EFFECTS OF BUTORPHANOL AND FENTANYL ON CEREBRAL PRESSURES AND CARDIOVASCULAR HEMODYNAMICS DURING TUNNELING PHASE FOR VENTRICULOPERITONEAL SHUNT INSERTION

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Summary

Purpose: Subcutaneous tunneling for ventriculoperitoneal shunt insertion is the most painful step of this surgery. It is associated with intense hemodynamic response, may influence the intracranial pressure, and thus may worsen the existing intracranial pathology. The purpose of this report is to evaluate the commonly used opioid fentanyl, along with butorphanol, an agonist-antagonist compound.

Methods: Twenty adult patients undergoing ventriculoperitoneal shunt surgery were induced with fentanyl 2-mcg.kg^{-1} and thiopentone 4-5 mg.kg^{-1}. Intubation followed the administration of rocuronium 1 mg.kg^{-1}. All patients were put on mechanical ventilation to maintain end-tidal

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carbon dioxide levels of 32 ± 2 mmHg. Anesthesia was maintained with isoflurane in N_2O and O_2 (MAC 1.0 ± 0.2). Routine monitoring, arterial blood pressure and intracranial pressures were measured. Three minutes prior to the tunneling phase, patients received either fentanyl 1 $mcg.kg^{-1}$ or butorphanol 1 mg in a randomized manner. Thereafter hemodynamic and intracranial pressure changes were noted during tunneling and each minute in the post-tunneling period for 5 minutes. The duration of the tunneling phase was also noted. Data were presented as number (proportion) or mean ± SD/median (range) as appropriate. Statistical analysis was done using Wilkoxon ranksum test and the repeated measures of ANOVA. The value of $p < 0.05$ was considered significant.

Results: A significant rise in the intracranial pressure and cerebral perfusion pressure along with the hemodynamic parameters was noted during the tunneling phase in both groups. The changes were of longer clinical duration in the butorphanol group.

Conclusion: Butorphanol must be used with caution in neurosurgical patients. The ventricular end of the shunt catheter should preferably be put before the tunneling phase to avoid rise in intracranial pressure.

Keywords: Opioids; Ventriculoperitoneal shunt surgery; Tunneling phase; Intracranial pressure; Cerebral perfusion pressure.

Introduction

The tunneling phase of ventriculoperitoneal shunt surgery is the most painful step of the procedure. Although analgesia for scalp and abdominal sites, is provided by infiltration with local anesthetic and a vasoconstrictor, the subcutaneous tunneling, the most painful step, occurs towards the end of the procedure. Systemic analgesia is often suboptimal, for fear of postoperative delayed recovery and respiratory depression[1,2]. This is critical in neurosurgical patients with previously altered levels of consciousness.

Hemodynamic responses to tunneling are usually blunted by increasing the concentration of the inhalational volatile anesthetic or the

use of intravenous anesthetic like propofol. However, this may produce cardiovascular depression compromising cerebral perfusion pressure. Neurosurgical patients with an altered cerebral physiology are always at risk with such fluctuations in arterial pressure[3].

The effect of tunneling phase on the hemodynamics has been studied earlier[1,4] and the changes in intracranial pressure and cerebral perfusion pressure are anticipatory. Fentanyl, a phenylpiperidine-derivative synthetic opioid agonist that is structurally related to meperidine, is a commonly used opioid in neurosurgical cases. Fentanyl has greater analgesic potency and a shorter duration of action than its congener. Butorphanol, an agonist-antagonist compound, however, that resembles pentazocine, is a less studied drug in neurosurgical cases. It is nonaddicting with limited depressant properties. The fact that butorphanol is an agonist-antagonist compound and so less likely to produce respiratory depression and drowsiness, when compared to fentanyl, lead us to select this drug for our study.

The purpose of the current observational investigation, a prospective randomized and double blinded, was to evaluate the effects of butorphanol and fentanyl on hemodynamics and intracranial pressure during the tunneling phase of ventriculoperitoneal shunt surgery.

