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Chung (John) Lee, Bachelor of Paramedicine (3rd Year) Victoria University, Victoria

Accuracy of student paramedics when measuring adult respiratory rate: A pilot study

Rami Fezai¹, Sarah Galka¹, Berrell¹, Louis Shabella¹, Dr Paul Simpson², Dr Liz Thyer²,

¹School of Science and Health, Western Sydney University, Second Year

²School of Science and Health Staff, Western Sydney University

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Will Septic Shock Patients Benefit from Prehospital Antibiotics?

Chung (John) Lee
Third Year Paramedic Student - VU

Background: Septic shock is defined as a systemic infection inducing organ dysfunction or tissue hypoperfusion. Millions of people around the world are affected by sepsis each year and its incidence is rising (Dellinger et al., 2004). **SEPSIS IS A MAJOR HEALTH-CARE PROBLEM WITH MORTALITY RATES SIMILAR TO POLY-TRAUMA, ACUTE MYOCARDIAL INFARCTION (AMI) OR STROKE** (Dellinger et al., 2004) . The Surviving Sepsis Campaign (SSC) Bundle recommends aggressive initial resuscitation by measuring lactate levels, obtaining blood cultures, administering broad spectrum antibiotics with 30ml/kg crystalloid for hypotension or lactate >4mmol/L (Dellinger et al., 2004). Ambulance Victoria Guidelines allow paramedics to begin fluid resuscitation and adrenaline infusions for septic shock patients but ceftriaxone is reserved for meningococcal septicaemia (Ambulance Victoria, 2014). This report examines the influence of delayed antibiotic treatment for septic shock on patient outcome.

Objectives: Evaluate hospital based research articles on delay to administration of broad-spectrum antibiotics and the impact on patient mortality.

Methods: Key words searched on databases included PubMed and The Cochrane Library. Randomised Control Trials were preferred but none were found so multi-center prospective studies from 2005 to present were included. Studies that measured relationships between mortality and hour increment delays in antibiotics were selected.

Findings:

Kumar et al., (2006) United States and Canada:

- Retrospective cohort study
- 2,731 patients with septic shock in 14 ICU’s and 10 hospitals
- Measured duration of hypotension before effective antimicrobials in hours
- **SURVIVAL RATE WAS 79.9% IN FIRST HOUR, DECREASED BY 7.6% FOR EVERY HOURLY DELAY FOR EFFECTIVE ANTIMICROBIALS** (Fig. 1)
- Multivariate analysis considering fluids, vasopressor and inotropic drug use revealed time to effective antimicrobials was strongly associated with outcome (p < 0.0001)
- Ineffective antimicrobial treatment was omitted from study
- Formed basis for updated SSC bundle recommending broad-spectrum antibiotics in first hour of patient contact

Puskarich et al., (2011) United States:

- Retrospective analysis of patients treated with Sepsis Protocol
- 291 patients with septic shock in 3 urban tertiary ED’s
- Measured mortality *versus* time to initial antibiotic treatment from triage and septic shock recognition
- **NO ASSOCIATION BETWEEN MORTALITY AND HOURLY DELAYS IN INITIAL ANTIBIOTIC ADMINISTRATION AFTER SHOCK RECOGNITION**
- **INCREASED RISK OF DEATH IF ANTIBIOTICS ARE DELAYED UNTIL AFTER SHOCK RECOGNITION**
- All ED’s followed same sepsis protocol and measured initial antibiotic administration regardless of effectiveness
- However 75% of patients received antibiotics within 3 hours of triage – difficult to conclude associations with longer delays

Ferrer et al., (2014) Europe, US and South America:

- Retrospective analysis of data collected from SSC
- **ONE OF THE LARGEST POPULATION TESTING OF BROAD-SPECTRUM ANTIBIOTIC TIMING AND MORTALITY WITH HOSPITALS COMPLYING TO SSC GUIDELINES**
- 28,150 patients with severe sepsis and septic shock in 165 ICU’s
- Measured time of presentation to first antibiotic administration
- **AFTER 1ST HOUR - MORTALITY STEADILY RISES REGARDLESS OF SEVERITY**
- Linear trend observed when Sepsis Severity Score (SSS), ICU admission source and geographic location were adjusted to their mean value (Figure 2)

Figure 1: Cumulative effective antimicrobial initiation following onset of septic shock and associated survival. Source: (Kumar et.al., 2006)

Figure 2: Predicted hospital mortality and associated 95% CIs for time to first antibiotic admin. Based on subject being from the US, admitted from ED and SSS is 52 (median of all)
Source: (Ferrer et al., 2014)

