Comparison of combined anaesthetic techniques or general anaesthesia on clinical outcomes and mortality rate in major surgeries

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ABSTRACT

Introduction: Anaesthesia may influence the perioperative period as well as the patients´ recovery. General anaesthesia (total intravenous or balanced intravenous/inhalation technique) is widely used for major surgeries. However, the association of general anaesthesia with a regional anaesthesia technique may represent a satisfactory alternative in several cases. However, there is a lack of population-based studies, particularly in Brazil, showing if this combined technique could be more effective with fewer complications for certain surgical procedures. *Objectives:* This study aimed to compare the use of opioids in general anesthesia and in combined techniques (general anaesthesia + epidural or spinal anaesthesia) regarding clinical outcomes and mortality rate in major surgeries. Methods: This retrospective cohort study included data from medical records of 305 adult patients who underwent elective major surgeries during the last five years in a tertiary hospital in a middle-sized city of the southern region of Brazil. Data from the individuals were included in two groups, according to the anaesthetic technique used: G1 (general anaesthesia group) and G2 (combined techniques group). The clinical outcomes analysed were: orotracheal intubation time (OIT), intensive care unit length of stay (ICU discharge time), hospital length of stay and in-hospital mortality. Data also considered the anaesthetic risk classification (ASA criteria). *Results*: In ASA I and II patients, there was no association between the anaesthetic technique and OIT, ICU time and length of stay (Mann-Whitney test, $p > 0.05$). However, for patients classified as ASA III and IV, longer OIT ($p=0.04$) was observed in patients undergoing general anesthesia compared to patients undergoing the combined technique, according to the Mann-Whitney Test. Similar results were observed concerning ICU time ($p=0.02$) and total length of stay ($p=0.03$). Regarding mortality rates, no differences between the groups were observed in ASA I and ASA II patients (*Chi* Square Test, $p=0.49$). On the other hand, in ASA III and ASA IV patients, lower mortality rates were observed in patients undergoing the combined anaesthesia techniques (Fisher Exact Test, $p=0.001$). *Conclusion*: It may be concluded that, in patients with higher anaesthetic risk, a combined anaesthesia technique (epidural or spinal anaesthesia combined with general anaesthesia) could reduce orotracheal intubation time, intensive care unit length of stay, hospital length of stay and mortality rate in patients submitted to major surgeries.

Keywords: General Anaesthesia; Epidural Anaesthesia; Spinal Anaesthesia; Orotracheal Intubation time; Length of Stay; Mortality; Major Surgery.

INTRODUCTION

Pain is one of the most common and significant postoperative events experienced by many surgical patients. Optimal postoperative pain management presents a challenge for healthcare providers across all surgical specialties worldwide [1].

The International Association for the Study of Pain (IASP) has stated that pain is a distressing experience associated with actual or potential tissue damage with sensory, emotional, cognitive, and social components [2,3]. Therefore, it is known that the painful experience involves the interpretation of the biological aspects of pain, but also its interaction with the social and cultural characteristics of everyone [4].

Considering its pathophysiology, pain may be classified as nociceptive, neuropathic, or mixed pain. Neuropathic pain is associated with damage to the somatosensory nervous system. Post-operative pain as well as pain related to trauma and ischemic conditions are known as nociceptive pain [5].

Immediate postsurgical pain affects four out of five patients [1]. In a national US survey of adults who had undergone surgery within the previous 5 years, 86% of overall patients experienced postsurgical pain, and 75% of those who reported pain described its severity as moderate–extreme during the immediate postoperative period [6].

The implications of poorly controlled postoperative pain are substantial, including cardiopulmonary complications, opioid-related side effects, unplanned hospital admissions, prolonged hospital stay, increase in health services costs and the subsequent development of chronic pain or opioid addiction [7]. Additionally, it is noteworthy that when surgeons prescribe more doses of opioids or potent opioids when other non-opioid analgesics might be able to control postoperative pain, they are contributing to the opioid epidemic [8].

