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ORIGINAL RESEARCH

The Effect of Intravenous Ketamine in Suicidal Ideation of Emergency Department Patients

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Abstract

Introduction: Suicidal ideation is an emergent problem in the Emergency Department (ED) that often complicates patient disposition and discharge. It has been shown that ketamine possesses fast acting antidepressant and anti-suicidal effects. This study was conducted to examine the effects of a single intravenous bolus of ketamine on patients with suicidal ideations in ED. **Methods:** Forty-nine subjects with suicidal ideations with or without an unsuccessful suicide attempt, received 0.2 mg/kg of ketamine. Scale for suicidal ideation (SSI) and Montgomery-Abserg depression-rating scale (MADRS) were evaluated before and 40, 80 and 120 minutes after drug intervention. The results were compared using the paired t-test and patients were followed up 10 days after ED admission for remnant suicide ideation. **Results:** SSI (df: 3, 46; F=80.7; p<0.001) and MADRS (df: 3, 46; F=87.2; p<0.001) scores significantly dropped after ketamine injection; the SSI score before and after 20, 40, and 80 minutes of ketamine injection were 23.0±6.7, 16.2±5.2, 14.3±4.3, and 13.6±4.0 respectively. The MADRS scores were 38.2±9.3, 25.6±7.1, 22.7±6.3, and 22.1±5.95 at the same time intervals. 25.5% of patients were hospitalized, 63.3% received medications and 12.2% discharged. 6.2% of patients had suicidal ideations ten days after ED disposition. **Conclusion:** It seems that Ketamine could not be a good choice for fast reduction of suicidal ideations in ED patients. Further studies are needed to determine the optimal dose of ketamine for different patients.

Key words: Ketamine; suicide; suicidal ideation; emergency

Cite this article as: Kashani P, Yousefian S, Amini A, Heidari K, Younesian S, Hatamabadi HR. The effect of intravenous ketamine in suicidal ideation of emergency department patients. Emergency. 2014;2(1):36-9.

Introduction:

Suicidal ideation is an emergent condition that demands immediate attention. It has been shown that the time between decision and attempt in patients with suicidal ideations is about ten minutes (1). Various therapeutic interventions to decrease suicide risk have been proposed in serious psychiatric disorders for long-term suicide prevention (2, 3). While the recognition of risk factors is very important for preventing suicide, they fail to clarify the timing of a suspected suicidal behavior. It has been shown that subjects with mood disorders are at greater risk of suicide in the first two years after discharge (4).

On the other hand it is known that during admission in emergency department (ED), immediately after discharge from ED, and after starting antidepressants are the time points which the subjects are very vulnerable to suicidal ideations (5-9). Therefore, it is crucial to quickly intervene and prevent suicidal behavior in such conditions. It has also been shown that 43% of suicides occur in the first month after discharge (5). This often complicates the disposition discharge of patient in the ED. A patient with significant suicide ideation cannot be safely discharged or admitted to general wards, regardless of the underlying medical condition.

Different interventions for decreasing the possibility of suicidal risks are effective in long term. For example, lithium, clozapine, and risperidone are used for such a condition in EDs (10-12). However, the acute pharmacological management of suicidal risk remains comparatively under investigation (13). Considering the crowdedness of the majority of EDs, it is often impossible to offer standard care to patients with suicidal ideation. In such settings, use of pharmaceutical interventions can play an important role with a rapid effect on diminishing suicidal ideation.

Numerous studies have shown the effect of single dose of intravenous (IV) ketamine on reducing depressive symptoms in approximately 70% of major depressive disorder (MDD) patients in 24 hours after infusion (14-18). The effects of Ketamine on reducing suicidal ideation in severely depressed patients have been supported by preliminary studies (19). Furthermore, a recent naturalistic study proved that a low-dose ketamine is

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Received: 29 January 2014; Accepted: 17 February 2014

effective on reducing the suicide ideation in patients refer to the ED (20) and those who have terminal illness(21).

Considering to other studies, Ketamine is a favorable choice for emergency physicians because of many reasons; its rapid effect as an anti-suicidal ideation causes that the patient can be discharged from the ED with early outpatient follow up. This is especially applicable in situations when an on call psychiatrist is not available. Therefore, this study was performed to reaffirm the ketamine effect on patients with suicidal ideation in the ED.

Methods:

Study design and setting

This single-blind clinical trial was done in Emergency Department of Imam Hossein hospital from October to September 2012. Participation in the study was voluntary and the consent form was obtained from their companions. Patients' files were completed by the emergency physician and the information was kept strictly confidential. This research was confirmed by ethical committee of Imam Hossein hospital.

