The Role of Ketamine Anaesthesia in Developed and Developing Countries: Assessing the Likely Impact of Changing the International Control of Ketamine to A Schedule I Drug

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Abstract

Introduction
The provision of safe anaesthesia is a worldwide aspiration but the drugs used in anaesthesia have the potential for abuse. Ketamine, a dissociative anaesthetic agent, is one such drug. In March 2015, the United Nations received proposals to make ketamine a schedule I drug internationally, which would limit its availability for anaesthesia.

Aim
To assess the likely impact of changes to the international scheduling of ketamine on the practice of anaesthesia in a developing country, Zambia and a developed country, Ireland.

Methods
A cross-sectional, questionnaire based survey of anaesthesia providers (APs) in Ireland and Zambia was performed. Inclusion criteria were any healthcare professional providing anaesthesia to patients who was willing to take part in the study. Data analysis techniques were carried out using IBM SPSS software and Microsoft Excel.

Results
Responses from 100 anaesthesia providers were included in this study, 50 from Zambian hospitals and 50 from Irish hospitals. 98% of Zambian APs use ketamine anaesthesia regularly versus 18% of the Irish APs. 86% of Zambian and 36% of Irish APs believe there would be a negative impact on their patients if ketamine was unavailable. 87% of the total participants believe ketamine should be readily available for medical use.

Conclusion
This study demonstrates the differences in the way ketamine is used in anaesthesia practice in a developing country, Zambia and a developed country, Ireland. These data suggests that the restrictions imposed by scheduling may have serious consequences for anaesthesia in many developing countries of the world.
that there are significant differences between Ireland and Zambia in both the need and use of ketamine for anaesthesia and suggests that restricting ketamine's availability worldwide would have a more serious effect in a developing country like Zambia which relies on ketamine for much of its anaesthetic needs. The wide availability of ketamine for medicinal purposes will continue to be under threat because increased illicit use of the drug will prompt ongoing debate regarding a change to its international schedule. Further research and information on the use of ketamine anaesthesia worldwide is necessary before an ethical and fair decision on its restriction can be made.

Introduction

The dissociative agent ketamine has established itself as having a major role in anaesthesia since it was first synthesised in 1962 [1]. In more recent years, ketamine has become a significant drug of abuse, with most reported ketamine abuse occurring in developed countries in Europe and China [2]. Concern regarding ketamine abuse has resulted in China, a major producer of ketamine, to make repeated proposals to the United Nations Commission on Narcotic Drugs (UN-CND) recommending that ketamine be classified as a schedule I drug internationally [3]. Placing a drug under schedule I would oblige countries worldwide, by law, to fully license ketamine dispensation and track its production, importation and exportation. Under article 7 of the UN convention on psychotropic substances, 1971; Schedule I "prohibits all use of a substance except for scientific and very limited medical purposes by duly authorized persons, in medical or scientific establishments which are directly under the control of their Governments” [4]. While these proposals may seem like a positive move for international drug control, they would also see significant restrictions placed on the availability of ketamine and raise issues for anaesthesia providers (APs), especially those practicing in resource poor or remote settings. Scheduling ketamine as a class I drug would not only require government authorization but require all participants to keep detailed records, require a system of limiting quantities and require a medical prescription for the supply and dispensation of the drug [4]. This increased bureaucracy in authorizing and supplying ketamine in developing countries, as well as the need to have a medical doctor prescribe ketamine, would likely significantly impact on the daily, routine use of ketamine for anaesthesia. Most anaesthesia in developing countries is delivered in rural remote areas by non-physicians and therefore such requirements are currently impractical.

Table 1. Control Status of the substances under the international control of the UN-CND. Sourced from the UNODC publications: Multilingual Dictionary of Narcotic Drugs and Psychotropic Substances under International Control 2006.

