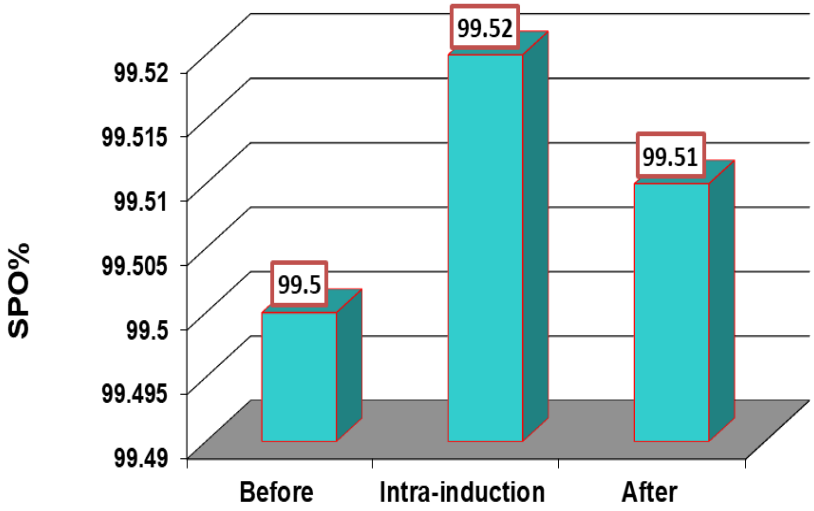

Fig. (2): Comparison between difference groups in SPO2.

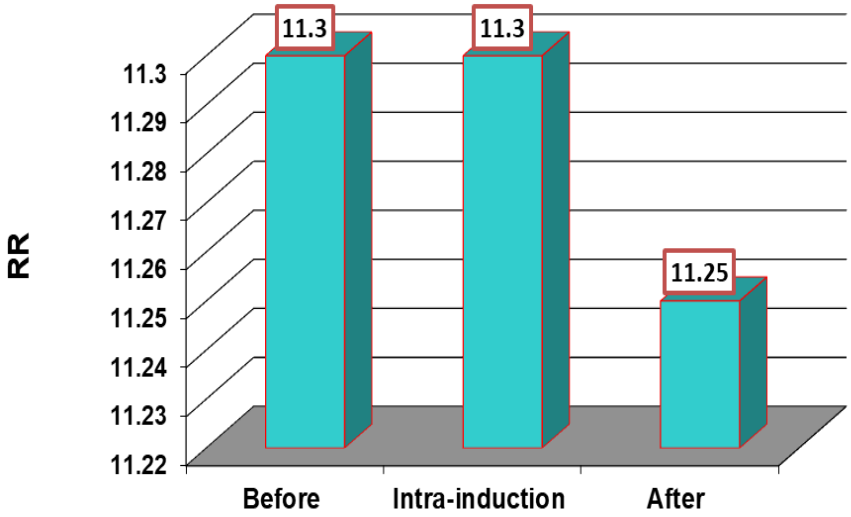

Fig. (3): Comparison between difference group in Respiratory rate.

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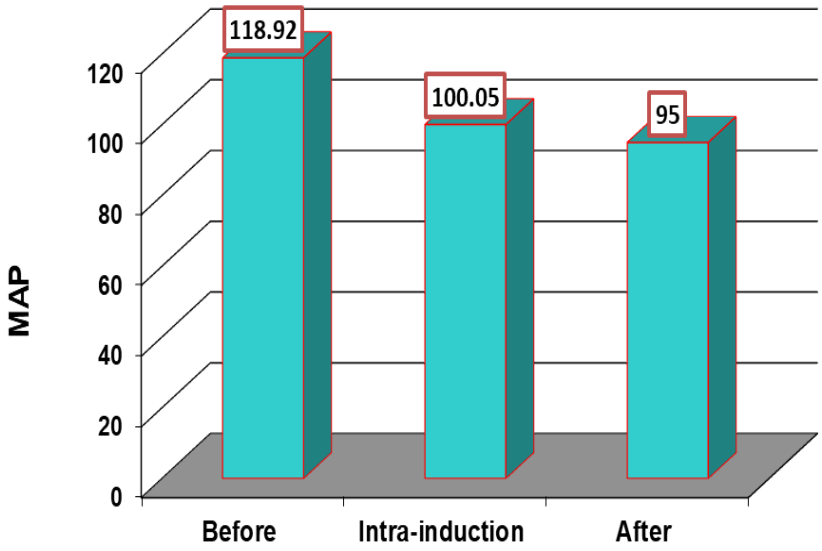

