EFFECT OF PRESSURE SUPPORT LEVEL, PATIENT’S EFFORT, AND LUNG MECHANICS ON PHASE SYNCHRONY DURING PRESSURE SUPPORT VENTILATION

GHAZI A. ALOTAIBI*

Abstract

**Background:** Pressure support ventilation (PSV) is used to encourage spontaneous breathing and facilitate weaning. During PSV, duration of the breath is not set, but controlled by the patient, and influenced by some ventilator settings. There is no guarantee that the PS breathe will match start and end of patient’s breathe. Indeed, patient-ventilator breath mismatching during PSV is the rule, not the exception.

**Objective:** This bench study was conducted to investigate effects of varying PSV, patient’s effort, and lung mechanics on trigger response time (TRT), and expiratory delay time (EDT).

**Methods:** We used an electromechanical lung simulator (ASL 5000) to create different clinical scenarios. The simulator was set at 15 b/min and inspiratory time of 1 sec. In experiment I, we used 5, 10, 15, and 20 cm H$_2$O of PS at each level of patient effort (Pmus) of 3, 6, and 10 cm H$_2$O. In the second experiment, we set airway resistance (R) at 5, 10, and 20 cm H$_2$O/L/s at each compliance (C) level of 30, 60, and 90 ml/cm H$_2$O. For each combination of setting, we analyzed 5 consecutive breaths and calculated TRT and EDT. Mean values of TRT and EDT for each scenario were reported and compared for trends and statistical significance.

**Results:** At each given Pmus, increasing PS produced shorter TRT. This effect seems to plateau at higher PS levels. Significant change ($p<0.01$) in EDT was noticed with increase in PS setting. Pmus alone did not affect trigger or cycle delay times. Increasing airway resistance caused an increase in TRT, except when R$_5$ was increased to R$_{10}$ at compliance levels of 30 and 60 ml/cm H$_2$O. Similarly, increasing compliance significantly lengthened TRT. Higher R and C produced extended EDT, casing major expiratory asynchrony.

**Conclusion:** This study delineates direction of effect for certain individual variables on patient-ventilator synchrony. Results of this study should help clinicians understand the complexity of synchrony issue.

**Keywords:** Ventilator synchrony, lung model, trigger synchrony, expiratory synchrony, lung mechanics.

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* PhD, RRT, Assistant Professor of Respiratory Care.
Affiliation: College of Applied Medical Sciences, University of Dammam, Saudi Arabia.
**Corresponding author:** Ghazi A. Alotaibi, PhD, RRT, Assistant Professor of Respiratory Care, King Fahad University Hospital, P.O. Box: 40269, Dammam 31952, Saudi Arabia. Tel: 00966500558006. E-mail: Galotaibi@ud.edu.sa
Introduction

There has been a trend in mechanical ventilation practice to allow early spontaneous breathing to share work of breathing between patient and ventilator. Studies have shown that maintaining spontaneous breathing during ventilatory support preserves diaphragmatic function, improves respiratory mechanics, and speeds up liberation from mechanical ventilation. Applying spontaneous breathing during mechanical ventilation requires a high degree of synchrony between patient and ventilator. The ventilator is synchronous with the patient when it delivers inflation in a timely manner with patients’ neural time, and provides flow and pressure sufficient to unload work of breathing. Literature indicates that level of synchrony in majority of ventilated patients may not be optimal. In a study of 60 ventilated patients on pressure support ventilation (PSV), significant asynchrony was reported in 27% of the patients. Mismatch between patient’s ventilatory needs and the ventilator settings can lead to many deleterious effects, such as discomfort, increased patient’s work of breathing, longer duration of ventilation, and longer hospital and intensive care unit (ICU) length of stay.

