A retrospective review of post-intubation sedation and analgesia practices in a South African private ambulance service

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ABSTRACT

Introduction: Adequate post-intubation sedation and analgesia (PISA) practices are important in the pre-hospital setting where vibration and noise of the transport vehicle may contribute to anxiety and pain in the patient. These practices are poorly described in the pre-hospital setting. This study aims to describe the current pre-hospital PISA practices in a private South African (SA) emergency medical service.

Methodology: Patient report forms (PRF) of intubated patients between 1 Jan 2017 and 31 Dec 2017 from a private ambulance service were reviewed. The data were analysed descriptively. Correlations between receiving PISA and various predictive factors were calculated with Spearman’s Rank correlations and differences between intubation method were calculated with independent t-tests and Mann-Whitney U tests. A binominal regression model was used to determine predictive factors of receiving PISA.

Results: The number of PRFs included for analysis was 437. Of these, 69% of patients received PISA. The estimated time from intubation to 1st PISA ranged from 9 to 12 min. There were statistically significantly more PISA interventions in patients who had received Rocuronium (p < 0.01). There was weak correlation between the number of interventions and the mean arterial pressure, (p < 0.05) and with the transport time to hospital (r_1 = -0.77, p < 0.01).

Conclusion: Sixty nine percent of patients who are intubated pre-hospital receive PISA, which leaves up to 30% without PISA. The time to 1st PISA appears to be shorter in the SA setting. There is an increased number of interventions in the patients who received Rocuronium, which may indicate practitioners being mindful of wakeful paralyzation. Patients intubated with RSI are more likely to receive PISA and practitioners take the blood pressure prior to and after intubation into account when administering PISA. Longer transport times attribute to patients receiving more PISA interventions.

African relevance

• This article describes the current pre-hospital post-intubation sedation and analgesia practices in the South African setting to determine if improvement or policy change is needed.
• The patient sample is representative of the high burden of trauma in the South African pre-hospital setting.
• Optimal post-intubation sedation and analgesia practices early on may contribute to improvement on the long-term outcome of patients.
• South Africa has one of the more advanced pre-hospital EMS in Africa and this research can act as a guideline for pre-hospital policy and procedure development in other developing African countries, as well as expanding and refining and otherwise improving our own local and national standard operating procedures, protocols or policies.

• As in South Africa, other African countries experience similar challenges such as rural infrastructure and long pre-hospital transport times which provides external validity of this research to Africa as a whole.

Introduction

Endotracheal intubation (ETI) in the South African (SA) pre-hospital setting can be facilitated by Rapid Sequence Intubation (RSI), and before the scope of practice changes in the year 2020, deep sedation (DS) intubation, or without medication by the advanced life support (ALS) paramedic [1,2]. The ETI process and proceeding mechanical ventilation procedure create discomfort and anxiety in patients, which are exacerbated by the unique, inherent challenges of the pre-hospital and aeromedical environment, i.e. increased noise, lack of space and significant vibration and jostling of the patient due to rough terrain [3].

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Consequences of inappropriate analgesia and sedation practices are numerous, particularly in the post-intubation period. Deeper sedation, whether long term or in the early post-intubation period in the emergency setting has been associated with increased mortality, hospital length-of-stay (LOS), longer ventilation days and delirium [4,5]. Conversely, inadequate sedation and analgesia (especially when pharmacologically paralysed) may lead to increased catecholamine release with a resultant multitude of undesirable consequences, including self-extubation with resultant asphyxia, hypoxia, or death [6–8]. Awareness during pharmacological paralysis may also lead to secondary psychological trauma and post-traumatic stress which may leave the medical practitioner open to litigation [9]. It is the medical practitioner’s ethical duty to first cause no harm and failure to provide adequate sedation may be construed as negligence.

After review of the literature, there appears to be only one recommendation, found in the Emergency Medicine Society of South Africa (EMSSA) RSI practice guidelines, for the pre-hospital administration of post intubation sedation and analgesia (PISA) in South Africa [10]. These guidelines are broad and open to interpretation, thus, sedation and analgesia of patients in this setting are at the discretion and clinical judgment of the medical provider [11].

Therefore, this study sought to assess the practice of ALS practitioners in the South African setting. The primary aim of this retrospective chart review was to investigate if patients were receiving PISA. The secondary aims were to determine the time frame of, and the total number of PISA administrations. It also attempted to determine if there was an association between PISA and paralytic use, and to describe the association, if any, of demographic or clinical parameters on the time to 1st PISA administration and the mean number of PISA interventions.