In major surgeries, postoperative pain can cause atelectasis and pneumonia, as it limits the patient's respiratory functions [9,10]. Besides that, pain also restricts patient mobility, increasing risk for thromboembolic events [10,11].

Despite of these findings, 50 to 70% of patients who underwent major surgery do not receive adequate analgesia control, which increases the risk for complications, resulting in a longer admission and more costs for the Health System [12].

Many studies have reported the advantages of spinal or epidural anaesthesia along with general anaesthesia for major surgeries [13]. Recently, a large transversal study involving 1540 patients which underwent elective surgery for correcting an aortic abdominal aneurism showed that the group under a combination of epidural and general anaesthesia had lower rates of mortality and respiratory complications [14]. The clinical trials on the subject, however, are inconclusive [15,16]. On the other hand, a previous randomised clinical trial by our research group (unpublished data), demonstrated that the combined anaesthetic technique is associated with better analgesic control and fewer postoperative complications in cardiac surgeries.

Therefore, this study aimed to compare the use of opioids in general anesthesia and in combined techniques (general anaesthesia + epidural or spinal anaesthesia) regarding clinical outcomes and mortality rate in major surgeries.

METHODS

This study was approved by the Ethical in Research Committee of Irmandade da Santa Casa de Londrina – BIOISCAL (Protocol #: 821.925).

This retrospective cohort study was developed in a tertiary hospital (Hospital Santa Casa de Londrina) located in Londrina, Paraná State, Brazil.

A random sample of medical records of adult patients (age > 18 years) of both genders which had been admitted to the Health System for elective major surgery in a period of 5 years were included. The study only included patients submitted to major surgeries in which the use of the combined techniques could be a good anaesthetic option.

The total number of patients at the referred centre during this period was 3500 patients. Coming from this data, the sample size formula for a finite population was used for sample size calculation, considering the following parameters: 5% sample error and 95% confidence interval. Therefore, it was determined that the minimum sample size was 224 patients. Considering possible dropouts, a sample of 305 medical records was used.

The patients were classified into two groups according to the anaesthetic technique used, as follows: G1 (group that underwent general anaesthesia) and G2 (group that underwent a combined technique) for further statistical analyses. Data were obtained through the patients' medical and anaesthetic records, including demographic information and anaesthetic risk classification according to the American Society of Anaesthesiologists (ASA). The ASA classification system divides patients into six groups according to their physical health. The groups are, in ascending order: I) a normal healthy patient, II) a patient with mild systemic disease, III) a patient with severe systemic disease, IV) a patient with severe systemic disease that is a constant threat to life, V) a moribund patient who is not expected to survive without the operation, and IV) a declared brain-dead patient whose organs are being removed for donor purposes.

The analysed clinical outcome variables were: orotracheal intubation time (OIT), intensive care unit length of stay, hospital length of stay and mortality rate.

A database on the Statistical Package for Social Sciences (SPSS) version 20.0 program was created for the statistical analysis, with a 95% confidence interval and 5% significance level ($p < 0,05$) for all the applied tests. The Mann-Whitney test was used for comparing the groups (G1 x G2) in terms of the following variables: orotracheal intubation time (OIT), intensive care unit length of stay (ICU discharge time), hospital length of stay. Moreover, *Chi* Square test or Fisher Exact test

was used for comparing the in-hospital mortality rate between the groups.

RESULTS

Data from 305 patients were included in this study. Clinical and general population traits are shown on table 1. There were 257 patients classified as ASA I or II and 48 patients classified as ASA III or IV.

For the ASA I or II patients, there was no relation between the anaesthetic technique and the OIT, ICU time and hospital length of stay (Mann-Whitney Test, p > 0,05).

However, for the patients classified as ASA III or IV, we observed a longer OIT for those on general anaesthesia, when compared to those on the combined technique (spinal or epidural anaesthesia + general anaesthesia), according to the Mann-Whitney Test (p = 0.04). Similar data were observed for ICU stay (p = 0.02) and length of stay (p=0.03).