Participants

The patients (age over 16 years) were included in the study based on subjective expression of suicidal ideations or recent suicidal actions at the time of admission to the department. Subjects were excluded if a diagnosis of alcohol or substance and drug abuse was made in the past three month or if they had received any medication for two weeks before ED admission.

Intervention

A single dose of ketamine hydrochloride infusion (0.2 mg/kg, over one minute) was administered to the selected subjects. This is the lowest dose of ketamine which has been described as effective in diminishing suicide ideation in previous studies (20, 21). Patients' suicidal ideations were assessed by using Montgomery-Asberg Depression Rating Scale (MADRS) and Scale for Suicidal Ideation (SSI). MADRS and SSI scales were completed for all of the patients in different times as follow: before injection and 40, 80, 120 minutes after infusion. The patients' treatment followed standard ED protocols regardless of the study results; the outcome was followed up ten days after admission by a telephone contact.

Statistical analysis

Descriptive analyses were performed by statistical software SPSS version 21.0 and graphs drawn by Excel 2013. The SSI≥4 was considered as significant suicidal ideations and SSI<4 without significant suicidal ideations. SSIs were compared before and after ketamine injection by paired t-test and repeated measures analysis of variance. The $p<0.05$ was considered statistically significant.

Results:

Forty-nine patients were included in this study. Fifty one percent of patients were female (n=25) and 49% were male (n=24). The mean age of patients was 32±10.8 years. Thirty-eight percent of patients (n=19) had a history of mental illness (bipolar and major depression), 30% (n=15) previous suicidal ideations, 12 % (n=6) psychiatric hospitalization, and 34% (n=17) self-injury.

Table 1 shows the mean and SD of patients' vital signs before and after injection of ketamine. Significant decrease was observed in the values of PR (89.8±8.8 vs. 87.8±7.5; $p<0.001$) and RR (18.5±5.0 vs. 17.4.0±2.0 respectively, $p=0.04$) ten minutes after ketamine injection. No significant difference was seen in the levels of BP (14.9±2.01 vs. 12.6±1.9; $p=0.32$) and O2SAT before and after ketamine injection (96.4±1.1 vs. 95.1±1.5; $p=0.35$).

Mean and standard deviation of SSI scores before injection and at 40, 80 and 120 min after ketamine injection were respectively, 23.0±6.7, 16.2±5.2, 14.3±4.3 and 13.6±4.0. The repeated measures analysis showed that the SSI scores decreased over time significantly.

The most significant reduction was seen in the first 40 minutes after injection ($p<0.001$) but, the score maintained a decreasing trend until 120 minutes (df: 3, 46; $F=80.7$; $p<0.001$). Mean and standard deviation of MADRS rating scales as well indicated a significant reduction in SSI scores at the times after injection (df: 3, 46; $F=87.2$; $p<0.001$). MADRS rating scales before injection of ketamine was 38.2±9.3 and at the time of 40, 80 and 120 minutes after injection were respectively 25.6±7.1, 22.7±6.3 and 22.1±5.95. Once again the highest rate of reduction was at 40 min after the injection ($p<0.001$).

25.5% of patients (n=12) were hospitalized, 63.3% (n=31) received medication, and 12.2% (n=6) discharged. Follow-up 10 days after admission in ED showed that 85.7% of patients (n=44) did not have any suicidal thoughts, 8.2% (n=4) had hospitalized and

Table 1: Vital signs measures before and after ketamine infusion ⇧

Vital signs	Time of injection		p
	Before	After 10 minute	
Pulse rate	89.8±8.8	87.8±7.5	<0.001
Respiratory rate	18.5±5.0	17.4±2.0	0.04
Blood pressure (Systolic/Diastolic)	12.6/8.1	12.6/8.2	0.32
O2 saturation	96.4±1.1	95.1±1.5	0.35