<table>
<thead>
<tr>
<th>Schedule</th>
<th>Harmfulness</th>
<th>Degree of control</th>
<th>Examples of listed drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Substances presenting a high risk of abuse, posing a particularly serious threat to public health, which are of very little or no therapeutic value</td>
<td>Very strict; use is prohibited except for scientific or limited medical purposes</td>
<td>Cocaine/coca leaf, MDMA (ecstasy), morphine, oxycodone</td>
</tr>
<tr>
<td>II</td>
<td>Substances presenting a risk of abuse, posing a serious threat to public health, which are of low or moderate therapeutic value</td>
<td>Less strict</td>
<td>Codeine, methamphetamine</td>
</tr>
<tr>
<td>III</td>
<td>Substances presenting a risk of abuse, posing a serious threat to public health, which are of moderate or high therapeutic value</td>
<td>These substances are available for medical purposes</td>
<td>Codeine preparations, cocaine preparations, morphine preparations</td>
</tr>
<tr>
<td>IV</td>
<td>Substances presenting a risk of abuse, posing a minor threat to public health, with a high therapeutic value</td>
<td>These substances are available for medical purposes</td>
<td>Alprazolam, diazepam, midazolam, zolpidem</td>
</tr>
</tbody>
</table>
The World Health Organisation’s Expert Committee on Drug Dependence (WHO-ECDD) has currently concluded that ketamine does not pose a significant enough public health risk to warrant changes to scheduling but this may change in the future [1]. The scheduling procedures of the UN-CND are set out by the 1971 Convention on Psychotropic Substances [5]. These procedures state that the UN-CND must act in accordance with the recommendations of the WHO-ECDD [4]. Concerns surrounding any changes to the international scheduling of ketamine require further investigation into the likely impact of such actions on the provision of anaesthesia in a worldwide setting and not just those that pertain to developed countries such as China. There currently exist vast differences in the way ketamine anaesthesia is used in developed countries and the way it is used in developing countries. Despite an excellent safety record, in the resource-rich developed world, ketamine has fallen out of favour due to its significant and unpleasant side effect profile and due to its potential for abuse. In developed countries ketamine’s use is confined mainly to analgesia and to emergency anaesthesia. In contrast, in many parts of the developing world, ketamine remains a key anaesthetic agent, its properties allowing it to be used when it may be impossible to use other agents [6]. Ketamine is included in the World Health Organization (WHO) list of essential medicines, one of two injectable anaesthetic agents on this list, alongside protocol [7]. There is currently a lack of up-to-date data on the use of ketamine and the how proposed restrictions on its use would be perceived by medical practitioners in both developed and developing countries. The aims of this study are to highlight any differences in the way ketamine anaesthesia is used in developed and developing countries and assess the likely implications of proposed restrictions on ketamine availability worldwide. We therefore conducted this study, comparing the use of ketamine anaesthesia in Ireland, a developed country in Europe, and Zambia, a developing country in Africa.

Methods

This study was approved by the Cork Clinical Research Ethics Committee (CREC) in March 2016.

The study was a cross-sectional, questionnaire-based survey of APs from a developed country and from a developing country. The criteria for inclusion in this study were any health-care worker providing anaesthesia to patients who consented to taking part.

Ireland was selected as an example of a developed country based on convenience and proximity to the project setting. Ireland has a population of almost 4.6 million people and has a current workforce density of anaesthetists of 8.8 per 100,000 of the population. We contacted a number of developing countries in Africa through medical societies and foreign embassies and invited them to take part in the study. Following contact with the Irish embassy in Lusaka, Zambia, the national anaesthesia coordinator for the Zambian Ministry of Health, Mr. Wisdom Chefu, expressed an interest in the project and offered to facilitate data collection in Zambia. Zambia has a population of almost 14 million people, with a workforce density of physician anaesthetists of 0.2 per 100,000 of the population.

The Human Development Index (HDI), an index used by the United Nations to measure the progress of a country, was used to define Ireland as a developed country and Zambia as a developing country. In 2014, Ireland’s HDI rating was 0.916, giving it 11th place in a table of 187 countries published. Zambia’s 2014 HDI rating was 0.586 giving it 141st place of 187 countries published, defining them as a developed and developing country respectively. For context, in 2014 the United States of America and the United Kingdom placed 5th and 14th respectively in the HDI rankings.