Fig. (4): Comparison between difference groups in MAP.

Table (2): The Effect of Remifentanil on SPO2%) Comparison between difference group SPO2%. There are non-significant changes in SPO2 during infusion of remifentanil.

Group	No	Mean ± SE of SPO%
Before	100	99.50 ±0.06
Intra-induction	350	99.52 ±0.03
After	150	99.51 ±0.04
LSD value	--	0.129 NS
P-value	--	0.937
NS: Non-Significant.		

Table (3): The Effect of Remifentanil on RR) Comparison between difference groups in RR. There a non-Significant changes in RR during infusion of remifentanil.

Group	No	Mean ± SE of RR
Before	100	11.30 ±0.09
Intra-induction	350	11.30 ±0.05
After	150	11.25 ±0.08
LSD value	--	0.222 NS
P-value	--	0.882
NS: Non-Significant.		

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Table (4): The Effect of Remifentanil on MAP) Comparison between difference groups in MAP. There are significant changes in MAP during infusion of remifentanil.

Group	No	Mean ± SE of MAP
Before	100	118.92 ±1.04 a
Intra-induction	350	100.05 ±0.71 b
After	150	95.00 ±0.93 c
LSD value	--	2.774 **
P-value	--	0.0001
Means having with the different letters in same column differed significantly. ** (P≤0.01).		

Table (5): Effect of gender in parameters study, there are significant changes in (HR, SPO2, and RR) Depending on gender

Parameters	Mean ± SE		T-test
	Male	Female	
HR	84.51 ±1.43	88.28 ±0.95	2.423 *
SPO2%	99.41 ±0.04	99.56 ±0.03	0.088 *
RR	11.43 ±0.07	11.23 ±0.05	0.153 *
MAP	102.61 ±1.13	101.67 ±0.71	2.498NS
***(P≤0.05), NS=Nonsignificant.**			

Table (6): The Effect of Age groups in parameters study. There are non-Significant changes depending on age except for SPO2%.

Parameters	Mean ± SE			LSD value
	<30 yr.	30-50 yr.	>50 yr.	
HR	86.73 ±1.63	86.92 ±1.06	88.39 ±1.75	4.020 NS
SPO2%	99.37 ±0.06 b	99.55 ±0.03 a	99.58 ±0.04 a	0.104 *
RR	11.35 ±0.08	11.31 ±0.05	11.18 ±0.08	0.180 NS
MAP	99.87 ±1.07	102.97 ±0.83	101.73 ±1.34	3.933 NS
*** (P≤0.05), NS: Non-Significant.**				

Table (7): Effect of Weight groups in parameters study, there are significant changes depending on weight in (HR and RR).

Parameters	Mean ± SE			LSD value
	<80 kg	80-100 kg	>100 kg	
HR	88.51 ±1.21 a	86.97 ±1.16 a	82.40 ±2.42 b	3.771 *
SPO2%	99.54 ±0.04	99.48 ±0.03	99.53 ±0.08	0.123 NS
RR	11.13 ±0.06 b	11.46 ±0.05 a	11.20 ±0.12 b	0.213 *
MAP	102.67 ±0.82	101.47 ±0.93	100.53 ±2.18	3.481 NS
*** (P ≤ 0.05), NS: Non-Significant.**				

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Discussion

The results from this study on remifentanil at hemodynamic reaction and SPO2 to common anesthesia in mellow hypertensive and normotensive patients, appeared that at a measurements of 1 mcg/kg/min of remifentanil managed over 30 minutes seem viably repress the intemperate increment of blood weight and heart rate in marginally hypertensive and normotensive patients.These results came in accordance many other study that reported the hemodynamic changes during intubation of trachea can be completely attenuate by using of a remifentanil (1mg/ kg) after administration over 30 seconds in adult patients by induction of anaesthesia [6 – 8].