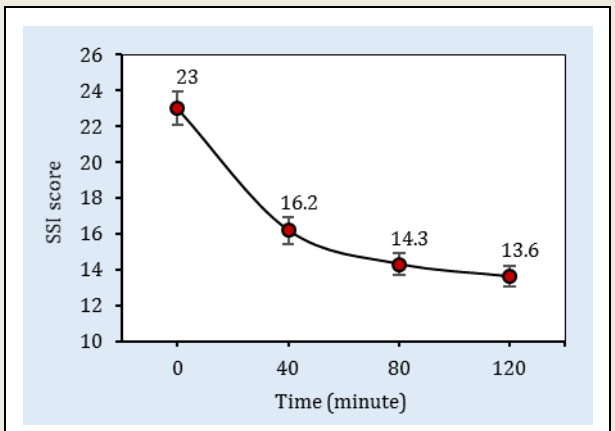

Figure 1: Scale for Suicidal Ideation (SSI) scores before and after ketamine infusion. ⇧

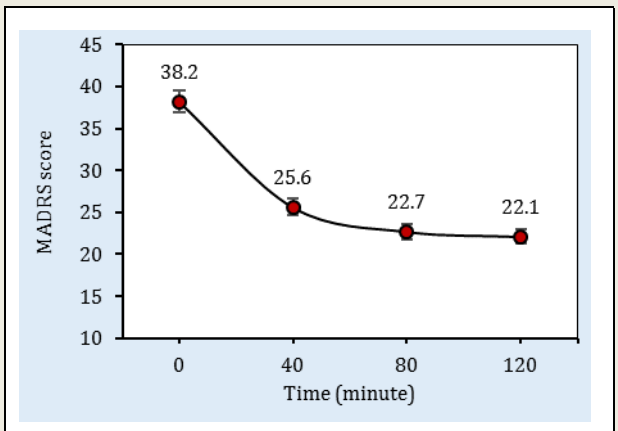

Figure 2: Montgomery-Abserg Depression Rating Scale (MARDS) scores before and after ketamine infusion. ⇧

6.1% (n=3) still had suicidal thoughts.

Discussion:

Suicide is one of the leading causes of death among young people especially those who have psychiatric disorders. In the past decade, many efforts have been done to prevent suicide attempts that the most important one was evaluating the risk factors of suicide and ways to prevent this problem (22). Suicidal ideation is a medical emergency that requires immediate attention and treatment. Unfortunately, therapeutics used now for the rapid decrease in suicidal thoughts is often followed up with unpleasant consequences (23).

In this study, the effect of ketamine was evaluated on 49 patients admitted in ED with suicidal ideations and actions. Although suicidal ideation did not remove after ketamine injection, evaluation at 40, 80 and 120 min after infusion showed a significant reduction in SSI and MADRS scores (Figure 1 and 2). Previous studies have assessed the effect of ketamine infusion in patients with treatment-resistant depressive disorder and demonstrated rapid beneficial effects on suicidal ideation (18, 19). The results like previous studies show that ketamine is effective in reducing suicidal ideations. Yet in our study, the SSI score 40 minutes after the injection of ketamine dropped from 23±6 to 16±5, which although is significant, still above the previously set limit of 4. This might be due to the lower dose of ketamine used in our study compared to prior ones (0.5mg/kg) (19). It means that injection of 0.2mg/kg to patients was unable to eliminate suicidal ideation.

A significant reduction was observed in the amount of RR and PR but all of the indices remained in normal limits and no danger threatened patients after injection of ketamine. The follow up of patients after ten days showed that some of them had still suicidal ideations (6.1%). This may reflect a shorter time of action for ketamine at the low dose of ketamine infusion (0.2 mg/kg) used in this study. Therefore, if such a dose were used, adjunct treatments or repeated dose maybe also needed.

It is clear that the results of current studies should be interpreted with more caution due to the small size of the population. The findings of this study showed that ketamine, as a modulating of glutaminergic system, could not be a good candidate for the quick treatment of suicidal ideations in the ED.

However, further studies should be done to confirm the findings of this and previous studies; so that the optimal dose of ketamine for different patients and its lasting impact could be determined.

Limitations

The main limitation of present study is the small sample size. Another limitation of this study is the lack of a control group. However, because ketamine does not have any effect on suicidal ideations, this limitation did not affect the findings.

Conclusion:

It seems that Ketamine could not be a good choice for fast decrease of suicidal ideations in ED patients. Further studies are needed to determine the optimal dose of ketamine for different patients.

Acknowledgments:

We would like to thanks from emergency ward staffs of Shohadaye Hafte Tir Hospital.

Conflict of interest:

None

Funding support:

None

Authors' contributions:

Parvin Kashani and Hamid Reza Hatamabadi designed the study. Shiva Yousefian and Somaie Younesian participated in data gathering. Kamran heidari analized the

data. Afshin Amini followed the patients and wrote the first draft of article. All authors approved the final version of manuscript.

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