Pressure support is a commonly used mode of gradual ventilatory support. PSV allows patient to control breathing profile. Breaths are triggered and terminated based on patient’s efforts, lung mechanics, and certain ventilator settings. Patient-ventilator interaction during PSV has been investigated by numerous research studies. Starting and ending the mechanical breath in relation to patients’ neural inspiratory time (Ti) have been a major concern during PSV. Phase synchrony refers to the extent at which ventilator breaths start and end with the patient’s. Optimal matching of mechanical inflation to patient’s breath seems to be the exception not the rule. Ventilator triggering is controlled by setting pressure or flow threshold that the patient must achieve in order to trigger the ventilator. Trigger sensitivity, ventilator sensor performance, patient’s effort, flow rise, and presence of dynamic hyperinflation are among factors that could interfere with triggering function. Dyssynchrony during trigger phase has been reported in 26-82% of patients receiving assisted ventilatory support. Work excreted during asynchronous trigger phase could be as high as 50% of total work of breathing. Breath termination, or cycle, is modulated in most commercially available ventilators by setting a flow threshold so that the breath is terminated when a threshold value is reached. Improperly set cycle criteria results in a mechanical breath that is either precedes (early cycle) or comes after patient’s neural timing (delayed cycle). In both situations, workload on patient increases, and discomfort ensues. Breath termination is affected by set expiratory threshold, flow profile, patient’s effort, and lung mechanics.

Based on available research work, timing mechanical breath to coincide with start and end of patient’s neural inspiratory time (Ti) is crucial for optimal patient-ventilator interaction. This interaction is affected by a delicate balance of several patient-and ventilator-related factors. Many investigators have studied effects of some ventilator settings and lung mechanics on patient-ventilator synchrony. However, effects of individual factor on phase synchrony during trigger and cycle have not been addressed clearly in these studies. Therefore, we conducted this bench research to study influences on varying PSV level, patient’s effort, airway resistance and lung compliance on trigger response and expiratory delay times.

Methods

Lung Simulator

To simulate different clinical scenarios, we used Active Servo Lung 5000 (ASL5000) (Ingmar Medical, Pittsburgh, USA). The ASL5000 is an electromechanical simulator, composed of a piston moving inside a cylinder. The simulator was connected to a software that allows variety of waveform depictions and calculated variables. Patients’ breathing profile can be configured and controlled by the application software, which uses Equation of Motion to achieve simulated settings. ASL5000 is classified as a high fidelity simulator with capability of initiating spontaneous breathing, varying breathing effort, and modulating resistance (R) and compliance (C).
Experimental Protocol

Puritan Bennet 840 ventilator (Galaway, Ireland) was connected the ASL5000 simulator via adult ventilator circuit with heated humidifier. Experimental setup is shown in Figure 1. The ventilator was set on 5 cm H₂O of pressure support (PS), 4 cm H₂O of positive end expiratory pressure (PEEP), 21% of oxygen, 2 L/min of flow trigger, and expiratory sensitivity (Esens) of 20%. Breathing rate on lung simulator was set at 15 b/min, inspiratory time (Ti) of 1 sec, rise time of 50%, breathing effort (reflected by muscle pressure, Pmus) of -3 cm H₂O with sine wave pattern, compliance (C) of 60 ml/cm H₂O, and resistance (R) of 5 cm H₂O/L/s. To study effects of changing PS level, patient’s efforts, and changes in lung mechanics on trigger and cycle functions, we conducted 2 experiments. See Table 1 for protocol settings.

Experiment I: Changing PS and Patient’s effort.

Using the baseline settings for the ventilator and lung simulator as above, we programmed a script file on the simulator to produce 3 levels of breathing efforts simulating low, medium, and high efforts. Pmus of -3, -6, and -10 cm H₂O were programmed in the script file to last for 300 breaths. For each Pmus setting, PS level was manually adjusted on the ventilator to achieve 5, 10, 15, and 20 cm H₂O every 20 breaths.

Experiment II: Changing Pulmonary Mechanics.