Although, some others study had revealed some other adverse effects, that includes (severe brady-cardia and hypotension.), by uses of the same or lower doses. So, these authors recommendation were to lower the total dose by slowing rates of remifentanil infusion or using vagolytic drugs that prevent hypotension and sever bradycardia associated with remifentanil administration. However, these studies results observed above might be due to occurrence of comorbidity, including cardiovascular pathology. [9 -11]

The results obtained from our study came in differentiate to past ponders the administration of Remifentanil asan infusion at a rate of 1mcg/kg/min over 30 minutes. This considered as an appropriate dose with no loading dose thus we didn't encounter problems with sever bradycardia and/or hypotension and didn't found any major changes in Respiratory rate RR and SPO2 other studies have showed a remarkable change [12،13].

During our work and procedure, the administration of remifentanil and dripping at arate of 1mcg/kg. /minute by 30 min., also it was used remifentanil during general anesthesia with an established airway, and controlled ventilation thus ventilatory depression was not a concern. The present study revealed that the heart rate decreased significantly after induction and throughout the infusion of remifentanil with non-significant between intra and after induction when compared with pre induction measures

The decreased of heart rate in this study suggest that remifentanil attenuated the hemodynamic response to laryngoscope and endotracheal intubation and other stimulation throughout the infusion of remifentanil or these might be attributed to vagolytic effect of remifentanil [14]. The results of present study revealed that the mean arterial pressure were significantly decreased after induction and throughout the infusion of remifentanil with non-significant between intra and after induction when compared with pre induction measures .The decreased of MAP in this study suggest that remifentanil alleviate the hemodynamic changes to laryngoscope and endotracheal intubation and other

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stimulation throughout the infusion of remifentanil or these might be attributed to vagolytic effect of remifentanil [14]

The present study revealed that the respiratory rate shows non-significant changes in values pre, during induction and throughout the infusion of remifentanil, the stationary in values is due to the established airway, and controlled ventilation [15]. The present study revealed that the peripheral arterial saturation shows non-significant changes in values pre, after induction and throughout the infusion of remifentanil, the stationary in values is due to the established airway, and controlled ventilation. There was significant difference between male and female with the female have slightly higher values than men in the parameters (heart rate HR, SPO2, and respiratory rate RR) with non-significant difference in MAP between them, these could be attributed to physiological and humoral differences between both genders [15]. There was non-significant different between age groups in the parameters (RR, HR, and MAP) with slightly difference in spo2. There were a significant difference between Weight groups in parameters (Respiratory rate RR, heart rate HR) with non-significant different between in (SPO2, MAP), the old group in our study needed a lower remifentanil concentration than the other groups. The pharmacokinetic and pharmacodynamics alterations of remifentanil among the elderly can help to explain this in part. The central volume of distribution, clearance, and potency of remifentanil are adversely correlated with age (16). However, there was no change in the remifentanil between the adult male and female groups, according to our research. It is well-known that women are more sensitive to the opioid than men [17]. However, according to Minto et al, gender had no effect on the remifentanil's potency [18]. Remifentanil's pharmacokinetics and pharmacodynamics are significantly influenced by advancing age [17]. The abolition and widespread distribution Age causes a reduction in remifentanil volume. Similarly, EC5%, the level required for 50% of maximum effect, as determined by the EEG, also significantly decreases over time. Thus, remifentanil is substantially more effective now. The elderly, and that it isn't more powerful cleaned as rapidly (blood and the affected area also balance) more gradually. Age-related modifications translate senior patients' dosages by 50%–70% (i.e., patients who are older than 60 on averages) [19].