Materials and Methods

Our local Ethical Committee granted permission for this human experimentation. Written consent was taken from patients or their guardians. Twenty adult patients, ASA I, II scheduled elective ventriculoperitoneal surgery for various intracranial pathologies, were selected. Patients with previous intracranial surgery, head injuries, shunt revision, hypertensives, diabetics and any other systemic illness, were excluded.

The 20 patients were equally divided and randomly allocated (by computer-generated random numbers) to receive either fentanyl 1.0 mcg. kg^{-1} (Group F) or butorphanol 1 mg (Group B), three minutes before the tunneling phase of shunt insertion.

Standard fasting intervals were applied to all the patients. All patients were premedicated with i. m Glycopyrrolate 0.2 mg, 1 hour prior to surgery. A baseline pre-induction heart rate, non-invasive blood pressure and SpO_2 were noted in the operation theatre, (Datex-Engstrom AS/3, Helsinki, Finland). An intravenous line was secured on the dorsum of the hand using an 18-G cannula.

General anesthesia was induced with fentanyl 2.0 $mcg.kg^{-1}$ and thiopentone 4-5 $mg.kg^{-1}$. Endotracheal intubation was facilitated with rocuronium 1 $mg.kg^{-1}$. Following intubation, an arterial line was placed in the dorsalis pedis artery of either foot. This helped us monitor the invasive blood pressure continuously. Anesthesia was maintained with isoflurane (MAC~1 ± 0.2) in a mixture of O_2 and N_2O (1:2). Mechanical ventilation was instituted to maintain and end-tidal carbon dioxide tension of 32 ± 2 mmHg. Neuromuscular blockade was achieved with vecuronium that was adequately reversed at the end of surgery. All patients received normal saline for rehydration and maintenance during the surgery.

Following local infiltration with 2% lignocaine with adrenaline at sites of incision, the surgeon was asked to place the ventricular end of the shunt catheter first. This intraventricular catheter was connected via an extension line to the pressure transducer. The transducer was zeroed to the atmosphere at the level of the mastoid. Three minutes prior to tunneling, the study drug was given intravenously. Steady state variables of heart rate, mean arterial pressure and intracranial pressure were noted.

The tunneling phases included the abdominal as well as the thoracic and scalp tunneling. During the entire tunneling phase, the maximum rise in heart rate, mean arterial pressure and intracranial pressure, were noted. The values of the three variables were recorded subsequently for another five minutes at one-minute interval. The total duration of the tunneling phase was also noted. Cerebral perfusion pressure was calculated as the difference of the mean arterial pressure and mean intracranial pressure (MAP-ICP). Towards the end of surgery, anesthetic gases were discontinued. Neuromuscular blockade was reversed with neostigmine and glycopyrrolate. All patients were extubated and transported to the neurosurgery ICU.

Statistical analysis was done using STATA 9.0 (College Station, TX, USA). Data are presented as either number (proportion) or mean ± SD/ median (range) as appropriate. The baseline characteristics such as age, weight, duration of tunneling and pre-tunneling parameters were compared between the groups using Wilcoxon ranksum test as the data was non-normal, whereas sex variable was analyzed using Fisher exact test. All cardiovascular and cerebrovascular parameters (HR, MAP, ICP and CPP) were compared between and within the group over a period of time using repeated measures of ANOVA followed by post-hoc analysis (Bonferroni correction). The value of P less than 0.05 was considered significant.

Results

A total of 10 patients of either gender were studied in Group B & Group F. Patients suffered of various intracranial pathologies. The demographic data along with the baseline characteristics of the patients were comparable between the two groups (Table 1).

Table 1

Baseline characteristics expressed as [number (proportion)/median (range)] of patients in butorphanol and fentanyl group. (M: male; F: female; HR: heart rate; MAP: mean arterial pressure; ICP: intracranial pressure; CPP: cerebral perfusion pressure; bpm: beats per minute).