Data regarding the comparison of anaesthesia technique groups and clinical outcomes can be seen on Figures 1, 2 and 3.

For the ASA I or II patients, the anaesthetic technique did not influence mortality prevalence (*Chi* Square Test, p = 0.49, Table 2). On the other hand, there was a smaller mortality rate among patients who underwent the combined anaesthetic technique (Fisher Exact Test, p= 0.001, Table 3).

Table 1 – General characteristics of the study population.

General features	Groups
Age (Mean ± SD)	65.7 ± 14.4
Gender (n, %)	
Female	118 (38.7%)
Male	187 (61.3%)
ASA classification (n, %)	
ASA I e II	257 (84.3%)
ASA III e IV	48 (15.7%)

SD: Standard Deviation.

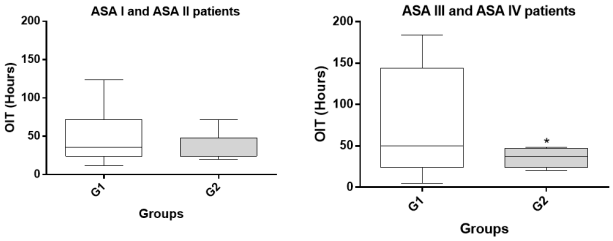

Figure 1 – Orotracheal intubation time (OIT, hours) related to anaesthesia technique (G1: General Anaesthesia and G2: General Anaesthesia + Epidural or Spinal Anaesthesia) in patients who underwent major surgeries. * Statistically different, Mann-Whitney Test, p=0.04.

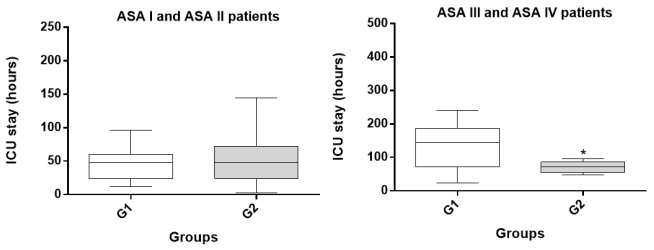

Figure 2 – Intensive Care Unit Length of Stay (ICU stay, hours) related to anaesthesia technique (G1: General Anaesthesia and G2: General Anaesthesia + Epidural or Spinal Anaesthesia) in patients who underwent major surgeries. *Statistically different, Mann-Whitney Test, p=0.02.

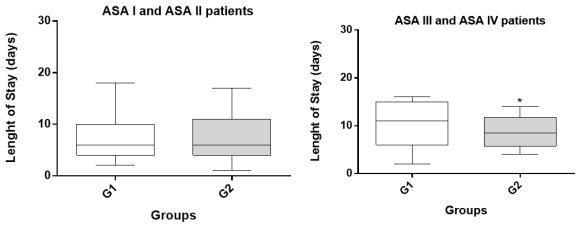

Figure 3 – Length of Stay (days) related to anaesthesia technique (G1: General Anaesthesia and G2: General Anaesthesia + Epidural or Spinal Anaesthesia) in patients who underwent major surgeries. *Statistically different, Mann-Whitney Test, p=0.03.

Table 2 – Prevalence of mortality rate related to anaesthesia technique (G1: General Anaesthesia and G2: General Anaesthesia + Epidural or Spinal Anaesthesia) in ASA I and ASA II patients.

Group	Mortality		
	Yes	No	Total
G1	14 (12.1%)	102 (87.9%)	116 (100.0%)
G2	11 (7.8%)	130 (92.2%)	141 (100.0%)
Total	25 (9.7%)	232 (90.3%)	257 (100.0%)

n.s. – Statistically not significance, Chi Square Test, p=0.49

Table 3 – Prevalence of mortality related to anaesthesia technique (G1: General Anaesthesia and G2: General Anaesthesia + Epidural or Spinal Anaesthesia) in ASA III and ASA IV patients.