Secondary aims were based on the following hypotheses:

1. Patients who received a long-acting paralytic would have less PISA administered as they would be unable to alert a provider when conscious [7,9,12,13];
2. Patients of female gender and older adults would receive less sedation and analgesia [14–16];
3. Hypotension would caution providers against administering PISA [17–19];
4. Longer prehospital times would necessitate more medication being administered [12].

Methods

A retrospective chart review of all cases where ETI was performed between the periods of 1 January 2017 to 31 December 2017 from a single, national South African emergency medical service (EMS)

South Africa’s EMS system consists of a free government service as well as multiple private ambulance companies that provide the service for an out-of-pocket fee or via medical insurance. During the study period, ETI could be performed by either RSI (induction and paralytic), DS or without any medication (in patients who are deeply unconscious or without a gag reflex). After 2020, scope of practice changes limited the performance of ETI to RSI, with intubation without medication limited to cardiac arrest management only. Despite these changes, no additional guidelines were created on PISA management, and current practice on PISA remains unknown.

Patient report forms (PRFs) from a single national private ambulance service were included for analysis in this study. These PRFs are filled out by hand by the treating practitioner and may be done retrospectively after the patient has been handed over. These PRFs are serially numbered and electronically scanned to PDF by an external company. The scanned electronic copies are available in a central billing system for record keeping and billing purposes. Various interventions performed (such as ETI) are manually captured during the billing process.

All PRFs that had an intubation attempt logged during the period of 1 January 2017 to 31 December 2017 were captured and scrutinised for the inclusion and exclusion criteria. PRFs included for analysis were patients of all ages successfully intubated by an ALS practitioner in the pre-hospital setting.

All intubation methods were included (RSI - when a paralytic was administered, DS – when only a sedative or analgesic agent was administered, and no medication intubation), since these practices were still in place in 2017. PRFs not included for analysis were patients in cardiac arrest or who had died on scene. Patients that required more than two attempts at intubation were excluded for analysis of the objectives where time played a role, such as time to 1st PISA and correlation with vital sign changes. All the PRFs were included for analysis of the primary objective and determination of the number of interventions.

Each PRF was scrutinised by a single data collector and variables were recorded according to pre-set criteria (see Appendix A). The variables recorded included patient age, gender, mechanism of injury categorised into medical or trauma, intubation method, heart rate (HR), blood pressure, including mean arterial pressure (MAP), and Glasgow Coma score (GCS) before and after intubation and after the 1st PISA intervention, medication used, dosages and administration times. The variables were recorded in a Microsoft Excel spreadsheet. The intubation time is not recorded on the PRFs and an estimation of intubation time had to be made according to the pre-set criteria (Appendix A).

To verify accuracy, a 10% random sample was generated in Microsoft Excel and a 2nd data collector was tasked to record the data for this sample according to the same pre-set criteria. The 2nd data collector was trained on the process of recording the variables prior to the process. Recorded information was compared during a scheduled meeting and consensus regarding differences was reached by discussion. The sampled data were compared to the corresponding PRF information that was captured by the 1st data collector for inter-rater agreement.

The data in the Excel spreadsheet (Microsoft Corporation, Redmond, WA, United States) were coded to numerical values (e.g., received PISA yes – 1, no – 2) to simplify statistical analysis. For missing vital sign variables, the case was excluded during the analysis where these variables were required. The descriptive data analysis was presented as proportions and percentages, and mean times pertaining to 1st PISA intervention and number of PISA interventions.

Analyses were done in aggregate, but also split into cohorts according to intubation method (RSI, as well as between RSI with rocuronium (ROC) and RSI with succinylcholine (SCH), DS and no medication). An independent sample t-test was performed to determine differences between number of PISA interventions in patients who had received ROC and patients who did not (patients who only received SCH or DS for induction). Patients who required no medication for intubation was excluded from this group.

Time from induction to 1st PISA was calculated but was not feasible for comparison between all the subgroups since this led to a prolonged time to 1st PISA in the DS group. This was due to the induction agents having a longer onset of action than those in the RSI groups. Analysis where this time frame was used was isolated to the RSI group between ROC and SCH subgroups.

An independent sample t-test was performed to determine differences in the number of interventions between the RSI group and the DS group. Mann-Whitney U tests were run to determine differences in time from estimated ETI to 1st PISA between the RSI and DS groups, differences in time from induction to 1st PISA between ROC or SCH groups and differences between the mean times from 1st PISA to 2nd PISA and 2nd PISA to 3rd PISA between the ROC and SCH groups, and between the RSI and DS groups.