Parameters	Group-B (n = 10)	Group-F (n = 10)	p-value
Age (yrs)	29 (18-40)	26.5 (21-55)	0.91
Sex			
M	6 (60%)	6 (60%)	1.0
F	4 (40%)	4 (40%)	1.0
Weight (kg)	60 (35-70)	53.5 (35-70)	0.73
Pre-tunneling values-			
HR (bpm)	71.5 (54-86)	72.5 (55-98)	0.94
MAP (mmHg)	81 (62-96)	87 (70-107)	0.43
ICP (mmHg)	28 (14-55)	19.5 (13-47)	0.38
CPP (mmHg)	51 (26-79)	62.5 (25-88)	0.15

The cerebral pressures and cardiovascular hemodynamic parameters during the study period are tabulated in (Table 2).

Table 2

Hemodynamic and intracranial pressure changes during tunneling phase of ventriculoperitoneal shunt insertion in the two study groups. (B: butorphanol group; F: fentanyl group; HR: heart rate; MAP: mean arterial pressure; ICP: intracranial pressure; CPP: cerebral perfusion pressure; bpm: beats per minute; PT: pre-tunneling; Tmax: Maximum rise during tunneling phase).

Variables	Mean ± SD							P value
	PT	Tmax	1	2	3	4	5	
HR (bpm)								
B Group	72.6±9.4	85.3±13.0*	79.2±11.7*	76.9±10.5*	75.1±10.9	74.3±10.0	73.6±10.8	0.96
F Group	73.8±16.2	86.0±21.0*	80.3±18.8*	77.6±16.9	75.0±15.7	73.7±15.9	72.8±15.5	
MAP (mmHg)								
B Group	81.6±9.4	108.2±13.2*	100.5±14.4*	96.4±11.8*	94.2±12.7*	91.7±12.8*	89.2±12.8*	0.99
F Group	87.7±13.5	111.7±14.5*	99.3±13.5*	93.7±12.8	90.7±13.0	89.5±12.8	89.0±13.3	
ICP (mmHg)								
B Group	27.9±12.2	37.4±18.0*	35.3±18.1*	34.5±16.6*	34.8±16.9*	34.4±16.1*	34.0±16.0*	0.31
F Group	24.0±11.4	32.3±17.4*	28.3±14.5*	27.6±13.7*	26.7±12.1*	26.3±12.1	25.5±11.3	
CPP (mmHg)								
B Group	53.7±14.8	70.8±15.9*	65.2±16.4*	62.5±16.0*	59.8±17.4	57.3±18.1	55.2±19.5	0.40
F Group	63.7±18.3	79.4±21.7*	71.0±21.4	66.1±19.7	64.0±18.7	63.2±17.7	63.5±17.8	

There was a statistically significant increase in all the parameters when compared with the base line values in both groups. The mean arterial pressure and the intracranial pressure in the butorphanol group (Group B) remained significantly high throughout the study period of five minutes after the tunneling phase. In the fentanyl group (Group F), the two parameters, mean arterial pressure and intracranial pressure, remained significantly raised till 1 minutes and 3 minutes, respectively. However, the trend in both the groups, when compared. were not significant ($p = 0.9$ and 0.3 respectively for MAP and ICP). The change in the cerebral perfusion pressure was noted to be significantly raised for 2 minutes in the butorphanol group.

The changes can be appreciated in the graphs showing the trends of heart rate, mean arterial pressure, intracranial pressure and the cerebral perfusion pressure (Fig. 1-4).

Fig. 1

Graphical trends showing changes in the heart rate during the tunneling phase of ventriculoperitoneal shunt insertion in Groups B & F.

HR: heart rate; B: butorphanol group; F: fentanyl group; PT: pre-tunneling; Tmax: Maximum rise during tunneling phase; T1-T5-1 to 5 minutes post-tunneling phase.

