Hyperchloremia and Diuresis in Children Undergoing Scoliosis Surgery: A Retrospective Cohort Study

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ABSTRACT: **Background:** Hyperchloremia is frequent in adult surgical patients and is associated with renal dysfunction. Studies in surgical pediatric patients are lacking.

Objectives: To identify both the incidence of postoperative hyperchloremia in children undergoing surgery for idiopathic and non-idiopathic scoliosis, and the association of postoperative hyperchloremia with intraoperative fluid management and postoperative diuresis.

Methods: The records of 74 children and adolescents who underwent elective scoliosis surgery were retrospectively evaluated. The primary endpoint was the incidence of serum chloride level ≥ 110 mEq/L at the end of surgery and 12 hours postoperatively. Secondary endpoints were the type and volume of administered fluids, 12 hours postoperative diuresis, and the incidence of postoperative oliguria.

Results: Hyperchloremia occurred in 55% of the patients at the end of surgery and in 52% 12 hours postoperatively. Hyperchloremic patients received larger intraoperative volume of 0.9% NaCl diluted cell-saver blood and 10% HAES than did normochloremic patients [median (interquartile range) 6.8 (2.5–11.0) ml/kg vs. 0 (0–7.3), $P = 0.003$ and 10.0 (0–12.8) vs. 4.4 (0–9.8), $P = 0.02$, respectively]. Additionally, when compared with normochloremic patients, diuresis during the first 12 hours postoperatively was lower in hyperchloremic patients. Postoperative oliguria (urine output ‹ 0.5 ml/kg/hr for 12 hours) was diagnosed in 7 children (9%), of whom 6 were hyperchloremic at the end of surgery.

Conclusions: Early postoperative hyperchloremia is common in children undergoing scoliosis repair surgery and may be attributed to the administration of 0.9% NaCl diluted cell-saver blood and 10% HAES. Postoperative hyperchloremia might be associated with postoperative oliguria.

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Animal and human studies have shown that hyperchloremia can cause renal vasoconstriction, decreased renal cortical perfusion, and reduced glomerular filtration rate [1-3]. In critically ill adult patients, the administration of chloride-restricted solutions was shown to decrease the incidence of acute kidney injury (AKI) [4], while higher chloride content fluids were found to be associated with unfavorable patient outcomes in the perioperative or intensive care setting [5].

In the pediatric population, chloride-rich solutions were found to cause hyperchloremia and metabolic acidosis in septic children as well as in children after cardiac surgery [6-8]. Acute kidney injury may occur as a complication in infants undergoing cardiac corrective surgery [9]. Thoracic surgery was found to be a predictive factor of increased relative risk of hyperchloremia [10]. Moreover, hyperchloremia was seen to be independently associated with mortality in critically ill children who ultimately require continuous renal replacement therapy [11]. A recent study has demonstrated an association of hyperchloremia with a complicated course and increased mortality in pediatric septic shock [12].

To the best of our knowledge, studies regarding hyperchloremia and diuresis in the pediatric non-cardiac surgical population are lacking. In the present study we aimed to identify the incidence of postoperative hyperchloremia in children undergoing surgery for idiopathic and non-idiopathic scoliosis. Additionally, the associations of postoperative hyperchloremia with intraoperative fluid management and postoperative diuresis were also assessed.

PATIENTS AND METHODS

Ethical approval for this study (Institutional Review Board # 0407-13-TLV) was received. The study protocol was approved in accordance with the Declaration of Helsinki and the principles of GCP. Informed consent was waived.

STUDY POPULATION

Data from the medical records of 91 children and adolescents who underwent elective scoliosis surgery at the Tel Aviv Sourasky Medical Center between May 2012 and May 2013 were retrospectively collected. Excluded were children who underwent surgery for scoliosis as an emergency, had received diuretic therapy, and had known renal impairment. Demographic data, patient's characteristics, procedural variables, anesthesia, and post-procedural variables in the pediatric

intensive care unit (PICU) were retrieved from the computerized medical records and from the anesthesia charts.

PERIOPERATIVE MANAGEMENT AND FOLLOW-UP

The study patients received standardized general anesthesia and mechanical ventilation. After tracheal intubation anesthesia was maintained with total intravenous anesthesia (propofol and remifentanil infusions). Minute ventilation was titrated to maintain normocarbia. Heating blankets and perfusion warming systems were used to prevent hypothermia. In addition to standard monitors, intraoperative monitoring included intra-arterial blood pressure and urine output (UO) monitoring as well as electrophysiological monitoring of the somatosensory and transcranial motor potentials of the upper and lower limbs. The protocol in our institution indicates the routine use of cell-saver in order to minimize allogeneic blood transfusion. The cell-saver blood is diluted in 0.9% NaCl before it is returned to the patient. Intraoperative fluids are given to maintain mean arterial pressure > 60 mmHg and systolic blood pressure between 80 and 100 mmHg to minimize blood loss, and at a ratio of 3:1 relative to blood losses approximated by the cell-saver. Vasopressor therapy is initiated if blood pressure goals are not achieved after a 20 ml/kg fluid bolus.

All patients are extubated at the end of surgery unless cardiovascular or hemodynamic instability prevents extubation. Following surgery all patients are transferred to the PICU for hemodynamic and respiratory monitoring and for pain management. On postoperative day 1, in the absence of any postoperative complication, children are transferred to the orthopedic ward. All children were followed until discharge from hospital with regard to creatinine level and the need for renal replacement therapy.