The association between patient variables and patients receiving PISA was determined with odds ratio calculations. Spearman’s rank-order correlation coefficients and independent sample t-tests were used to determine the relationships between the groups receiving PISA, number of PISA interventions and time from induction administration/estimated ETI to 1st PISA and the remaining variables recorded.
A binomial logistic regression was performed to ascertain the predictive value of variables that had a statistically significant correlation in the above-mentioned groups on the likelihood of patients receiving PISA. Significance was two-tailed and determined at a value of p < 0.05. The descriptive statistics were performed in the original spreadsheet and the correlation and between-group comparisons were calculated using Statistical Product and Service Solutions (IBM, Armonk, New York, United States).

**Results**

There were 801 PRFs identified that had an intubation event logged over the study period, but 364 were excluded according to the exclusion criteria (Fig. 1). Of the 437 that were included for analysis, 68 patients had multiple intubation attempts (included for primary objective analysis). Three hundred and sixty-nine PRFs were included for analysis of all of the objectives. There was a 95.2% inter-rater agreement between the data abstractors.

Of the 437 patients, 217 (49.6%) were intubated with RSI; 105 (24%) had ROC administered either as a primary or as a secondary neuromuscular blocking agent (NMBA) and 112 (25.6%) had only received SCh during the intubation process, 162 (37.1%) were intubated with DS and 58 (13.3%) were intubated with no medication. Table 1 describes the demographic and basic distributions of the sample.

Three hundred and two (69.1%) of the patents in the total sample had received some type of PISA intervention (Fig. 2). Patients who were intubated with RSI overall were more likely to receive PISA compared to patients who were intubated with DS (OR 5.45 (95% CI, 3.26 to 9.12 p < 0.01)); the odds of receiving PISA between RSI and no medication intubation was 16.33 (95% CI, 8.18 to 32.58 p < 0.01) and between DS and no medication was 3.00 (95% CI, 1.58 to 5.67 p < 0.01). There was no significant difference in odds of receiving PISA between those who had received ROC and SCh during RSI: OR 2.32 (95% CI, 0.96 – 5.60, p = 0.06).

The time from estimated time of intubation to 1st PISA was fairly similar between the groups, ranging from 9 to 12 min (Table 2) with no significant differences between the subgroups.

Median time from 1st to 2nd PISA between RSI with ROC (15 min) and RSI with SCh (10.5 min), was statistically significantly longer, p < 0.01. No significant differences were found between the other subgroups.

There was a statistically significant difference (p < 0.01) between the mean number of PISA interventions in the ROC and the non-ROC group. The ROC group received 0.72 (95% CI, 0.47–0.97) more interventions than in the non-ROC group. There was also a significant difference (p < 0.01) between the RSI and DS groups, with the RSI group receiving 0.95 (95% CI, 0.737–1.169) more interventions than the DS group.

Pre-and post-ETI MAP had a statistically significant impact on patients receiving PISA with a higher pre-ETI (t = 2.09, 95% CI, 0.36–12.82) and post-ETI MAP (t = 2.35, 95% CI, 1.1–12.67, p<0.05) resulted in receiving PISA. The odds of receiving PISA were found to be lower in females than in males (OR 0.62, 95% CI, 0.40 to 0.96 p < 0.03) but there was no difference in trauma vs medical patients who received PISA (OR 1.42, 95% CI, 0.91 to 2.21 p < 0.13). There was weak but statistically significant correlation between age of the patient and receiving PISA $r = 0.11$ (p = 0.03) with an increasing age more likely to receive