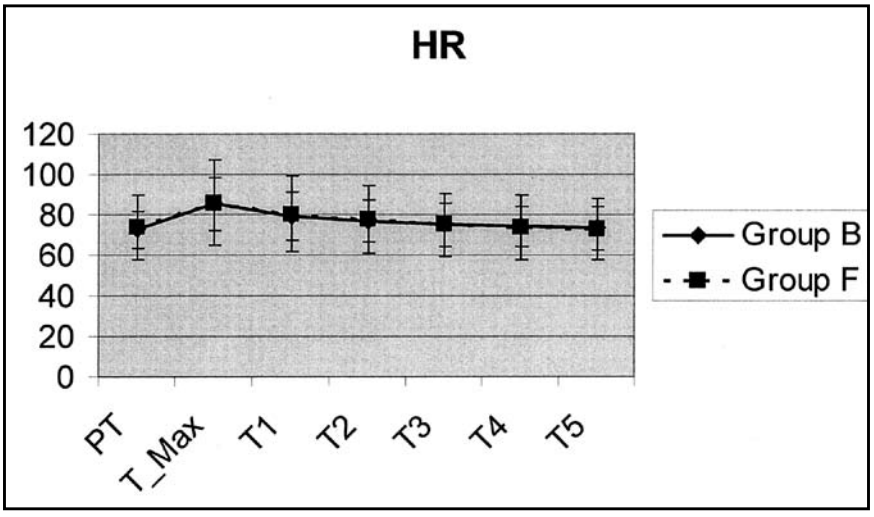


Fig. 2

Graphical trends showing changes in the mean arterial pressure during the tunneling phase of ventriculoperitoneal shunt insertion in Groups B & F.
MAP: mean arterial pressure; B: butorphanol group; F: fentanyl group;
PT: pre-tunneling; Tmax: Maximum rise during tunneling phase;
T1-T5-1 to 5 minutes post-tunneling phase.

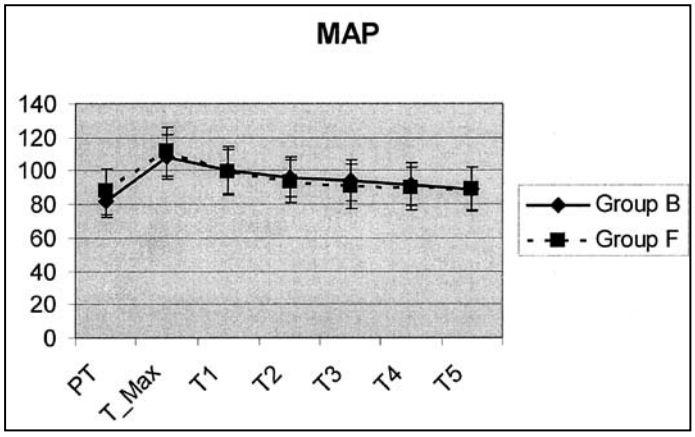


Fig. 3

Graphical trends showing changes in the intracranial pressure during the tunneling phase of ventriculoperitoneal shunt insertion in Groups B & F.
ICP: Intracranial pressure; B: butorphanol group; F: fentanyl group;
PT: pre-tunneling; Tmax: Maximum rise during tunneling phase;
T1-T5-1 to 5 minutes post-tunneling phase.