A questionnaire was designed as the data collection tool for this study, with reference to two other data collection tools, the validated [8]. World Health Organisation tool for situational analysis to assess emergency and essential surgical care and the Surgeons Over Seas PIPES tool (Personnel, Infrastructure, Procedures, Equipment, Supplies). A copy of the questionnaire is included as appendix 1. The questionnaires were distributed in five hospitals in 2 of 4 provinces in Ireland and in 29 hospitals in six of Zambia’s ten provinces. Participant demographic information such as country of practice, level of medical training and hospital characteristics and information pertaining to the participants use and opinion of ketamine anaesthesia was collected. The data collected was anonymous and analysed using Microsoft Excel 2016 and IBM SPSS statistics v22 using a qualitative approach.

Results

We included responses from 100 anaesthesia providers in our study, 50 responses from Ireland and 50 from Zambia. Participant demographic information can be found in Table 1. A total of 5 hospitals in Ireland took part (2 tertiary centres and 3 secondary centres) and 29 hospitals in Zambia, (5 tertiary healthcare, 9 secondary centres and 15 primary healthcare centres).

100% of the Irish participants were physician anaesthetists, compared to 18% of Zambian participants. The remaining 82% of Zambian participants were non-physician clinical officer (CO) anaesthetists who have qualified with a four-year higher diploma in healthcare.

In Zambia, 98% of APs reported using ketamine anaesthesia regularly in their practice compared to 18% in Ireland. 98% of Zambian APs and 34% of Irish APs had used ketamine as a single anaesthetic agent in the past (Figures 1 & 2).

Overall, 89% of all participants had a positive opinion of ketamine anaesthesia, 8% had a negative opinion and 3% did not respond. In the Irish group, 84% had a positive opinion, 12% had a negative opinion and 4% did not respond. In the Zambian group, 94% had a positive opinion, 4% had a negative opinion and 2% did not respond.
Participants were asked hypothetically; if ketamine was unavailable, whether there would be a negative impact on their practice of anaesthesia. In Zambia and Ireland, 88% and 58% of participants, respectively, believed their work would be negatively impacted if ketamine was unavailable to them. In the same hypothetical situation, participants were asked whether there would be a negative impact for patients under their care, 86% of Zambian and 36% of Irish participants believed there would.

When asked their opinion on the availability of ketamine, 87% of the total participants believe ketamine should be readily available for medical use, 92% of the Zambian group and 82% of the Irish group.

Table 2. Participant demographics. N (%)(Senior House Officer - 2+/3-Year Resident, Registrar – at least 3 years of anaesthesia training completed)

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Ireland</th>
<th>Zambia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Country</td>
<td>N=100</td>
<td>N=100</td>
</tr>
<tr>
<td>Level of Training</td>
<td>50 (50%)</td>
<td>50 (50%)</td>
</tr>
<tr>
<td>Consultant</td>
<td>41 (41%)</td>
<td>30 (30%)</td>
</tr>
<tr>
<td>Registrar</td>
<td>25 (25%)</td>
<td>4 (25%)</td>
</tr>
<tr>
<td>Senior House Officer</td>
<td>4 (4%)</td>
<td>4 (4%)</td>
</tr>
<tr>
<td>Consultant</td>
<td>28 (56%)</td>
<td>18 (36%)</td>
</tr>
<tr>
<td>Registrar</td>
<td>18 (36%)</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>Senior House Officer</td>
<td>4 (8%)</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>Clinical Officer</td>
<td>41 (82%)</td>
<td>41 (82%)</td>
</tr>
<tr>
<td>Registrar</td>
<td>7 (14%)</td>
<td>7 (14%)</td>
</tr>
<tr>
<td>Consultant</td>
<td>2 (4%)</td>
<td>2 (4%)</td>
</tr>
</tbody>
</table>

**Conclusion**

Our data has demonstrated that there are significant differences between Ireland and Zambia in both the need and use of ketamine for anaesthesia. In Ireland, concerns regarding ketamine availability focus more on its analgesic properties than anaesthetic usefulness. In our study it is notable that all anaesthesia was provided by physicians in Ireland compared with only 18% in Zambia. Over half of the anaesthesia in Zambia was delivered in primary healthcare centres, a practice that does not occur in Ireland.