Using the baseline settings for the ventilator and lung simulator as above, we programmed another script file on ASL5000 simulator to produce 3 levels of lung compliance, simulating stiff, normal, and high compliance. Compliance settings of 30, 60, and 90 ml/cm H₂O were programmed in the script file to last for 200 breaths. For each compliance level, Resistance of 5, 10, and 15 cm H₂O/L/s were programmed so that each resistance setting lasts for 20 breaths.

Fig. 1
Experimental Setup

Fig. 2
Representative Tracings of Muscle Pressure (Pmus), Airway Presser, and Flow to illustrate definitions of studied variables.
Table 1
Protocol for Pressure Support (PS), Muscle Pressure (Pmus), Resistance, and Compliance during Experiments I and II

<table>
<thead>
<tr>
<th>Experiment I</th>
</tr>
</thead>
<tbody>
<tr>
<td>PS (cm H₂O)</td>
</tr>
<tr>
<td>5  10  15  20</td>
</tr>
<tr>
<td>Pmus (cm H₂O)</td>
</tr>
<tr>
<td>3  3  3  3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Experiment II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resistance (cm H₂O/L/s)</td>
</tr>
<tr>
<td>5  10  20</td>
</tr>
<tr>
<td>Compliance (ml/cm H₂O)</td>
</tr>
<tr>
<td>30  30  30</td>
</tr>
</tbody>
</table>

Table 2
Mean Measured Parameters during Experiment I

<table>
<thead>
<tr>
<th>Pmus (cm H₂O)</th>
<th>3</th>
<th>6</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>PS (cm H₂O)</td>
<td>5</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>TRT (ms)</td>
<td>165</td>
<td>136</td>
<td>127</td>
</tr>
<tr>
<td>PFR (l/min)</td>
<td>56</td>
<td>90</td>
<td>124</td>
</tr>
<tr>
<td>PIP (cm H₂O)</td>
<td>9.8</td>
<td>14.9</td>
<td>20</td>
</tr>
<tr>
<td>VT (ml)</td>
<td>357</td>
<td>659</td>
<td>952</td>
</tr>
<tr>
<td>EDT (ms)</td>
<td>0</td>
<td>54</td>
<td>88</td>
</tr>
</tbody>
</table>

Table 3
Mean Measured Parameters during Experiment II

<table>
<thead>
<tr>
<th>Compliance (ml/cm H₂O)</th>
<th>30</th>
<th>60</th>
<th>90</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resistance (cm H₂O/L/s)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>10</td>
<td>20</td>
<td>5</td>
</tr>
<tr>
<td>TRT (ms)</td>
<td>142</td>
<td>160</td>
<td>169</td>
</tr>
<tr>
<td>PFR (l/min)</td>
<td>59</td>
<td>38</td>
<td>24</td>
</tr>
<tr>
<td>PIP (cm H₂O)</td>
<td>9.7</td>
<td>9.4</td>
<td>9.2</td>
</tr>
<tr>
<td>VT (ml)</td>
<td>349</td>
<td>279</td>
<td>204</td>
</tr>
<tr>
<td>EDT (ms)</td>
<td>-150</td>
<td>-41</td>
<td>55</td>
</tr>
</tbody>
</table>

Pₘus = muscle pressure, PS = pressure support, TRT = trigger response time, PFR = peak flow rate, PIP = peak inspiratory pressure, VT = tidal volume, EDT = expiratory delay time.
**Data Collection and Measurement**

Measurements were taken for each level of PS during the 3 settings of patient’s effort (12 combinations), and for each level of Resistance during the 3 settings of compliance (9 combinations). Trigger response time, expiratory delay time, peak flow rate, peak inspiratory pressure, and exhaled tidal volume were recorded. For each combination of set parameters, measurement were recorded from 5 consecutive breaths after one-minute of stabilization period. As depicted in Figure 2, trigger response time (TRT) was measured as the time from the start of patient effort (drop in Pmus) to the point where airway pressure returns back to baseline (ie. PEEP). Expiratory delay time (EDT) was defined as the time from the end of patient’s effort (Pmus returns back to zero) to the time when ventilator’s flow reaches zero. Referring to Figure 2, EDT is positive when the ventilator ceases flow after end of patient’s effort (late termination), or negative when the ventilator ends inflation while patient’s effort still in action (early termination).