Conclusion:

PATIENTS WITH SEPTIC SHOCK ARE TIME CRITICAL AND ALL THREE STUDIES AGREE THAT THE TIMING OF ANTIBIOTIC INFLUENCE MORTALITY. Kumar et al., (2006) and Ferrer et al., (2014) identified changes in outcomes for septic shock patients that had delayed antibiotics in just hours whereas Puskarich et al., (2011) refuted their findings. Ferrer et al., (2014) has research methods that resemble Puskarich et al., (2011) and its higher power may have revealed associations missed before. Additionally, the sample group in Puskarich et al., (2011) had a lower mean mortality than Kumar et al., (2006) and Ferrer et al., (2014) (18.9% vs. 56.2% vs. 29.7% respectively) which could be indicative of the patient’s severity.

Fluids, vasopressors and inotropes are initiated for septic shock patients by paramedics. But the implementation of prehospital blood cultures, blood lactate and broad-spectrum antibiotics means complete SSC bundle resuscitation can be initiated earlier for better patient outcomes but they all carry logistical issues. Research in the prehospital field needs to be conducted to measure cost and benefit.

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Accuracy of student paramedics when measuring adult respiratory rate A Pilot Study

Rami Fezai¹, Sarah Galka¹, Berrell¹, Louis Shabella¹, Dr Paul Simpson², Dr Liz Thyer²,
¹School of Science and Health, Western Sydney University, Second Year
²School of Science and Health Staff, Western Sydney University
Email: fezai.rami@gmail.com Mobile:0457252442

WESTERN SYDNEY
UNIVERSITY

INTRODUCTION

Abnormal respiration rate (RR) is commonly undervalued in the out-of-hospital environment despite its use as a predictive marker for physiological decline [1, 2, 3]. Failure to accurately measure RR may lead to delayed recognition of the deteriorating patient [4]. While accuracy of measurement and recording of RR has been reported in allied health settings [5], no evidence exists in the context of paramedicine.

METHODS

This pilot study utilizes a double-blinded cohort design. Student paramedics manually record RR along with a range of vital signs including non-invasive manual blood pressure (NIBP), heart rate (HR), oxygen saturation (SpO₂), temperature (Temp) and 4 lead ECG on healthy volunteers [Fig. 1]. Neither the subjects nor the students were aware of the specific aims of the study. Capnography was used as the gold standard (as in hospital environments) to confirm observed respiratory rates.

RESULTS

Thirty-six complete sets of data (pre and post exercise RR with manual measurement and capnography) were recorded. An even gender split was achieved in the healthy volunteers, whilst 42% of paramedic students were male.

Intraclass correlation (ICC(3,k)) was used to assess agreement between manual RR and capnography and showed strong agreement, ICC 0.77 (95% CI 0.54 to 0.88). This was supported by Bland Altman plots indicating a mean difference of 0.11 breaths between student measured (mean=17.53 SD = 3.89) and capnography (mean=17.42 SD = 3.59).

It is noteworthy that the 95% limits of agreement indicate variation as large as 6 breaths (-6.2 to 6.4) in measurement [Fig 1]; whilst this may not be statistically significant, it could be clinically significant.

Due to the need to look at a patient's chest during manual RR measurement, accuracy of student paramedics of a particular gender to measure patients of the opposite gender was assessed [Fig 2]. Although the boxplot appears to show a large variance, a one way stratified ANOVA showed no statistical difference when female students (F=0.05, P=0.83) or male students (F=0.04, P=0.84) measured RR.

CONCLUSION

The manual RR measured by paramedic students agrees well with capnography irrespective of the gender of the patient or student paramedic. These two measurements could be used interchangeably, although the difference between statistical and clinical significance should be further investigated.

These results suggest teaching and learning methods of UWS undergraduate paramedicine students for this skill are suitable for the majority of the cohort.

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AIM

The study aims to:

1. Determine the accuracy of manually measured RR when taken by University of Western Sydney (UWS) second year student paramedics on healthy volunteers in a simulated environment and
2. Inform study design of a larger study.

Figure 1. Student paramedic undertaking manual vital signs

Figure 2. Plot of agreement between student paramedic measurements and capnography

Figure 3. Difference in gender between student paramedic and healthy volunteer

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FUTURE DIRECTIONS

This pilot study showed promising results that indicate a larger study,, including students from other universities, would be worthwhile.

Further research may also consider a qualitative component, assessing student paramedics' perceptions of measuring RR accurately and understanding of the importance of this physiological marker in the declining patient.