In developing countries there are many barriers to the safe provision of anaesthesia such as a lack of infrastructure and funding for healthcare and a low workforce density of anaesthetists. Medical research conducted in resource poor countries in Africa like Somalia and Gambia report deficiencies in basic infrastructure for healthcare, shortages in oxygen supply, electricity and running water [9,10]. Low workforce densities of physician anaesthetists are also found in Malawi, Gambia, Somalia and Cameroon and many of these areas rely on informally trained anaesthesia providers and nurse anaesthetists [9-12]. The ease of administration of ketamine and its safety profile make it indispensable in these circumstances, when other anaesthetic agents may be impossible to use due to lack of basic infrastructure or equipment.

Changing the international control of ketamine to a schedule I drug under the United Nations-CND would almost certainly restrict its availability for anaesthesia. Morphine is an example of a drug controlled internationally under schedule I of the UN-CND. As a result of these restrictions placed on its availability, in many countries, cancer patients and patients suffering from other painful conditions are not receiving morphine [13]. There currently exists a large imbalance in the distribution of morphine worldwide. In 2002, the WHO estimated that 78% of the worldwide morphine use went to just six countries, which are all developed countries, including the UK, Canada and the USA, while just 6% went to other countries in the world [1].

Our study suggests that a similar and more serious situation of restricted availability of anaesthesia could arise in a country like Zambia, which depends on ketamine for much of its anaesthetic needs.

The decision to schedule ketamine can only be taken with consideration of the impact worldwide and not taken to suit the interests of the developed world as may often be the case with international policies. The recent phenomenon of ketamine abuse is an issue that is mainly confined to the developed world and there are few reports from developing countries. Scheduling ketamine may reduce the incidence of ketamine abuse in the developed world but in the developing world may serve to remove a safe and relied upon anaesthetic agent from clinical use.

There is a relative lack of data regarding the use of ketamine anaesthesia worldwide. However, a large study assessing anaesthetic capacity in 590 facilities in 22 low- and middle-income countries showed that the availability of ketamine anaesthesia (71.5%) exceeded the availability of running water (62.4%), electricity (59%) and supplemental oxygen (45.2%) [14]. The proposed restriction of ketamine availability could have a negative impact in many developing countries across the world that find themselves relying on ketamine to meet anaesthetic needs. The safe provision of anaesthesia is a worldwide aspiration and it is a basic human right to enjoy the highest attainable standard of health [15]. Changing the international scheduling of ketamine could prevent many of the world’s poor from accessing a relatively safe and heavily relied upon form of anaesthesia.
There are a number of limitations of our study. We could only recruit 50 participants in Zambia and hence only a similar number were recruited in Ireland. Recruiting participants from developing countries proved difficult, even, in this case with the help of the Zambian Ministry of Health. This study also only included participants from one developing and one developed country. Studies investigating the use of ketamine and the assessment of the likely impact of restrictions on its use would be useful coming from multiple countries in the respective categories to get a more representative picture.

The continued wide availability of ketamine for anaesthesia will depend on whether increased illicit use will prompt ongoing debate regarding a change to its international schedule. Further research and information on ketamine anaesthetic use in developed and developing countries is necessary before an ethical and fair decision can be made.

Acknowledgements

Mr. Wisdom Musonda Chelu. Clinical Officer Anaesthetist, National Anaesthesia Co-ordinator, Zambian Ministry of Health.

His Excellency, Seamus O’Grady, Ambassador, Embassy of Ireland, Lusaka, Zambia.

All members of the Surgeon Noonan Society, University College Cork, Ireland.

References