Another crucial consideration when creating remifentanil dosing regimens is body weight. Lean body mass is more strongly correlated with remifentanil pharmacokinetic characteristics than is total body mass. In other words, patients who weigh more may not continuously have an increment in metabolic capacity that's weight-proportional. This is in line with the finding that lean tissue is where more than 90 % of metabolic processes are thought to take place [20]. This indicates that people who are obese, especially those who are severely obese, do not require a greater dose (i.e. a weight normalized dose).

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Remifentanil dosages should be determined using optimal body weight or lean body mass rather than total body weight. Patients who are truly obese and are given a dosage based on add up to body weights are more inclined to involvement bradycardia, hypotension, and other side impacts [21]. Remifentanil has hemodynamic effects that are similar to those of the opioids in the fentanyl family. Heart rate, arterial blood pressure, and cardiac output all decrease with remifentanil dosage [22]. Remifentanil has been linked to severe bradycardia at large doses [23]. It is believed that these cardiovascular effects are at least partially attributable to a centrally mediated rise in vagal tone

Conclusion

It is clear from our study remifentanil will eventually play within the conveyance of anesthesia (and in other settings). It is obvious; in any case, that remifentanil could be a modern pharmacologic device with energizing potential that was not conceivable with the longer-acting opioids. On the premise of its commonplace, fentanyl-like pharmacodynamics behavior and its short-acting pharmacokinetic profile, remifentanil could be beneficial in a assortment of settings in which significant opioid impact with consequent quick return of unconstrained ventilation and awareness is alluring, Remifentanil successfully attenuate the increase in heart rate HR and MAP due to different stimulation in the surgery. the (MAP) and heart rate (HR) declined after induction and during infusion remifentanil in this study, the decrease in HR and MAP might not be of importance in the healthy patients, but it could be of importance in the patients with preexisting hypotension and/or bradycardia. The respiratory rate RR and SPO2 remained stationary and haven't shown any remarkable changes during induction and infusion of remifentanil in general anesthesia with endotracheal intubation and controlled ventilation.

Recommendations

we are recommended to avoid using remifentanil in patient with shock and low circulatory and blood volume state also It is recommended Remifentanil infusion rate of at least 0.1 microgram/kg/min (6 microgram / kg / h) should be maintained for at least 5 minutes prior to the start of the stimulating procedure, so We recommend the use of remifentanil in painful surgeries and procedure but pay careful attention to the respiration and ventilation, our opinion were to encourage medical students to do more researches in different situation on remifentanil since it is new drug with special pharmacodynamics and pharmacokinetic Characteristics, One of the special features of employing remifentanil is the ability to switch from remifentanil intraoperatively to a longer-acting analgesic postoperatively. Remifentanil is metabolized so quickly, therefore unless an analgesic infusion of remifentanil is maintained or unless the switch to another longer-acting analgesic is done

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before to emergence, there is a risk of a rapid drop in analgesia after emergence from anesthesia. In the post-anesthesia care unit, anesthesiologists are accustomed to moving from the intraoperative opioid—typically one of the fentanyl congeners—to the postoperative opioid—typically morphine or meperidine. With remifentanil, this transition must be made before the end of anesthesia (for example, 100 mg of fentanyl around 15 minutes prior to the end of the procedure or 5-10mg of morphine about 30 minutes prior to the conclusion of the procedure). Upcoming applications. Remifentanil could have a variety of potential uses in addition to those that are related to surgery. Remifentanil, for instance, can be used as a bolus injection to reduce pain during quick, uncomfortable diagnostic or therapeutic procedures like lumbar puncture, central venous catheterization, or wound dressing changes. In the intensive care unit, it may also be helpful as a continuous infusion for the conscious sedation-analgesia of patients who are being mechanically ventilated. Remifentanil may be helpful as a diagnostic tool in the treatment of chronic pain in ambulatory clinics to ascertain whether a understanding highlights a complex ceaseless torment clutter and is responsive to opioid analgesics. Remifentanil is being researched for these and other possible uses.

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