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**Table 1**

| Description                  | Total | ROC | SCH | DS | No meds |
|------------------------------|-------|-----|-----|----|---------|
| Age distribution             |       |     |     |    |         |
| Child (< 18) n (%)           | 39 (8.9) | 6 (1.4) | 12 (2.7) | 18 (4.1) | 3 (0.7) |
| Mean age (range)             | 8.6 (1–17) | 6.2 (3–9) | 8.7 (3–17) | 9.3 (1–17) | 9.7 (7–15) |
| Adult (≥ 18) n (%)           | 344 (78.7) | 80 (18.3) | 84 (19.2) | 131 (30) | 49 (11.2) |
| Mean (range)                 | 43.5 (18–99) | 40.2 (19–92) | 39.7 (18–84) | 46.8 (20–99) | 46.6 (18–49) |
| Unknown n (%)                | 54 (12.4) | 19 (4.3) | 16 (3.7) | 13 (3) | 6 (1.4) |
| Total Age (±SD)              | 40 (±20.4) | 38 (±17.6) | 36 (±18.5) | 42 (±22.8) | 44 (±19.6) |
| Gender n (%)                 |       |     |     |    |         |
| Male                         | 315 (72) | 82 (18.8) | 85 (19.5) | 107 (24.4) | 41 (9.4) |
| Female                       | 122 (28) | 23 (5.2) | 27 (6.2) | 55 (12.6) | 17 (3.9) |
| Classification n (%)         |       |     |     |    |         |
| Medical                      | 118 (27) | 15 (3.4) | 24 (5.5) | 57 (13.1) | 22 (5.1) |
| Trauma                       | 319 (73) | 90 (20.6) | 88 (20.1) | 105 (24) | 36 (8.2) |

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**Fig. 1.** Inclusion of cases.
PISA. There was also a statistically significant correlation between time from induction to destination and receiving PISA $r = -0.77$ ($p < 0.01$) with an increasing time to destination resulting in one or more PISA administrations.

The binomial logistic regression was performed to ascertain the effects of age, gender, mechanism (trauma or medical), MAP prior and after ETI, GCS prior to ETI, ETI method and time from induction to destination on the likelihood of participants receiving PISA. Only time from induction to destination and ETI method were statistically significant predictors. Patients intubated with RSI had 6.6 times higher likelihood of receiving PISA (OR 6.6, 95% CI, 3.4 – 12.97, $p < 0.01$) than those intubated with DS.

Additional analysis was performed on the type of PISA interventions. These interventions ranged from Morphine only, Midazolam only, a combination of Morphine and Midazolam, Ketamine, Diazepam, Ketamine and Morphine combination, Ketamine and Midazolam combination, Lorazepam and one instance of Etomidate. The majority of the interventions were Morphine, Midazolam or a combination thereof (76.6% of the patients who had received some type of PISA). Basic descriptive statistics were performed on these groups of PISA interventions. The average dose of Morphine ($±SD$) when administered as a singular agent for the 1st intervention post ETI was 4.1 mg ($±1.1$), as the 2nd intervention 4.6 mg ($±0.5$) and as the 3rd intervention 3.4 mg ($±1.2$). The results for Midazolam as a singular agent post-ETI was 4.4 mg ($±2.5$), 4 mg ($±2.2$) and 3.6 mg ($±1.1$) for 1st, 2nd and 3rd intervention respectively, and for a Morphine/Midazolam combination, the results were 3.6 mg ($±1.4$)/3.6 mg ($±1.3$) for 1st intervention, 3.4 mg ($±1.2$)/3.2 mg ($±1.2$) for 2nd intervention and 3.2 mg ($±1$)/3 mg ($±1$) for the 3rd intervention.

### Discussion

This study described the PISA practices of ALS practitioners in a private ambulance service in the South African pre-hospital setting. Sixty nine percent of all the patients intubated had received PISA. Of this, 88% in the RSI group, 57.4% in the DS group and 31% in the no medication group had received PISA. Therefore, 75% of patients intubated with the help of an induction agent in this environment received some type of PISA. This is similar to that in a 2017 study by Stein in a similar South African setting, where it was found that 72% of patients received Morphine and 63% received Midazolam post-intubation [20].

The demographic descriptors of the patients were similar to other studies done in the South African pre-hospital setting with the predominant population being young males with trauma [17,20–22]. Interestingly, males were more likely to receive PISA than females. There is evidence in the literature that analgesia administration discrepancies exist between genders but none specifically pertaining to PISA [14–16]. The reason for this finding therefore remains unclear, however, gender bias may play a role.

Recommendations regarding PISA in the international prehospital setting varies according to local protocols [23–28]. The consensus in the majority of the guidelines is to titrate benzodiazepines and opioids to smaller, more frequent doses, based on physiological indicators, to limit haemodynamic side effects. Other guidelines advocate administer-

![Fig. 2. Distribution of PISA between subgroups.](https://example.com/image-url)
ing an opioid (fentanyl being the preference) first, and adding sedation as needed, if at all, for patient comfort [18,26]. EMSSA RSI practice guidelines states 1–2 mg of morphine, midazolam or a combination of both, every 10 min as required [10]. These guidelines are vague and give no indication as to the initiation of the PISA or the considerations of physiological parameters to direct PISA use.