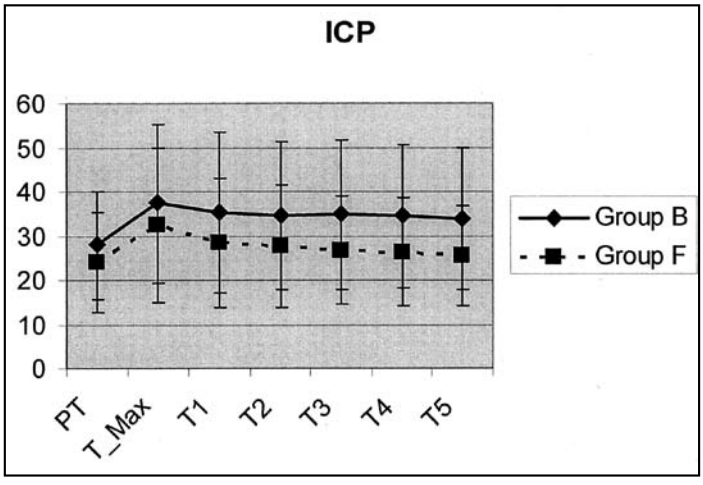
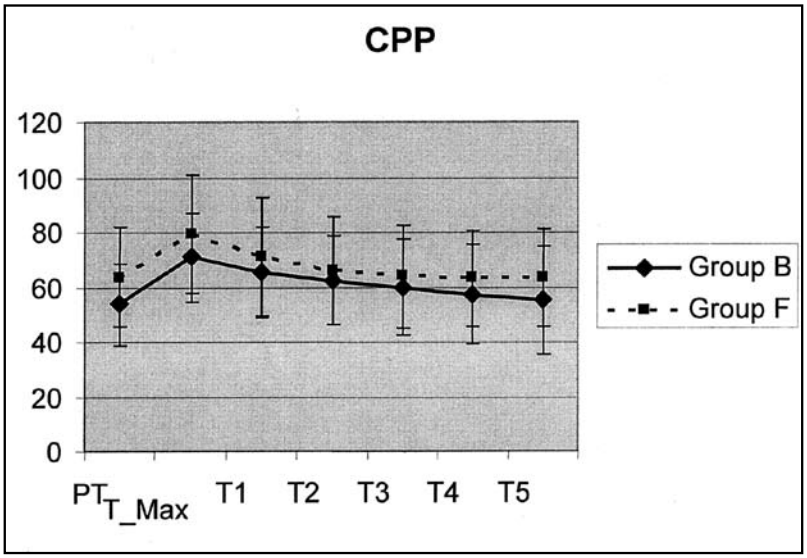


Fig. 4

Graphical trends showing changes in the cerebral perfusion pressure during the tunneling phase of ventriculoperitoneal shunt insertion in Groups B & F.
CPP: Cerebral perfusion pressure; B: butorphanol group; F: fentanyl group;
PT: pre-tunneling; Tmax: Maximum rise during tunneling phase;
T1-T5-1 to 5 minutes post-tunneling phase.



The total median duration of the tunneling phase was 2.12 minutes (1.0-3.3) in fentanyl group and 2.4 minutes (1.0-4.0) in butorphanol group, the values being comparable ($p = 0.38$).

All patients were awake at the end of the surgery and were extubated. All patients were assessed neurologically and shifted to the neurosurgery ICU.

Discussion

One of the objectives of neurosurgical procedures is to achieve an early recovery after anesthesia to facilitate the neurologic evaluation of the patient. This inadvertently results in suboptimal anesthetics in short procedures such as ventriculoperitoneal shunt.

In a preliminary study, Prabhakar and colleagues[4] observed during the tunneling phase of ventriculoperitoneal shunt insertion, a tremendous rise in the intracranial pressure as a result of increased arterial blood pressure despite fentanyl administration prior to tunneling. In the present study it was also found that there was a significant increase in the hemodynamic and intracranial pressures in both groups. The rise was remarkably persistent in the butorphanol group unlike the fentanyl group where the parameters returned to their base line values within the study period of five minutes post tunneling phase. The effect of butorphanol on the intracranial pressure, as documented by our study, warns us of the use of this drug in neurosurgical cases.

Although arterial pressure is the principal determinant of cerebral perfusion pressure, changes in the intracranial pressure and central venous pressure will influence cerebral perfusion pressure, and unless extreme are also compensated for by the autoregulatory changes in cerebrovascular resistance[5]. In the setting of an already compromised cerebral perfusion pressure, sudden upsurge in intracranial pressure and arterial pressure can predispose to intraventricular hemorrhage and cerebral ischemia. In our study, the anesthetic agents used were appropriate for neurosurgical cases. There is no clinical evidence of meaningful intracranial pressure increase during craniotomy following narcotic administration, rather narcotics in the absence of hyperventilation, tend to cause either no change or a small decrease in intracranial pressure in patients with intracranial mass lesion. Because narcotics do not alter cerebral carbon dioxide reactivity, their combination with hypocapnia accounts for the resulting favorable effect upon the brain bulk and intracranial pressure[6,7].

