Use of Ultra Rapid Opioid Detoxification in the Treatment of US Military Burn Casualties

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Background: The purpose of this case series was to review the management of burn patients who requested ultrarapid opioid detoxification under anesthesia after extended duration of narcotic use for chronic pain related to burn injury.

Methods: The treatment plan of six opioid-dependent burn patients was analyzed to assess the effectiveness of our detoxification practice to date. Demographic and clinical information was used to characterize the patient population served: age, burn size, injury severity, duration of narcotic use before detoxification intervention, and length of hospitalization stay. Daily narcotic consumption, in morphine equivalent units, was noted both before and after detoxification.

Results: Six burn patients (average age, 31 years) underwent detoxification at the Burn Center during a hospitalization lasting between 1 day and 2 days. Average burn size was 38% total body surface area (range, 17–65); average Injury Severity Score was 30 (range, 25–38). Mean duration of narcotic use was 672 days (range, 239–1,156 days); average use of narcotics at time of detoxification was >200 units daily. Mean outpatient consumption for opioids after the intervention was minimal (<25 units/d). No complications were noted during any procedures.

Conclusions: The results of ultrarapid opioid detoxification under anesthesia suggests that it is safe and effective for treating opioid addiction in military burn casualties when a coordinated, multidisciplinary approach is used. Safety and effectiveness to date validate current practice and supports incorporation into clinical practice guidelines. Further clinical research is warranted to identify those patients who may benefit most from detoxification and to determine the timing of such treatment.

Key Words: Rapid opioid detoxification, Opioid dependence, Rehabilitation, Narcotic, Opioid.

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Combat-related injuries, particularly burn trauma, are often associated with chronic pain. Combat veterans are often treated with opioids for both acute and chronic pain related to their injuries. Opioid dependence and addiction is a very real issue for both patients and their providers in military and civilian trauma populations secondary to prolonged therapies and requisite pain control. Opioid dependence has been classified as a physiologic state that manifests when an opioid medication is abruptly stopped. In contrast, opioid addiction is a disorder that results in continued opioid use despite physical, psychologic, or social dysfunction.[1,2] Patients with physical dependence or addiction often develop tolerance from chronic use of exogenous opioid medications, requiring escalating doses to control pain. Sudden discontinuation of opioids after prolonged use has often resulted in opioid withdrawal syndrome, which may lead to debilitating symptoms for patients, including fever, diaphoresis, anxiety, insomnia, rhinorhea, lacrimation, chills, myalgias, irritability, abdominal cramping, nausea/vomiting/diarrhea, tachycardia, and other adrenergic symptoms.[1,3]

Early treatments using prolonged detoxification techniques for opioid addiction in civilian heroin addicts focused on treatment of withdrawal symptoms, but this cohort suffered high relapse rates.[4,5] More recent rapid and ultrarapid detoxification trials have been viewed as high-risk from sedative and anesthetic complications but low-yield or benefit because relapse rates are often greater than 80%.[6–8] Although the temptation of euphoric effects may have contributed to abuse and relapse in opioid addicts, the intense discomfort experienced during withdrawal is the most likely cause of relapse during and after the more time-consuming detoxifications.[9] Ultrarapid opioid detoxification under anesthesia (URODA) following extended duration of narcotic use for chronic pain is one option available to the provider to assist patients in reversing dependence or addiction to narcotics. According to founder and chairman of the International Institute for De-Addiction Research and Therapy, psychiatrist Dr. Sanjay Chugh, "URODA is a painless way of withdrawal of opiate addicts".[10] URODA has been used successfully to avoid the protracted course of debilitating physical and psychologic withdrawal symptoms by compressing the detoxification process into an abbreviated symptomatic period and precipitating withdrawal while the patient is under general

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anesthesia.[10–12] Experience with military burn casualties has revealed patients had opioid dependence, not addiction, and URODA was used to facilitate discontinuation or decrement in opioid dosing.