Group *	Mortality		
	Yes	No	Total
G1	26 (68.4%)	12 (31.6%)	38 (100.0%)
G2	0 (0%)	10 (100.0%)	10 (100.0%)
Total	26 (54.2%)	22 (45.8%)	48 (100.0%)

* Statistically different, Fisher Exact Test, p=0.001.

DISCUSSION

Major surgeries have a huge potential for postoperative pain, with an estimated 50 to 75% of patients not receiving adequate analgesia control. Pain is associated with more frequent occurrences of many

undesirable postoperative events, such as: pulmonary (atelectasis, pneumonia) and vascular (thromboembolic) complications [11, 12,17-20].

At this study, in patients classified as ASA I or II, the anaesthetic technique did not seem to influence the orotracheal intubation time, length of stay at the intensive care unit, total length of stay, or mortality rate.

On the other hand, our results show that patients who are classified as ASA III or IV had different postoperative outcomes according to the anaesthetic technique and opioid administration route. The individuals who received general anaesthesia associated with spinal or epidural anaesthesia with opioid administration via spinal route, were submitted to a significantly shorter period of mechanical ventilation when compared to the group which received only opioids via parenteral route through general anaesthesia. The same finding was found regarding total length of stay. Regarding mortality rates, the combined technique has been shown to be equally superior to general anaesthesia, with significantly lower mortality rates.

These findings agree with previous studies, which list the advantages for spinal or epidural anaesthesia with opioid administration [13]. Moreover, Bardia et al. [14] reports that spinal or epidural anaesthesia alongside general anaesthesia has been shown to be a good technique. However, there is lack of evidence comparing different anaesthesia techniques and mortality rates in patients submitted to major surgeries.

An explanation for these results is that, with adequate postoperative pain control, the patients present themselves in clinical conditions favourable to an evolution with less complications: without pain, less postoperative opioids are needed, easing the occurrence of *fast track*. Besides that, the patient tends to awake calmer at the Intensive Care Unit, which makes it easier for his extubating and return to spontaneous ventilation; the ambulation starts earlier and abilities such as eating on one's own and returning to biological functioning are established more precociously. The combination of these factors results in an overall shorter length of admission, which significantly reduces the risks for complications and mortality.

The main advantage for administering opioids in spinal or epidural anaesthesia is that, since it is an administration on target organs, low doses cause a potent, long-lasting pharmacological effect of analgesia (up to 24 hours), parameters far superior to those obtained with intravenous administration during general anaesthesia. In fact, spinal or epidural anaesthesia have the potential to block the afferent nociceptive route. This results in a significant reduction of central sensibilization which occurs on medullar level, and is one the events responsible for hyperalgesia, allodynia, and chronic pain [21-23].

It is also known that, when postoperative analgesia is often superior, it can reduce systemic opioid consumption, orotracheal intubation time (OIT), and pulmonary morbidity [24]. The choice of an adequate anesthetic technique and the conduction of the organic changes intrinsic to these procedures are of major importance for the survival and quality of life of the individuals who undergo this type of treatment.

This study has some drawbacks that need to be considered. In the opinion of the authors, the major limitation is related to the fact that the present study has a retrospective design, which may influence the results reported here. Another important point is related to the diversity of surgeries included in the analysis, which may have directly affected the observed mortality rates. Therefore, future studies are necessary to confirm these results.

There is not a consensus relating to the most adequate anaesthetic protocol for patients submitted to major surgery. There is also a lack of population- based studies showing whether this combined technique is more effective or even more advisable for certain surgical procedures. In this context, our work contributes towards the establishment of more adequate conducts in the anaesthetic management of patients which underwent major surgery, aiming for lower rates for complications and mortality.

CONCLUSION

It may be concluded that, in patients with higher anaesthetic risk, a combined anaesthesia technique (epidural or spinal anaesthesia combined with general anaesthesia) could reduce orotracheal intubation time, intensive care unit length of stay, hospital length of stay and mortality rate in patients submitted to major surgeries.

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