Narcotics are routinely use as analgesics in neurosurgery. The term “narcotic” describes a class of drugs that exhibit properties similar to morphine. Opioid drugs with morphine-like properties may be strong agonists, partial agonists, or competitive antagonists at receptors that share common characteristics. Fentanyl citrate is a semisynthetic derivative of meperidine and provides analgesia in low doses of 1-2 $mcg.kg^{-1}$. Butorphanol tartrate is a totally synthetic nonaddicting analgesic of high

potency and with limited respiratory effect in humans[8]. Butorphanol is an agonist-antagonist compound and so respiratory depression is generally less due to its antagonistic action at the mu receptors. Its moderate affinity for kappa receptors produces analgesia and antishivering effect[9]. However, this drug has not gained popularity in neurosurgical cases. This formed the basis for selecting butorphanol as our study drug. Higher doses of opioids are usually avoided for fear of postoperative delayed recovery and respiratory depression. This is of particular importance in neurosurgical cases where respiratory depression may lead to hypercapnia increasing intracranial volume or may require postoperative artificial ventilation. Studies have shown that fentanyl affects intracranial pressure and cerebral perfusion pressure less than other opioids in patients with supratentorial mass lesion[10,11]. Newer opioids, like remifentanil. Has been shown to be effective analgesic with good recovery in pediatric neurosurgical patients undergoing ventriculoperitoneal shunt insertion[2].

There is tendency to increase the concentration of volatile anesthetic during the tunneling phase to obtund the stress response. In clinical studies, cerebral autoregulation is impaired during 1.5 MAC isoflurane[12,13]. We kept a constant minimum alveolar concentration less than 1.5 to avoid any alteration in the cerebral physiology. From their study, Fraga and colleagues[14] concluded that in normocapnic patients with their supratentorial tumoral pathology without midline shift on the CT scan, administration of 1 MAC isoflurane decreases cerebral perfusion pressure because of decrease in the mean arterial pressure, but it does not increase the intracranial pressure.

The muscle relaxant vecuronium has an intermediate duration of action with minimal hemodynamic side effects in humans. In fact, Stirt and co-workers[15] noted a decrease in the intracranial pressure and mean arterial pressure after vecuronium, without significant changes in the cerebral perfusion pressure in patients with supratentorial tumours.

In our study a standard technique of placing the ventricular end of the shunt in the more dilated lateral ventricle was applied to all patients. This avoided the bias of differential intracranial pressures in patients who had a unilateral mass lesion[16]. Although studies have compared butorphanol and

fentanyl in various groups of patients before[17], our study is the first of its type.

Every attempt was made to minimize bias by conducting the study in a double-blind manner. The volume of drugs was the same and the liquids were clear and odorless. All our patients had a good postoperative recovery. All patients were successfully extubated and showed no signs of drowsiness and respiratory depression in the neurosurgical intensive care unit. This could be because of the lower doses of fentanyl and butorphanol used.

Finally one has to consider the ethics of doing such a trial. For instance, having recorded a rise in the intracranial pressure, we took no measures to reduce it till the end of our study period of five minutes. Later though, we did resort to CSF withdrawal via a three-way stopcock present in the ICP monitoring assembly. This was the most feasible method of ICP reduction at that time. We recommend that the ventricular end of the drain always be placed before the tunneling phase. This would not only help us monitor the intracranial pressure but also drain the cerebrospinal fluid in case of rise of intracranial pressure during the tunneling phase.

To conclude, our study compared the effects of fentanyl and butorphanol on the hemodynamic and intracranial pressure changes during the tunneling phase of ventriculoperitoneal shunt insertion. There occurs a statistically significant rise in the parameters noted but the changes were for a clinically longer duration in the butorphanol group as compared to the fentanyl group. This definitely warns us of the use of butorphanol in neurosurgical patients.

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