SOMATIC AND AUTONOMIC UPREGULATION
IN THE QUADRIPLEGIC PATIENT

Patients with chronic spinal cord transection develop both somatic and autonomic denervation below the level of denervation. This can result in “up-regulation” of both the somatic and adrenergic receptors below the level of the cord transection, with a subsequent increased sensitivity to the chemical transmitter at both the neuromuscular junctions and the adrenergic receptors.

The number of postjunctiional receptors can be influenced by the ambient concentration of the chemical transmitter. As a rule, there is an inverse relationship between the concentration of the transmitter and the number of its receptors. Alteration in the number of the receptors is referred to as either “up-regulation” or “down-regulation”. Patients with chronic spinal cord transection will develop both somatic and autonomic denervation, which can result in “up-regulation”, and hence a supersensitivity response at both the neuromuscular junction and the adrenergic vascular receptors.

Somatic denervation will be followed by extrajunctional spread of the receptors beyond the motor endplate into the whole muscle membrane, with a subsequent increased sensitivity to the chemical transmitter acetylcholine. A similar response will follow sympathetic denervation, resulting in extrajunctional spread of the adrenergic receptors, with a subsequent adrenergic supersensitivity to the chemical transmitter norepinephrine which can trigger the so-called “autonomic hyperreflexia”.

The “autonomic hyperreflexia” is not secondary to an increased secretion of the chemical transmitter norepinephrine, but rather to an increased sympathetic response of the expanding adrenergic receptors, resulting in severe hypertension, associated with reflex slowing of heart rate via the innervated carotid sinus baroreceptors. It has been shown that plasma catecholamines (epinephrine and norepinephrine) are subnormal in patients with cord transaction. During autonomic hyperreflexia, the level of norepinephrine increases, but still does not exceed the resting level of the control normal patients. These findings demonstrate that patients with chronic spinal cord transection have a subnormal sympathetic tone, even during an attack of autonomic hyperreflexia. These findings suggest the excessive reflex elevation of the blood pressure in patients with spinal cord transaction is not secondary to autonomic hyperreflexia, but is rather due to a denervation supersensitivity response of the adrenergic receptors to the released norepinephrine.

The somatic “up-regulation” will explain the marked hyperkalemia following the administration of succinylcholine to the quadriplegic patient. That is why, succinylcholine is contraindicated in the quadriplegic patient, while the nondepolarising relaxants may be safely administered whenever indicated.
The autonomic “up-regulation” will explain the marked vasopressor response to stimulation below the level of cord transection. The autonomic response consisting of severe hypertension associated with reflex bradycardia can follow bladder distension, uterine contractions during pregnancy and labor, as well as surgical stimulation. About 85 percent of patient with cord transection above T6 will exhibit the reflex, since vasodilation in the neurologically intact portion of the body is insufficient to offset the effects of vasoconstriction below the level of transection.

The vasopressor response can be decreased by the use of epidural meperidine or intrathecal morphine which act on the substantia gelatinosa in the spinal cord, blocking the response to nociceptive stimulation. The technique has been used to block the autonomic hyperreflexia in the quadriplegic patient undergoing delivery or surgery below the level of cord transection.

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References

The key to

Lock-up

Postoperative Pain

STEP I

Initial bolus

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

STEP II

Ways of administration after initial bolus

Infusion
Inject 3 ampoules Tramal®, each 100 mg, in 500ml of infusion solution.
Infusion rate 12-24 mg Tramal® (16-20 drop/min or 30-60ml/h)

Subsequent increments of 50 mg with a lock-out time of 5 minutes.

If needed further doses of Tramal® up to a total of 200 mg (excluding the initial bolus) within the first 60 min.

STEP III

Follow-up

1-2 capsules every 4-6 hours

50 mg

20-40 drops every 4-6 hours

1 suppository every 4-6 hours

100 mg

slow release

100 mg, 150 mg, 200 mg

1 tablet every 12 hours

STEP III

Loading Dose

2.5 - 3 mg/kg

at wound closure

Loading Dose

2.5 - 3 mg/kg

at wound closure

Post-Anaesthesia Care Unit

If intra-operative dose not given then:
BOLUS I.V.*
100 mg over 2-3 mins

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.
For patients with localized burning, shooting, stabbing, and neuropathic pain.

VERSATIS®
5% lidocaine medicated plaster
WORKS WHERE IT HURTS
BRIDION—*for optimal neuromuscular blockade management* and improved recovery

**Predictable and complete reversal**
- 98% of BRIDION patients recovered to a TOF ratio of 0.9 from reappearance of T2 in 5 minutes
- 97% of BRIDION patients recovered to a TOF ratio of 0.9 from 1 to 2 PTCs within 5 minutes

**Rapid reversal**
- BRIDION rapidly reversed patients from reappearance of T2 in 1.4 minutes
- BRIDION rapidly reversed patients from 1 to 2 PTCs in 2.7 minutes

**Important safety information**
BRIDION is indicated for the reversal of neuromuscular blockade induced by rocuronium or vecuronium. In children and adolescents (aged 2-17 years), BRIDION is only recommended for routine reversal of moderate rocuronium-induced neuromuscular blockade.

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 pregnant women are available.

BRIDION has not been investigated in patients receiving rocuronium or vecuronium in the intensive care unit (ICU) setting. If neuromuscular blockade is required within 24 hours of BRIDION administration, a non-depolarizing neuromuscular blocking agent should be used instead of rocuronium or vecuronium. The most commonly reported adverse reactions were dyspnea (oral or laryngeal) and anaphylactic complications (anaphylaxis, coughing, pruritus, or flushing on the endotracheal tube). In patients treated with BRIDION, a few cases of awareness were reported. The relation to BRIDION was uncertain. In a few individuals, allergic-like reactions (coughing, urticaria, rash) following BRIDION were reported. Clinicians should be prepared for the possibility of allergic reactions and take appropriate precautions. In a trial of patients with a history of previous complications, hemodynamic events reported in 2 patients and a causal relationship could not be fully excluded.

Volunteer studies have demonstrated a slight (1.9±1.2%) and transient (<30 minutes) prolongation of the proximal time (axilla to elbow) with BRIDION. However, clinical studies have demonstrated no clinically relevant effect on postoperative hemodynamic complications with BRIDION alone or in combination with antibiotics. An RIFAXON has demonstrated no in vitro pharmacodynamic interaction with anticoagulants, corticosteroids should be continued in patients on anticoagulation for acute, moderate, or severe renal failure. This pharmacokinetic interaction is not clinically relevant for patients requiring routine postoperative prophylactic anticoagulation. Although formal interaction studies have not been conducted, no drug interactions were observed in clinical trials. Preliminary data suggest that clinically significant drug interactions are unlikely with the possible exceptions of corticosteroids, furosemide, and hormonal contraceptives.

**REFERENCES**

Please see summary of product characteristics for full prescribing information.
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