Although the efficacy of URODA is debated, careful patient selection may predict successful therapeutic intervention. Although sparse, available civilian studies point to several notable explanations for failure: patient composition, poor access to medical care, suboptimal follow-up, or a return to negative habit-forming environments.[13,14] Military cohorts may demonstrate higher success rates and minimal relapse when compared with civilian programs. Service members have favorable risk-to-benefit ratios due to access to medical specialists, lack of direct financial costs, and close-knit social support networks. Burn trauma causes one of the most severe forms of chronic pain and requires large doses of opioids for relief. URODA in the severely burned military population has not been previously studied and is the focus of this patient review. Although URODA has been studied using various combinations of agonists, antagonists, and pain adjuncts, there are no reports in medical literature of the use of ketamine and naloxone combined with dexmedetomidine, an alpha-2-agonist seven times more alpha-2b-selective than clonidine.

Since 2003, more than 900 military burn casualties have received comprehensive care at the US Army Institute of Surgical Research Burn Center, located at Brooke Army Medical Center. The purpose of this case series was to review the management of burn patients who requested URODA following extended duration of narcotic use for chronic pain related to burn injury. The patient's hospital course was reviewed and their response to the treatment assessed. The rationale and multidisciplinary processes used to implement URODA at a contemporary burn center are described.

METHODS

As part of a multidisciplinary process improvement project, all URODA procedures completed in the 12-month period from March 2008 through February 2009 were examined. Of note, our standard clinical practice uses URODA exclusion criteria of age greater than 65 years, American Society of Anesthesiology (ASA) physical classification III or greater, and patient refusal for behavioral medicine follow-up. Preprocedure baseline narcotic usage was determined by chart review of medical records at the time of initial consultation for and immediately before URODA, with standardized opioid conversion calculator yielding morphine equivalent units (MEUs). This preprocedure usage was compared with the postprocedure baseline narcotic usage by calculating average daily MEUs after URODA as determined by both patient interview and medication review. A paired *t* test was used to compare the average daily consumption of MEUs before and after URODA and the percentage of opioid-dependent days before and after URODA across all six patients. The objective was to review experiences with rapid opioid detoxification in a contemporary military burn center using dexmedetomidine, ketamine, and naloxone in efforts to reduce the daily opioid consumption or narcotic requirement of chronic pain patients undergoing URODA by at least 50%.

Multidisciplinary medical specialists including anesthesiologists, physiatrists, surgeons, physician assistants, social workers, occupational therapists, and the behavioral medicine team assessed potential candidates for URODA. After initial multidisciplinary screening, each patient was referred and independently evaluated for URODA eligibility by the behavioral medicine team, a physiatrist, a senior burn surgeon, and an anesthesiologist. After the clinical decision was made to clear the patient for participation, discussion with the attending burn surgeon ensured that no operative plans were imminent so as to minimize persistent opioid administration after URODA. Each patient would also undergo extensive counseling with behavioral health and psychologic assessments and a thorough discussion of the risks, benefits, and options with regard to the care plan before, during, and after the therapeutic intervention. Written informed consent was obtained from every patient.

On admission for URODA, patients were pretreated with an aspiration prophylaxis regimen and clonidine to reduce some withdrawal symptoms. Standard ASA and awareness monitors were used as part of the general anesthesia induction and mechanical ventilation period in the Intensive Care Unit. Propofol and subanesthetic ketamine infusion were initiated for sedation and analgesia. The alpha-2 agonist dexmedetomidine infusion was also administered to abolish the sympathetic response to opioid antagonism after naloxone administration. All infusions were titrated to maintain general anesthetic depth per a standard protocol using standard ASA monitors and BiSpectral Index (BIS; Aspect Medical, Norwood, MA) awareness monitors.

Escalating naloxone doses were then deliberately administered for reversal of opioid receptor complexes until a sympathetic hemodynamic response was no longer observed. The dosages were personalized for the patient. Doses increased until the patient did not show a significant rise of heart rate or blood pressure. This point marked an assumed surrogate for maximal opioid antagonism resulting from saturation of the mu (μ) receptors with the competitive antagonist—naloxone. A maintenance naloxone infusion (dictated by the maximum dose per patient) was then continued for approximately 24 hours to effect complete reversal of agonist ligands to the μ opioid receptors.

