MB – IDEAL SHOCK THERAPY

Methylene blue is exceptionally beneficial for both infections in general and for hypotensive shock. This makes it a particularly optimal therapy for the very common cause of intensive care unit death around the planet: septic shock.

Refractory septic shock, a state of disseminated infection with vascular collapse and hypotension often *unresponsive to all traditional measures*, consistently responds positively to MB therapy, sometimes saving the patient from otherwise certain death.

As with vitamin C and many other non-traditional treatments, nearly all clinicians simply will not take the "leap" from clear-cut positive results in the literature to the application of those results in their patients. At best, they use these non-traditional therapies almost like a final gesture that they have done everything possible to save the patient, even though those therapies have little to no toxicity and should not be relegated to the last option in a treatment protocol. And, of course, this only applies to the clinicians who are even remotely aware of the existence of the data showing how effective and nontoxic these non-traditional therapies are. The many pearls in medical literature remain completely unharvested by most clinicians. And many more clinicians are very diligent in doing everything possible to maintain the "mainstream status quo" to the point of ignoring and even suppressing anything that might threaten it.

An experienced and honest clinician will tell you that just one dramatic case report that is accurately reported has enormous value. When a patient is on the verge of death despite all that has been done, and one single intervention quickly stops the clinical deterioration and starts a clear recovery, the alert clinician does not need a large prospective, double-blind, and placebo-controlled clinical trial to take such a clinical response seriously. Such a trial would be unethical when the placebo group is not being given the benefit of some inexpensive, nontoxic, and highly effective agent. Especially in the setting of an advanced and rapidly progressing infection with unresponsive shock secondary to sepsis, seeing the patient normalizing only a short time after a treatment is administered compels serious attention.

A clear example of such a case report was reported on a 38-year-old male patient who presented with bilateral pneumonia that subsequently worsened and resulted in bacteria (*Klebsiella pneumonia*) being released into the bloodstream (septicemia). Lethargic with low blood oxygen when admitted to the hospital, he was given IV fluids with insulin and antibiotics. The oxygen levels continue to decline with increased difficulty breathing, and he was then intubated and supported on a ventilator. Hypotension requiring vasopressor infusion ensued. Broader antibiotic coverage was added. Metabolic acidosis with declining renal function followed, and a few hours later he had a cardiac arrest. Four hours after regaining a heart rhythm and only 25 hours after initial presentation, extracorporeal membrane oxygenation (ECMO) support was started. Nevertheless, critically low blood pressure *unresponsive* to multiple vasopressors continued.

At this point in time, a 172 mg IV bolus of MB was administered, and an infusion of MB at 0.51 mg/kg/hour was maintained for the next 10 hours. Blood pressure *quickly improved*, and vasopressor support could be decreased. At the conclusion of the infusion, the clinical status stabilized for another 22 hours, but fever with a dropping blood pressure unresponsive to combinations of vasopressors at the highest doses returned. The MB infusion was restarted, and blood pressure *again responded promptly*. This time the infusion was continued for 54 hours, and about seven days after this longer infusion was completed the patient was fully recovered and discharged from the hospital.

Another impressive case report on a clinically similar patient showed that MB had to be continually infused for a full 120 hours to prevent repeated clinical relapses, after which the patient stabilized and was eventually discharged.

These case studies, in which the patients effectively serve as their own controls, showed clear improvement on MB when severely ill, clear deterioration back to a life-threatening point after MB discontinuation, and prompt improvement with complete clinical resolution when the MB was restarted and continued for a long enough period. No sincere and competent clinician giving his/her highest priority to patient welfare would ignore the importance of such a clinical response when treating similar patients in the future. And this is especially the case when it is realized that MB, dosed appropriately, has an impeccable safety profile, just like vitamin C. Also, like vitamin C, MB also *enhances antibody production* in the body. This begs the question: Why not use MB *first* in such situations, rather than last, or never?

Multiple studies have demonstrated the benefits of MB in stabilizing and even resolving septic shock, which is the worst stage that any infection can reach before the inevitable progression to death. No reports of MB worsening the overall clinical status of septic patients could be found. Studies consistently show that MB always improves hypotension when appropriately administered. Furthermore, it has been shown that MB improves survival in shock of all causes (vasodilatory shock), including the shock of advanced sepsis.

The refractory hypotension in septic shock is consistently seen in the setting of excessive nitric oxide production, which causes too great a decrease in vascular tone. MB promptly counteracts this in restoring normal blood pressure. Furthermore, over 120 years of MB use has clearly established the lack of significant toxicity. Toxic levels exist, as with nearly every other agent (including water), but the amounts needed are far beyond the recommended dosing in established treatment protocols.

An open-minded clinician reviewing literature for the first time, to learn about the best treatment for septic shock, would certainly utilize methylene blue as a first-line agent. Even low doses of MB and one-time boluses of MB consistently show clear benefit in septic shock. However, the clinical response is much better and consistently achieved with a properly dosed continuous infusion. Septic shock still claims a lot of lives regardless of the therapy, and some clinical studies add MB seemingly as a last-ditch afterthought, after which MB is then reported to be ineffective for improving survival. And even now, some of the most recent clinical research continues to assert that "more studies are needed" on the impact of MB in septic shock, even though the very positive research on MB and septic shock now spans *decades*. MB infusions in hypotensive neonates have also been shown to increase blood pressures rapidly and safely.

The impact of MB on septic shock was addressed above in some detail since a patient cannot really be much sicker than having severe hypotension with massive infection and enormously increased oxidative stress throughout the body. However, it is important to realize that MB has also been shown to be very effective in treating different types of hypotensive shock that are unrelated to advanced degrees of infection.

Shock with unresponsive hypotension secondary to the ingestion of multiple drugs has responded rapidly to MB infusions, allowing the weaning of other vasopressor agents. Shock, secondary to anaphylaxis also responds well to MB. One patient with profound refractory hypotensive shock, following a dihydropyridine calcium channel blocker overdose, only responded positively to MB infusion, and was eventually discharged. Prior to the MB infusion, no improvement in blood pressure was seen with saline infusion, several doses of calcium gluconate, glucagon, various vasopressor agents, and even high-dose insulin euglycemic therapy over a period of several hours. Another type of hypotensive shock, cardiac vasoplegia, is also sometimes seen following cardiac surgery. This is effectively treated by methylene blue as well.

All forms of hypotensive shock should be treated with MB, and it should be part of the treatment protocol at the outset. It should not just be held back as a last-ditch intervention to save the patient.

Regarding ARDS secondary to COVID, a massive production of pro-inflammatory agents known as a cytokine storm typically precedes imminent death if not effectively terminated and neutralized. MB has been uniquely shown to inhibit the production of all three of the major classes of pro-oxidants involved in the cytokine storm clinical picture (reactive oxygen species [ROS], reactive nitrogen species [RNS], and cytokines). And as a potent antioxidant, MB is highly effective in neutralizing the wide array of pro-oxidants that have already been produced in the ARDS lungs. MB also combines well with other antioxidants in providing clinical benefit. MB combined with vitamin C and N-acetyl cysteine was very effective in treating advanced COVID.

Furthermore, patients who were severely ill with COVID but showing a steady clinical recovery still greatly benefit from MB. Many "recovered" COVID patients have significant neurocognitive problems that are lessened or even blocked with adequate dosing of MB. With the known antioxidant properties of MB along with its predilection for targeting increased oxidative stress in the nervous system, it should be part of any COVID treatment, *regardless of how well the infection is responding to other therapies*.