Finally, a repeat study should consider comparison of all components of the vital signs survey to investigate variation in results and determine if trends in accuracy become apparent.

Recombinant Human Factor VIIa: A novel solution for severe, refractory postpartum haemorrhage in the prehospital setting?

Rachel Kluck, Bachelor of Paramedic Science (3rd Year), The University Of Queensland

Rachel Kluck
kluckrachel@gmail.com
0437 639 389

BACKGROUND

Obstetric haemorrhages pose a serious albeit rare challenge in the prehospital environment. Management options for post-partum haemorrhage (PPH) are traditionally limited to standard cares, a few manual manoeuvres and uterotonic drugs in some instances. In the case of severe PPH (>1500mL) that is refractory to available management, the threat of patient deterioration and death are great. Recombinant human factor VIIa (RhuFVIIa) is a novel, off-label treatment option being considered in hospital settings for these patients as a last-line management in these patients prior to hysterectomy. Previous case reports and case series have reported success rates of 63-100% [1], and it is already included in a number of PPH guidelines [6][7]. RhuFVIIa, normally reserved for treating haemophilia and congenital factor VII deficiencies, acts by directly activating factors IX and X on platelets, enhancing thrombin generation. This facilitates increased conversion of fibrinogen to fibrin in clots that cross-links, strengthening thrombi and assisting haemorrhage cessation. Many hospital interventions such as hysterectomy, arterial ligation and artery embolization are not feasible prehospitally. However, an easily administered drug such as RhuFVIIa, if effective, could be useful in prehospital patients with severe, refractory PPH.

OBJECTIVE

To determine the effectiveness of RhuFVIIa in treating severe, refractory PPH.

METHOD

A search strategy was developed using key words from the primary research question. PubMed, Web of Science and the Cochrane Library were searched, producing 6 articles. An exclusion criteria was then applied (Figure 1), leaving 3 articles for review.

FIGURE 1 – Primary Outcome Literature Search

FINDINGS

Only three studies were found in the literature search. However, the limited results available are consistent, with evidence of a large potential clinical impact.

Hossain et al conducted the first study for review. The retrospective cohort study examined 34 women, with both a treatment and control group [2]. They found that although there was not a significant reduction in mortality of patients who received RhuFVIIa, there was a dramatic reduction in the number of transfusions required (mean -5.61 transfusions), as well as haemostatic times (Table 2). **Of patients who *did* receive RhuFVIIa, 83.3% had a complete response (decreased/ceased bleeding and improved coagulation) with the first dose** (Table 1). This study obviously has significant limitations, in that it was not randomised or blinded, and treatment prior to RhuFVIIa administration was not consistent; this casts some doubt over the reliability of these results. The sample size was quite small at 34 patients, and there were a few minor differences in the baseline characteristics of subjects that may have affected outcomes [2]. These results must therefore be assessed with regards to how agreeable it is with other available evidence.

TABLE 2 – Beneficial changes in treatment group after RhuFVIIa administration

Hossain et al., 2007	Huber et al., 2012	Lavigne-Lissalde
↓ RBC transfusions, P<0.007	↓ RBC transfusions, P<0.001	↓ haemoglobin loss, P<0.0377
↓ thromboplastim times, P<0.0001	↓ plasma substitutions, P<0.001	↓ fibrinogen administered
↓ prothrombin times, P<0.0001	↓ platelet transfusions, P<0.001	No change in transfusions, NS
	↑ haemoglobin levels, P<0.001	
	↑ fibrinogen levels, P<0.001	

The second study, by Huber et al, investigated RhuFVIIa after failure of all medical and surgical interventions prior to emergency hysterectomy [3]. They found it to have a huge success rate, **removing the requirement for last-line hysterectomy in 91% of cases** (Table 1). In addition, the need for post-RhuFVIIa interventions such as red blood cells, plasma and platelet transfusions decreased significantly compared to pre-RhuFVIIa requirements, with reductions of 2.6 units, 1.8 units and 1 unit respectively (Table 2) [3]. Furthermore, haemoglobin and fibrinogen levels increased significantly after administration (Table 2). Despite these impressive results, there are major design limitations with this study. There was no blinding or control groups, with a relatively small sample size of 22 women [3]. This drastically increases the risk of bias and error within the data. In addition, the lack of a standardised pre-RhuFVIIa treatment algorithm may have affected the results; it is difficult to assess the true efficacy of an

intervention when other treatments are varied between patients and may have an independent impact on patient outcome. However, despite the huge study flaws, the results produced are impressive. No thromboembolic events occurred following RhuFVIIa administration.