Maintenance dexmedetomidine, ketamine, and propofol infusions were continued after intubation to attenuate the cardiostimulatory effects during naloxone administration and to provide sedation during mechanical ventilation. Although only peripheral intravenous (IV) tubes were placed for venous access, orogastric/nasogastric tubes and urinary catheters were placed to monitor fluids and allow for decompression and enteral medication if needed. After URODA, propofol, ketamine, and naloxone infusions were discontinued. Dexmedetomidine infusion was continued for endotracheal tube tolerance and light sedation, but it was weaned off after extubation. Once all infusions had been discontinued, the patient remained monitored in the ICU until clinically cleared for transfer to an intermediate care unit or step-down ward within 12 to 24

TABLE 1. Patient Characteristics Before URODA

Patient	Age (yr)	Total Body Surface Area (%)	Injury Severity Score	No. of Days After Injury	No. of Opioid Days	Pre-URODA Opioid Use (MEU)	Post-URODA Opioid Use (MEU)
1	30	34	25	568	568	275	0.1
2	38	65	38	1156	1156	260	20
3	36	34	25	675	675	315	75
4	28	48	38	742	742	240	25
5	28	17	29	239	239	120	0.1
6	27	31	25	657	657	100	10
Average	31.2	38.2	30.0	672.8	672.8	218.3	21.7

Note that average opioid consumption was in excess of 218 MEUs per day before URODA.

hours. Diet was judiciously advanced and the in-dwelling tubes (gastric tube and urinary catheter) were removed. Sleep hygiene protocols were routinely used in an effort to maximize return of the normal sleep-wake cycles which are often extremely fragmented in patients with a chronic pain history and opioid addiction.

Before hospital discharge, both nonopioid adjunct treatments and follow-up plans were established. Extensive coordination and communication between the healthcare team, the family, and the patient was emphasized. Patients were followed up per the standard clinical routine for outpatients in the burn clinic, which is prolonged surveillance and treatment as needed. In addition, they were also interviewed telephonically by the anesthesiologists as part of the postprocedure assessment at approximately 1 month and 6 months after the URODA procedure.

RESULTS

Six burn patients underwent URODA in the 12-month period from March 2008 through February 2009 at the Army Burn Center at Brooke Army Medical Center. As shown in Table 1, all patients were male with an average age of 31 years. Mean burn size was 38% total burn surface area (TBSA; range, 17–65%), distribution ranged from mostly isolated extremities to involvement of the majority of the body. The average Injury Severity Score (ISS) was 30 (range, 25–38), signifying major trauma, usually defined as ISS >16.[15]

Each patient in this small cohort was classified as a 2 on the American Society of Anesthesiologist physical status classification system (ASA 2) indicating patients have a mild to moderate systemic disease, but have minimal risk during treatment. Each patient carried a formal diagnosis of both chronic pain and opioid dependence. Individual chart reviews for each patient supported the development of opioid dependence secondary to chronic opioid prescription as part of the multimodal pain management therapy. The mean duration of narcotic use was 672 days (range, 239-1156 days) or 1.9 years. The mean daily consumption of opioid medications at the time of URODA was 218.3 MEUs per day (range, 100–315 MEUs). The mean daily consumption for opioid medications after intervention was minimal, 15.9 MEUs per day (range, 0–55 MEUs; Table 1 and Fig. 1; $p = 0.0006$). In addition, the number of opioid-dependent days also decreased significantly for all six patients from an average of 100 to 9.2% (Fig. 2; $p < 0.0001$).

Patients were hospitalized 1 day to 2 days in the ICU during the acute phase of this therapeutic intervention. They were then transferred to the intermediate care unit within the burn center, where they stayed until discharge to home. The post-ICU stay averaged 3 days. No complications were noted during any of the URODA procedures, although one patient was prophylactically readmitted within 1 week of discharge to rule out pneumonia.

DISCUSSION

The physiologic and psychologic impact of chronic opioid therapy for severely burned service members should not be underestimated. Chronic pain management for these patients may pose a challenge for even the most experienced clinician. A constant struggle exists between creation of opioid treatment plans and the development of opioid tolerance from chronic therapy. Solutions to minimize opioids in burn patients can be problematic when combining multiple surgeries with unpredictable postoperative pain courses, long-term rehabilitation programs, baseline pain unresponsive to nonopioid pain medication adjuncts, and suboptimal pain control. Efforts to walk the tight-rope of effective pain management in opioid-tolerant patients often leave them either in pain because they are undermedicated or at risk for cardiorespiratory compromise because they are overmedicated and sedated.