Patients intubated with RSI were more than 6 times more likely to receive PISA than those intubated by other methods. Historically, a common indication for the administration of sedation was purported to be patient movement, a sign that is masked by long-acting NMBA [7]. As such, patients at risk of awake paralysis is twice as high in patients who received a long-acting NMBA as opposed to those who did not [7,9,13]. This did not occur in the current study. The time to the 1st intervention after intubation was administered at similar times between the different intubation methods. The average number of interventions however, were significantly higher in the patients who had received ROC, possibly alluding to the mindfulnes of awake paralysis by practitioners.

There was a statistically significant difference between the time of the 1st and 2nd PISA administrations between the ROC and SCH groups. Earlier 2nd PISA administration in the SCH subgroup may be due to patient physical movement once the half-life of the short acting SCH was reached, alerting the practitioner to their wakefulness sooner than those in the ROC cohort. The 1st PISA administration may therefore be due to mindfullness of the EMSSA guidelines, whereas the 2nd dose is due to patient factors. Furthermore, the delay may be caused by the singular practitioner in the treatment compartment with the patient, possibly preoccupied with other life-saving interventions, only administering subsequent PISA doses when promoted by physical signs of patient distress. Despite this delay, the time frame noted (10 – 15 min) was still an improvement when compared to a 2013 emergency center study done by Watt et al., where it was found that the mean time to initial PISA was 27 min after RSI with ROC [29].

This study found that there was a small but significant correlation between the MAP before and after intubation and receiving PISA, suggesting that practitioners consider the patient’s haemodynamic status before administering PISA. In the context of South African EMS scope of practice, where only medications that have a profound effect on haemodynamics and exacerbate hypotension are available for PISA, pre- and post-intubation hypotension may result in a reluctance to administer PISA [17,30]. Importantly though, hypotension in and of itself should not be seen as a justification for withholding PISA. In the creation of prehospital PISA guidelines, the approach to the hypotensive/ unstable patient should be stipulated.

The strongest correlation for receiving PISA and the number of administrations was seen with transport time to hospital, with a longer transport time resulting in a higher likelihood of receiving more frequent PISA. This was to be expected as the stressors of transport were experienced by the patients for a longer period of time (during which the effects of a single ROC administration for intubation would subside), with the subsequent signs of distress. A short transport time may therefore account for some of the patients not receiving any/multiple PISA administrations.

Limitations

This study was a retrospective chart review and subject to the common limitations of this type of study. This included the possibility of inaccurate or missing information in the documentation (PRFs) and poor external validity since the study population was derived from a single private company with their own policies and procedures. The PRFs are often completed by the practitioners retrospectively after patient handover and the times recorded may therefore not be accurate, since it is based on the practitioner’s memory if they did not record it during the procedure. ETI times were not recorded on the PRFs and multiple timeline estimates had to be made. The results should be interpreted in light of this limitation.

There was a wide variety of post-intubation medications administered in the population. This made the analysis of these interventions difficult to compare. These medications have different durations of action which also fluctuate based on the dosages administered. This may have had an effect on the timings of PISA administration as well as the number of interventions. The data were from a 2017 cohort, however the scope of practice has since changed in the South African pre-hospital setting. RSI is the only recommended method for ETI and the report on the other methods may be less relevant. Despite this, these results may be taken into account as future changes in scope of practice or clinical guidance are undertaken on the continent.

Conclusion

Sixty nine percent of patients intubated in the South African pre-hospital environment received some type of PISA. This unfortunately means that 31% of patients did not receive any PISA. Without evidence-based guidelines for PISA practice or patient outcome data, it is not possible to conclude if the current practices regarding the number and timing of interventions were optimal for patient management, nor is it possible to determine the effect on the patients’ outcome. The authors recommend that the administration of PISA be aided by guidelines tailored to the South African pre-hospital setting and that the administration of PISA not be left up to the discretion of the practitioner alone.

Dissemination of results

The results of the study, including the full article, were made available to the private ambulance company from where the patient report forms originated. The deidentified raw data will be made available upon request.

Authors’ contribution

Authors contributed as follow to the conception or design of the work; the acquisition, analysis, or interpretation of data for the work; and drafting the work or revising it critically for important intellectual content: JMDK contributed 50%, WS and CB contributed 25% each. All authors approved the version to be published and agreed to be accountable for all aspects of the work.

Declaration of competing interests

The authors declare no conflict of interests.

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