The final study for review was an open RCT of 84 women by Lavigne-Lissalde et al. They administered RhuFVIIa after failure of all interventions except arterial ligation, embolisation and hysterectomy [4]. **PPH cessation occurred significantly more frequently where RhuFVIIa was given**, with success rates in the control group and treatment group at 7% and 48% respectively, P<0.0001 (Table 1). This efficacy was demonstrated in a Number Needed to Treat (NNT) of just 2.6 [4]. Decreased fibrinogen concentrates were required in the treatment group after administration, at 67% versus 48% (Table 2), however there was no difference in

TABLE 1 – Efficacy of RhuFVIIa in severe refractory PPH

Author	Study Type	Pre-RhuFVIIa Interventions	RhuFVIIa Dose (mcg/kg)	Control Group Efficacy (%)	RhuFVIIa Group Efficacy (%)
Hossain et al, 2007	Retrospective Cohort	• Fluid resuscitation • Uterotonics* • Internal iliac ligation	70	NA	83.3
Huber et al., 2012	Prospective Cohort	• Uterotonics* • Fluid resuscitation • RBCs • Fresh frozen plasma • Platelets • Surgery**	71	NA	91.0
Lavigne-Lissalde et al., 2015	Open RCT	• Fluid resuscitation • Bladder catheterisation • Removal of retained placenta • Uterine exploration • Oxytocin & Sulprostone	60	7.0 P<0.0001	48.0 P<0.0001

*Oxytocin, methylergometrine, misoprostol

**Lesion repair, uterine curettage, balloon catheter, laparotomy, compression sutures or artery embolization

transfusion requirements. In terms of haemoglobin, the fall in serum levels in the 30 minutes post-RhuFVIIa was less in the treatment group (Table 2). This study had some similar limitations to Huber et al, in that it was not blinded and although there was a generalised treatment algorithm in place prior RhuFVIIa administration, many first-line treatments were left performed at the doctors’ discretion [4]. This adds a large risk of bias, as it is difficult to ascertain if the reduced need for invasive second line was truly because of RhuFVIIa or a variation in adjunctive interventions. However, the study was powered to detect significant outcomes and as the only RCT carried out so far, the available results are promising. In terms of adverse events, 5% of women in the intervention group experienced mild thromboembolic events which were easily resolved with post PPH enoxaparin administration [4]. It should be noted that no thromboprophylaxis protocol was included in this study and adding such a regime in future RCTs may alleviate these risks.

CONCLUSIONS

- RhuFVIIa is a promising alternative to invasive surgical management of severe, refractory PPH >1500mL that slows/ceases haemorrhage, decreases transfusion requirements and improves coagulation while preserving fertility.
- Large, double-blind RCTs assessing RhuFVIIa efficacy and safety are required before strong recommendations can be made. The reviewed studies were not powered to assess safety. These studies should also include a pre-RhuFVIIa treatment algorithm.

PREHOSPITAL APPLICATION

- Despite a weak evidence base, **the potential benefits of RhuFVIIa *may* be greater than the risks associated with side effects and the probable poor outcome of a deteriorating, refractory patient** with no remaining prehospital treatment options.
- RhuFVIIa may significantly decrease transfusion requirements and improve coagulation in patients with massive, refractory PPH. **Since RBCs, plasma and platelets are rarely readily available prehospitally, RhuFVIIa may compensate for this** and effectively ‘buy some time’.
- Surgical treatments are not feasible prehospitally; having an effective drug such as RhuFVIIa would be an appealing alternative where traditional prehospital interventions have been exhausted.
- RhuFVIIa is expensive at approximately \$5000-\$10000 per dose [5]. Given the rarity of these patients prehospitally, **it may be appropriate to restrict this drug to rural areas and specialist crews** such as the Trauma Response Team in South-East Queensland. A full cost-benefit analysis may be required should implementation be considered.

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The role of morphine in acute coronary syndromes, are there safer alternatives?