Although the goal for traditional opioid detoxification is to eliminate opioid use and prevent relapse, most patients treated in early studies did not suffer from chronic pain syndromes.[4,6] In burn patients with chronic pain syndromes, total elimination of opioid use may not be the immediate goal, in contrast to other patient populations that have been studied with rapid detoxification. The goal is to achieve adequate pain control while minimizing opioid dependence and preventing addiction. URODA treatment for burn patients with chronic pain syndrome should be considered a success with reduction of opioid usage by greater than 50%.

Although this small series of military burn patients had a much greater reduction in their opioid usage as calculated by daily MEUs, decreasing the opioid burden by as much as half would certainly make a profound difference in the

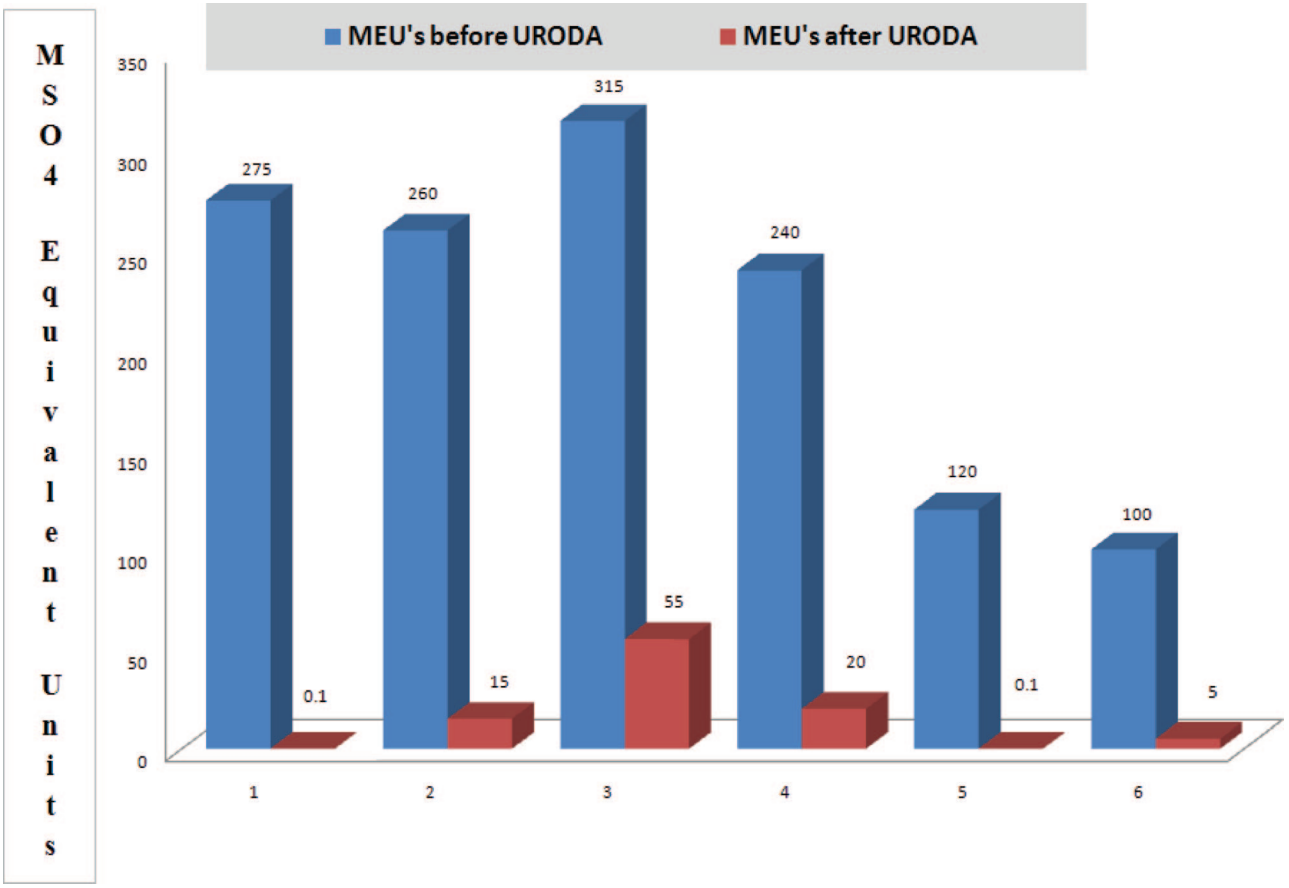

Figure 1. Daily opioid consumption per patient as expressed in MEUs both before and after URODA. The graph demonstrates statistically significant reduction in daily opioid consumption after URODA. *$p = 0.0006$.