**Data Analysis**

Data was analyzed using SPSS version 16.0. The variables were described using means and standard deviations. All comparisons were tested for statistical significance using one-way ANOVA. Post hoc analysis was performed using Bonferroni’s correction method. Significance level was considered as $p$ value < 0.01.

**Results**

Mean values of measured parameters are shown in Tables 2 and 3. Because of high precision of the lung simulator used in this study, standard deviation for each set of measurements was very small. Therefore, it was not shown in the tables.

**Experiment I**

Effect of changes in PS and Pmus on TRT are shown in Table 2 and Figure 3. As PS increases, TRT decreases at all levels of Pmus. Within each Pmus level, all reductions in TRT were statistically significant ($p<0.01$), expect when PS10 was increased to PS20 at all Pmus levels. Table 2 shows effect of increased effort on TRT. Increasing Pmus did not significantly affect TRT at the same PS level, expect comparison between Pmus 3 and Pmus 10 at PS of 5, and comparison between Pmus 6 and Pmus 10 at PS of 5. As shown in Figure 3, it is notable that the effect of increased effort on TRT is mitigated by the increase in PS. Figure 4 depicts effect of PS and Pmus on EDT. At each given Pmus level, increases in PS increased EDT significantly ($p<0.01$). Increased Pmus alone did not change EDT at all PS.
levels, except when Pmus was increased from 3 to 10 cm H₂O at PS of 15 and 20 cm H₂O. This finding suggests that the effect of increased patient’s effort on EDT becomes more apparent at higher PS settings.

Experiment II

Changes in pulmonary mechanics and their effects on TRT and EDT are shown in Table 2 and Figures 5-6. Figure 5 plotted effect of changes in compliance and resistance on TRT. At each given compliance level, there was a trend towards increase in TRT as resistance increases. That trend was statistically significant (p<0.01) in all comparisons except when R5 was increased to R10 at C30 and C60. Similarly, increases in lung compliance increased TRT at every given resistance. Effects of compliance on TRT were statistically significant (p<0.01) for all comparisons except when C30 was increased to C60 at R10, and C60 was increased to C90 at R5. In Figure 6, EDT is plotted as a positive bar when ventilator ends inspiration after the patient, and a negative bar when ventilator terminates inspiration prematurely. At any given compliance level, increases in resistance made the breath to terminate later, leading to delayed termination. All changes on EDT as a result of increased resistance were statistically significant (p<0.01), except when resistance was increased from 10 to 20 at higher lung compliance (C90). Similarly, increases in
lung compliance at any given resistance led to delayed breath termination. All comparisons were statistically significant ($p<0.01$).

**Discussion**

The main findings of the present bench study can be summarized as follow; (1) As level of set PS increases, time required to trigger the ventilator becomes shorter but expiratory delay time increases; (2) patient’s effort seems to have little effect on trigger and cycle delay times; (3) higher pulmonary resistance was found to be associated with longer trigger time and delayed breath termination; (4) as lungs become stiffer, trigger time becomes shorter and mechanical breaths tend to terminate earlier.