Michael Toussaint-Australian Catholic University Canberra-third year bachelor of paramedicine/bachelor of nursing-Mobile 0411 152 097

Introduction	Results
<p>Ischaemic heart disease remains the leading cause of death in Australia (ABS, 2015) and has been estimated to cost around \$3.5 billion a year (Access Economics, 2009). Fortunately, acute coronary syndrome (ACS) is an area where quality prehospital care greatly effects outcomes, research has shown mortality rates are halved with prehospital diagnosis and treatment of ACS (Chan et al., 2012). Paramedics have traditionally treated ACS with morphine, oxygen, nitrates and aspirin (ARC, 2012), however recently some services have moved away from this treatment, introducing changes including using fentanyl as the preferred analgaesic. The purpose of this research is to assess the evidence for this change and question its value to patient outcomes.</p>	<p>Drug interactions identified in ACS treatment with the potential to affect patient outcomes the most were those between morphine and P2Y12 antiplatelet agents such as clopidogrel, prasugrel and ticagleror. Research also found a possibility that morphine may interact with the antiplatelet medication aspirin.</p> <p>In 2014, a randomised, double blind, placebo-controlled trial found that morphine delayed clopidogrel absorption (P=0.025) and reduced levels of its active metabolite by 34% (P=0.001). The study also found that use of morphine prior to clopidogrel delayed inhibition of maximum platelet aggregation by an average of 2 hours (P=<0.001) (Hobl et al., 2014).</p> <p>Another paper assessed three hundred patients who had undergone PCI and had received the antiplatelet agents prasugrel or ticagleror (Parodi et al., 2015). Researchers found that in patients suffering from ST elevated myocardial ischaemia, morphine use was associated with delayed onset for both prasugrel and ticagleror. Other research has confirmed this finding even stating the effects are more pronounced when patients are treated in a pre-hospital setting (Silvain, 2015).</p> <p>A double blind, randomised control trial is currently underway to assess if morphine administration lowers the rate of absorption of aspirin (Hobl, 2015). The rationale for this research is given as follows <i>“Opiates reduce the intestinal reabsorption of orally administered drugs such as paracetamol. Because morphine is often injected to relieve pain in patients with myocardial infarction, it is of particular interest if morphine may decrease the rate of absorption of antiplatelet drugs”</i> (Hobl, 2015)</p> <p>Other findings of note: No research could be found comparing morphine to fentanyl directly in patients suffering from ACS. It can be assumed that morphine is often preferred due to its anxiolytic effects (O’Gara et al., 2013). Fentanyl has been shown to have the potential to react negatively with amiodarone, a medication often utilized for pre-arrest patients. Despite this, research by Victorian Ambulance Service concluded that the use of amiodarone after fentanyl is justified as it is indicated for life threatening arrhythmias for which there is no alternative. Fentanyl should however be avoided post amiodarone administration (Ambulance Victoria, 2009).</p>
Why Morphine?	
<p>Although there are several aspects of paramedic practice in ACS, morphine was identified as a potential area of improvement due to the findings of the CRUSADE quality improvement initiative. This assessment of 17000 patients showed an increase in mortality amongst patients who had received morphine during ACS (Meine et al., 2005).</p>	
Methods	
<p>Protocols and guidelines from each state were assessed to compile a list of pharmacological interventions used in ACS. Morphine and fentanyl were found to be the most commonly used analgesics with morphine being indicated in the majority of states. Other pharmacological interventions identified included aspirin, glyceryl trinitrate and P2Y12 antiplatelet agents such as clopidogrel, prasugrel and ticagleror. These were primarily used in preparation for percutaneous coronary intervention (PCI). Some services also utilised fibrinolysis medications such as heparin, enoxaparin and tenectopase. These pharmacological interventions coupled with MeSH-compatible search terms were used in searches of databases such as Cochrane, PubMed, Uptodate, Google scholar and the U.S clinical trials register. Research regarding potential drug interactions and patient outcomes where assessed for quality with preference given to randomised, double blind control trials and systematic reviews of other evidence.</p>	<div><div> </div><div><div><div>Why morphine doesn’t play well with others...</div><div><div>Clopidogrel</div><div>Prasugrel & Ticagleror</div><div>Aspirin</div></div><div><div>It has been shown to reduce Clopidogrel’s active metabolite by 34% and delay maximum inhibition of platelet aggregation by an average of 2 hours.</div><div>It has been shown to delay the absorption of both prasugrel and ticagleror.</div><div>Research is currently underway to assess if morphine influences the absorption of aspirin. The hypothesis is that morphine will delay absorption.</div></div></div></div></div>
Conclusion	
<p>Despite morphine's dual analgaesic and anxiolytic effects; both of which are important in the treatment of the ACS patient, the move towards fentanyl by some services seems to be supported as the right one by current evidence. This is primarily due to morphine inhibiting the absorption and efficacy of other medications used in the treatment of ACS, both in a prehospital setting and during PCI. There is strong evidence to suggest a double blind randomized control trial comparing the two directly is needed to assess patient mortality and outcomes following ACS treatment.</p>	
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