well-being of most chronic pain populations. The findings reported here illustrate the utility of URODA when using a multidisciplinary approach and well-advised patient selection to achieve a decrease in opioid dependence and minimize opioid addiction as part of the comprehensive care for severely wounded military burn patients. The objective impact of URODA on narcotic use in this military cohort was very significant. The postprocedure opioid consumption was less than 1/14 the preprocedure consumption in MEUs. When opioid-dependent days were evaluated as a percentage of total days compared before URODA (since initial injury) and after URODA, there was a marked decrease as well. There was a 90% reduction in opioid-dependent days after rapid detoxification.

There still remains significant debate over the safety and efficacy of URODA when compared with traditional, more conservative opioid detoxification techniques that extend over weeks to months.[14,16,17] Many insurance companies label rapid detoxification as experimental based on mixed results in the medical literature and the evident risks of sedation and general anesthesia.[18] Although one patient from the URODA group was readmitted to rule out pneumonia, it was not felt to be a complication associated with the detoxification procedure itself. Microbiological speciation revealed bacterial pathogens consistent with community-acquired pneumonia, and the patient endorsed exposure to sick contacts within his community. Neither the clinical course nor the bacterial isolate from sputum was suspicious for an aspiration event and the patient was discharged home on oral antibiotics within 48 hours of admission.

Based on this initial experience with anesthesia-assisted rapid detoxification in this population, albeit a small sample reviewed here for a limited duration, there is a suggestion that an effective institutional URODA program can be safely implemented to improve patient outcomes and quality of life while minimizing many of the negative consequences of chronic opioid prescription. Future studies may validate decreases in sedation, constipation, and appetite and the improvements in patient satisfaction, alertness, mood, social/familial interactions, and healthcare spending. Most importantly, further interrogation of the clinical utility of URODA will allow for refinement of the technique and optimization of patient selection.

Successful opioid detoxification requires highly motivated patients, accessibility to treatment facilities and medical professionals, and funding revenues for treatment costs.[17,19] Although the acute detoxification phase is led by the anesthesiologist, the family and the multidisciplinary team becomes the pivotal extensions into the follow-up phase. Continued patient education and awareness of their