Pressure support is a very common mode of partial ventilation and waning. Pressure support level is adjusted to achieve optimal work of breathing and patient’s comfort. In our study, we report inverse relationship between PS level and TRT when other factors are unchanged. Speed of pressurization was set at a medium value (50%) throughout this study. Reduction in TRT as a consequence of increased PS level can be explained by the sharp rise of flow that accompanied higher PS. Increasing PS level involves higher $V_T$ and flow, pushing the negative airway pressure to return to baseline faster as compared to lower PS level. As a result, TRT becomes shorter. Reduction in TRT was attenuated when PS increases from 15 to 20 cm H$_2$O at all Pmus levels. We speculate that the rate at which negative airway pressure decays to baseline has reached its maximum at PS of 15 cm H$_2$O. Therefore, further increase in PS would not significantly affect TRT. Murata et al$^{17}$ studied the effect of different levels of inspiratory rise time and reported that faster rise time reduced duration of post-trigger phase (the time from maximum drop in airway pressure during trigger to the return to baseline). This finding support our explanation of TRT reduction as a result of increased PS. In real clinical situations, effect of increasing PS on TRT is extenuated by reduction in patient’s effort as a response to PSV unloading. In such case, less trigger effort will be exerted by patient, extending TRT or even causing missed trigger. The net effect may be unappreciable change in TRT, but depends on level of trigger work unloading by PS. This relationship between PS level and TRT has clinical implications. In clinical practice, it is common to wean PS level as patient recovers to allow more spontaneous breathing and muscle reconditioning. When PS reaches an under-assist level, effect on TRT becomes more exaggerated, prolonging trigger delay time and worsening patient-ventilator synchrony. Contrary to our finding, Thille et al$^7$ found that patient-ventilator synchrony was improved with lower PS. As explained by the authors, improvement in synchrony reported in their study was attributed to lower $V_T$, shorter inflation time, and reduction in intrinsic PEEP associated with lower PS. As a result, ineffective triggers were eliminated. In our study, intrinsic PEEP and ineffective triggers were not part of the protocol.

Manipulation of PS does not only affect trigger

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**Fig. 6**

*Effect of Changes in Resistance (R), and Compliance (C) on Expiratory Delay Time (EDT)*

![Diagram showing effect of changes in resistance and compliance on expiratory delay time](image-url)
phase, it extends to influence breath termination. Higher levels of PS produce larger \( V_T \) and longer inflation times. If patient’s neural Ti does not change considerably, mechanical breath continues beyond patient’s neural timing. Because expiratory trigger point is set as a percent threshold (20% in our protocol), higher \( V_T \) and flow will cause cycle point to be reached late, causing delayed breath termination. Delayed breath termination is uncomfortable to patient and could recruit active expiratory muscles, increasing work of breathing. In patients with airflow limitation diseases, such as asthma and COPD, late termination of the breath could be very harmful. Less time will be available for expiration, leading to dynamic hyperinflation and worse patient-ventilator synchrony.

According to our study, lowering PS led to shorter EDT. This could be clinically important during weaning process of PSV mode. Clinical experience supported by literature findings indicate that higher PS is associated with poor patient-ventilator synchrony. When PS is reduced, cycle synchrony is expected to improve. It should be noted that as PS is further reduced, shorter mechanical breaths and early termination could occur. Our observations about PS and EDT support the mathematical analysis by Yamada and Du\(^{18}\), who suggested that expiratory synchrony improves when PS is reduced.

We simulated 3 different levels of muscle pressure (Pmus) to reflect low, medium, and high patients’ efforts. Our findings indicated that the degree of effort did not significantly affect TRT or EDT. However, there was a trend towards reduction in TRT and increase in EDT as Pmus increases. With higher patient’s efforts, trigger threshold is expected to be reached sooner, decreasing TRT. The fact that the observed reduction in TRT did not reach statistical significance can be attributed to the pattern chosen for Pmus. At all Pmus levels used in this study, we configured the drop in pressure to simulate sine wave pattern. We chose to use this pattern of Pmus to study the effect of merely drop in Pmus when other factors are unchanged. We realize that in a real patient with increased effort, Pmus may decrease sharply reaching maximum drop at early stage of the trigger phase. We also used a neural timing of 1 sec at all 3 levels of Pmus. Using the same pattern of Pmus and fixed Ti for all levels of efforts in our experiment could be the reason for the non-significant effect of changing effort on TRT. However, our protocol revealed an important finding about effect of purely increase in Pmus on trigger delay time. It will be interesting to study effect of more vigorous efforts with different waveform pattern and inspiratory times on TRT.

In their mathematical modeling, Yamada and Du suggested that expiratory cycle of a breath is affected by the ratio of applied PS and patient’s generated pressure (PS/Pmus). According to this model, when Pmus becomes the main generator of flow and VT, expiratory synchrony improves. In our study, we found that all 3 levels of Pmus did not significantly affect EDT, except at higher PS levels (15 and 20 cm H2O). In line with the mathematical proposition, we can speculate that Pmus did not affect EDT because flow and \( V_T \) were predominantly controlled by PS.

Our study also provides insight into effect of changes in pulmonary mechanics on both trigger and cycle phases of the breath. Increases in pulmonary resistance or compliance shifted synchrony window to the left. In such case, the mechanical breath will lag after neural breath and end well after patient finishes his breath. Reduction in resistance and compliance will produce the opposite effect. Both scenarios disrupt patient-ventilator synchrony. For a given PS setting, as resistance increases, required \( V_T \) and flow necessary to maintain the target PS level are reduced. Lower inspiratory flow, in particular at the onset of the breath, may explain longer TRT observed with high resistance. On the other hand, larger \( V_T \) and faster flow observed when ventilating high compliant lungs contribute to long TRT. Effect of resistance and compliance on EDT can be explained by the concept of time constant (\( T_c \)). Time constant is the time needed to empty about two thirds of exhaled volume\(^9\). It is the product of resistance and compliance. At longer \( T_c \) (as the case of increased resistance and/or compliance), expiratory flow decays at a slower rate. Therefore, it takes longer time to reach expiratory trigger point. This is the underlying cause for longer EDT that is associated with higher resistance and compliance. Our findings corroborate results of Tassaux et al\(^{12}\) who reported improvement in ventilator synchrony in COPD patients when expiratory trigger point was increased to 70%. Longer \( T_c \) in these patients was
curtailed by setting expiratory trigger so that EDT is shortened. In patients with acute lung injury (short Tc), synchrony and work of breathing improved when expiratory trigger was decreased from 45% to 1%, preventing early cycle of the breath. According to the mathematical model mentioned above, expiratory synchrony is not affected by Tc alone, rather it is the effect of time constant divided by neural inspiratory time (Tc/Ti). In the present study, we tested different levels of Tc (as reflected by resistance and compliance) at a fixed Ti of 1 sec. Further research is needed to investigate effect of different Tc/Ti ratios on cycle synchrony.

Patient-ventilator interaction has been the subject of study for many research works that aimed to understand factors influencing synchrony. Of particular interest, two technical developments have been introduced recently to improve phase synchrony. Neurally adjusted ventilatory support (NAVA) is a mode of ventilation that uses electrical activity signals of the diaphragm to trigger and cycle the breath. Research studies indicated that this mode of ventilation produced better synchrony and imposed less work of breathing when compared to PSV. Special algorithm to automatically select breath termination criteria was incorporated in Newport ventilator. A preliminary study compared automated vs. fixed expiratory criteria reported improvement in synchrony and patient’s comfort with the automated algorithm.

This study has some limitations. First, we used an electromechanical lung model to simulate breathing. In a laboratory environment, we were able to test specific parameters while controlling possible confounding factors. This may not reflect clinical reality where outcomes are influenced by many interrelated variables. Therefore, direct extrapolation of this study findings to clinical practice should be done cautiously. Secondly, we did not use active exhalation feature of the lung model, which could have produced different results. The use of active exhalation seems more realistic clinically, but our aim was to investigate effect of some single variables on breath start and end. Thirdly, although we used clinically plausible settings, interpretation of our data should be limited to the range of settings used in this study. Finally, statistical differences reported in this study cannot be directly translated into clinical relevance. Because of high precision produced by the lung simulator, small changes in parameters could reach statistical significant. We used a stricter p values (< 0.01) to signify statistical significance. In one study, 15% increase in work of breathing was reported when trigger delay time increased from 89 to 115 ms.