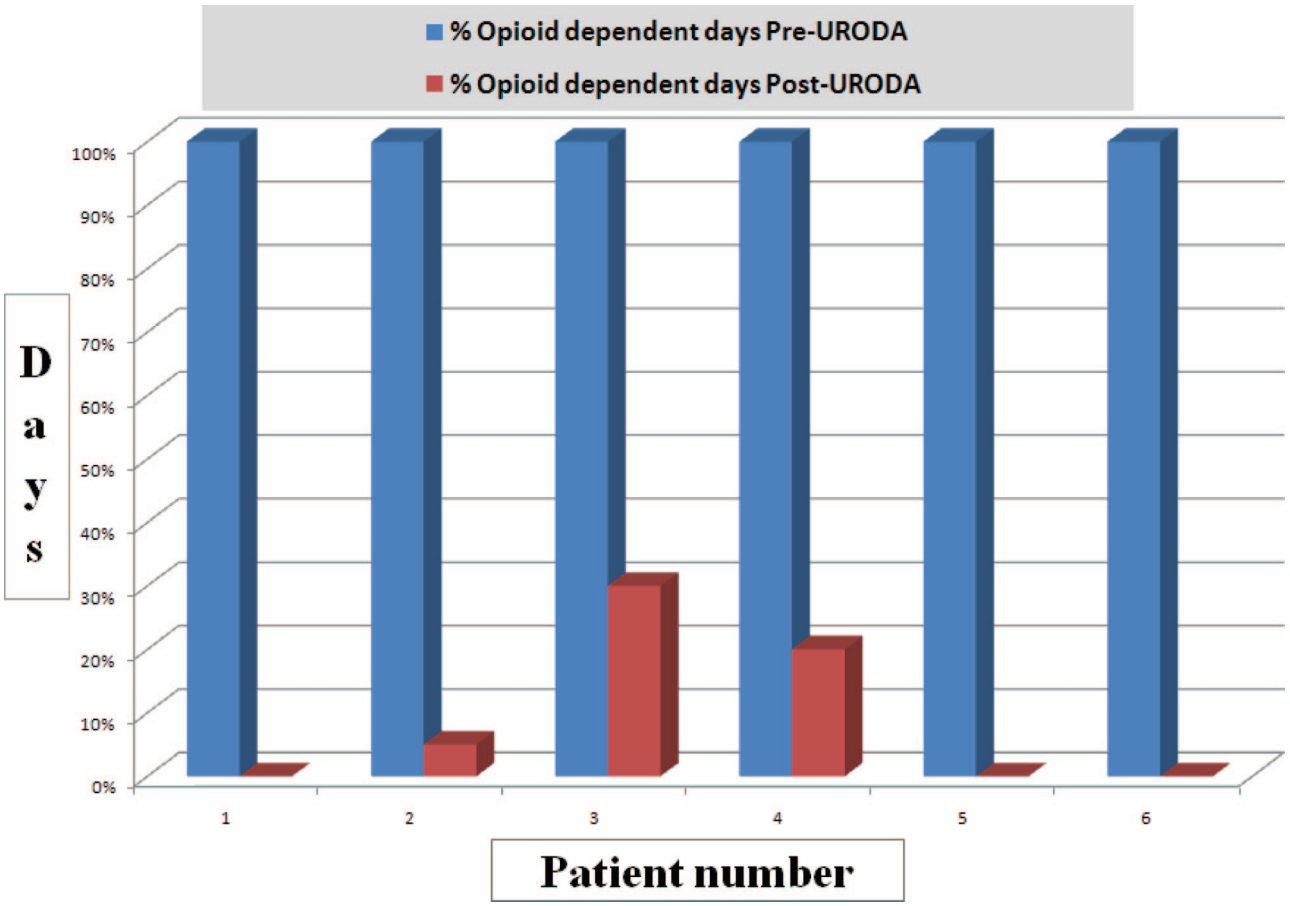

Figure 2. Percentage of opioid-dependent days per patient both before and after URODA. The graph demonstrates statistically significant reduction in opioid-dependent days after URODA. *$p < 0.0001$.

newfound opioid naiveté (a functional opioid sensitivity) by all care providers, including all ward/clinic nurses, pharmacists, and family, must be prioritized to minimize the significant risk of catastrophic narcotic overdose should prior opioid tolerance be assumed.[19] The existence of a Sole-Provider Program, with patients having a single, dedicated prescribing authority for pain medications, and the closed unit status of our Burn Center with frequent patient follow-ups created an environment of care ideally suited for implementation of the URODA intervention. Along with judicious patient selection, this support infrastructure is crucial for successful detoxification and relapse prevention.

URODA procedures performed at specialized facilities are expensive and resource-intensive[16]; however, they provide evaluation, detoxification, and extensive follow-up to ensure success. Military service members have access to world-class medical facilities, are motivated and cooperative patients, have excellent family/social support networks, and are entitled to no-cost healthcare in a Military Treatment facility. Military Treatment facility has the ability to schedule, admit, monitor, and follow-up with these patients. This capability allows the provider team and the patient to remain very engaged and involved in the care plan. Military healthcare beneficiaries on active duty may prove to be an ideal patient population for successful URODA based on extensive and readily available support systems and resources.

Successful detoxification of military burn patients may demonstrate the utility of URODA as outweighing the potential risks in this unique patient population. Results obtained from opioid detoxification reviews such as this one could be used as proof of feasibility for future prospective randomized studies using ketamine and dexmedetomidine during URODA. In addition, success in the military population may shine a beacon of hope toward the civilian sector plagued by opioid addiction. By demonstrating a practical model for successful therapeutic intervention to manage opioid dependence and addiction, studies could further the arguments calling for civilian insurance coverage of URODA procedures when clinically indicated for patients to significantly improve their overall health and well-being.

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