In conclusion, using a high fidelity lung simulator, we created several scenarios resembling clinical conditions and studied “pure” effects of changes in PS, breathing effort, resistance and compliance on trigger and cycle delay times. Higher PS was associated with shorter trigger time but lengthened time to cycle the breath. Patient’s effort alone did not affect time to trigger or cycle the breath. Increased airway resistance and/or lung compliance disrupt phase synchrony by delaying time to trigger and extending mechanical breath beyond neural time.

**Financial Support**

None.

**Conflict of Interest**

None.

**Acknowledgment**

I would like to thank Mr. Ahmed Mansi for his assistance in setting up the lung simulator.
References


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Initial bolus
Inject 1 ampoule Tramal® 100 mg i.v. or i.m. slowly over 2-3 minutes.

**Ways of administration after initial bolus**
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  - Usual dose 150 mg or 100 mg 4-6 hours up to a total daily dose of 400 mg except in special clinical circumstances which might necessitate daily doses up to 800 mg. Further treatment with Tramal® bolus on demand.

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  - 1 suppository every 4-6 hours

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If intra-operative dose not given then BOLUS i.v.
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An intra-operative loading dose of Tramal® will reduce PONV rates

*If needed further doses of 50 mg up to a total of 200mg (incl. the initial bolus) may be given within the first 60 min.


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- 97% of BRIDION patients recovered to a TOF ratio of 0.9 from 1 to 2 PTCs within 5 minutes

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- BRIDION rapidly reversed patients from 1 to 2 PTCs in 2.7 minutes

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**Important safety information**
BRIDION is not recommended in patients with severe renal impairment. Studies in patients with hepatic impairment have not been conducted and, therefore, patients with severe hepatic impairment should be treated with great caution. Caution should be exercised when administering BRIDION to pregnant women as no clinical data on exposed pregnancies are available. BRIDION has not been investigated in patients receiving neuromuscular blocking agents in the intensive care unit (ICU) setting. If neuromuscular blockade is required within 24 hours of BRIDION administration, a nondepolarizing neuromuscular blocking agent should be used instead of rocuronium or vecuronium. The most commonly reported adverse reactions were hypotension (headache or dizziness) and anaphylactic complications (fainting, coughing, rhinorrhea, or swelling of the oral/pharyngeal areas). In patients treated with BRIDION, a few cases of Awareness were reported. The case reports to BRIDION were consistent with those observed with other products. In a few instances, anaphylactic reactions (e.g., flushing, hypotension, rash) following BRIDION administration were reported. Physicians should be prepared for the possibility of allergic reactions and take appropriate precautions. In a few instances, patients with a history of hypotensive complications, benzodiazepines were reported in 2 patients and a causal relationship could not be fully excluded. Volunteer studies have demonstrated no clinically relevant effect on peak or postoperative recovery from the effects of BRIDION in patients undergoing open abdominal surgery. Anaphylactic reactions should be treated with other antihistamines, corticosteroids, or epinephrine. A 1% solution of lidocaine with epinephrine, 1:200,000, should be used in patients undergoing open abdominal surgery. Although formal interaction studies have not been conducted, no drug interactions were observed in clinical trials. Preclinical data suggest that clinically significant drug interactions are unlikely with the possible exceptions of cimetidine, furosemide, and hormonal contraceptives.

**REFERENCES**
1. BRIDION Summary of Product Characteristics (SPC)

Please see summary of product characteristics for full prescribing information.
TAP Block And InfiltraLong
For Effective Treatment
Of Long And Deep Incisions

Sono Cannulas
For Single Shot UltraSound
Guided Nerve Blocks

SonoSystem And SonoLong Curl
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