DATA COLLECTION

The relevant perioperative data were extracted from the medical records at our medical center (patient files, ADA, NMR, IMD Soft MetaVision™), and included:

- Demographic and anthropometric data: age, gender, weight, American Society of Anesthesiology (ASA) score, non-idiopathic scoliosis (congenital or acquired)
- Duration of surgery
- The amount of time with systolic blood pressure ≤ 80 mmHg during surgery (SBP ≤ 80 mmHg)
- Need for vasopressor agent administration, type, duration, and amount of vasopressor usage
- Complete blood count, electrolytes, serum creatinine and blood urea nitrogen recorded before surgery, at the end of surgery and 12 hours postoperatively. Arterial blood gases recorded at the end of surgery and 12 hours postoperatively
- UO during the operation and PICU stay, and need for renal replacement therapy (i.e., hemodialysis or continuous hemofiltration)
- Fluid volume administration during surgery and up to 12 hours postoperatively: total volume administered (crystalloids and colloids) as well as the volume of administered packed red blood cells (PRBC) and cell-saver blood.

We defined intraoperative oliguria as UO < 0.5 ml/kg/hr after dividing the total amount of urine collected during the surgery by duration of the surgery. Postoperative oliguria was defined as UO < 0 .5 ml/kg/hr for 12 hours as in the Kidney Disease Improving Global Outcome (KDIGO) criteria [13].

In light of the PICU length of stay we chose to assess serum chloride and UO 12 hours postoperatively.

STUDY ENDPOINTS

The primary endpoint was the incidence of serum chloride level (SCl) ≥ 110 mEq/L at the end of surgery and 12 hours postoperatively. Secondary endpoints were the type and volume of administered fluids, 12 hours postoperative diuresis, and the incidence of postoperative oliguria.

STATISTICAL ANALYSIS

Statistical analyses were performed using SPSS (version 21). Categorical variables are reported as frequencies and percentages, and continuous variables as medians and interquartile ranges (IQR). Categorical variables were compared between SCl groups using the chi-square test or Fisher's exact test and continuous variables by the Mann-Whitney test. A two-tailed $P < 0.05$ was considered statistically significant.

RESULTS

A total of 91 patients underwent scoliosis surgery during the study period. Seventeen patients were excluded due to emergency surgery (n=2), anaphylactic shock during anesthesia that postponed surgery (n=1), and lack of accurate data regarding the amount of perioperative IV fluids and UO (n=14). Of the 74 patients included in the study 28 (38%) were male. Median age and weight were 14.3 years (IQR 12.3–15.8 [5.1–18.5]) and 44.5 kg (IQR 33.7–53.0 [15–72]), respectively. Forty-six patients (62%) had non-idiopathic scoliosis secondary to: cerebral palsy (n=14), meningomyelocele (n=4), neurofibromatosis type 1 (n=5), vertebral anomalies (n=3), spinal muscular atrophy type 2 (n=2), Duchene muscular dystrophy (n=1), central core myopathy (n=1), achondroplasia (n=1), trauma (n=2), collagen disease (n=2), Beckwith–Wiedemann syndrome (n=1), DiGeorge syndrome (n=2), neuroblastoma (n=2), syringomyelia (n=1), and undiagnosed neurological syndrome (n=5). The median duration of surgery was 5.3 hours (IQR 4.6–6.4 [3.5–9.8]).

Perioperative data regarding fluids administration, UO, and laboratory data are depicted in Table 1. During surgery all children received Ringer's lactate (RL) as the crystalloid

Table 1. Perioperative fluids **[A]** and laboratory **[B]** data

A	Intraoperative	12 hours post-op
Urine output (ml/kg/hr)	1.4 (0.8–2.8 [0–6.8])	0.8 (0.6–1.3 [0.2–11.7])
Packed red blood cells volume (ml/kg)	0 (0–9)	0 (0–0)
Cell-saver blood volume (ml/kg)	5.6 (0.0–9.7)	Not applicable
10% HAES (ml/kg)	8.2 (0–11.9 [0-31.2])	Not applicable
Ringer's lactate (ml/kg/hr)	9.6 (7.5–11.9 [1.7–22.2])	2.4 (0.9–3.8 [0–11.7])
0.9% NaCl (ml/kg/hr)	Not applicable	3.4 (2.6–5.3 [0.5–11.1])

B	Preoperative	End of surgery	12 hours post-op
Creatinine (mg/dl)	0.7 (0.6–0.8 [0.15–1])	0.6 (0.5–0.7 [0.2–1])	0.6 (0.5–0.7 [0.2–1])
Blood urea nitrogen (mg/dl)	12 (10–15 [6–23])	10 (9–13 [2–16])	10 (7–13 [3–22])
Serum Na (mEq/L)	140 (138–142 [132–148])	138 (136–140 [132–145])	135 (133–137 [127–145])
Serum Cl (mEq/L)	104 (103–105 [96–111])	110 (108–112 [104–117])	110 (106–112 [100–118])
pH	Not applicable	7.33 (7.29–7.36 [7.2–7.5])	7.37 (7.34–7.41 [7–7.5])
Serum base excess	Not applicable	-2.2 (-3.7--0.9 [-15.5–1.7])	-0.4 (-2.1–1.1 [-7.5–5])

Values are median (IQR [range]) unless stated otherwise

solution, and none received 0.9% NaCl. 10% HAES was administered to 47 patients (63%) who were found to spend significantly longer time with SBP ≤ 80 mmHg during surgery as compared to 27 patients who did not receive 10% HAES [median (IQR) 58 (24–108) minutes vs. 18 (6–34), respectively, $P = 0.0002$]. Cell-saver blood diluted in 0.9% NaCl was returned to 47 patients (63%) and a third of the patients required PRBC transfusion.

PRIMARY ENDPOINT

Acute hyperchloremia (SCl ≥ 110 mEq/L) was observed in 55% of the operated patients at the end of surgery and in 52% at 12 hours post-surgery [Table 2]. Hyperchloremic patients 12 hours after the surgery, as compared to normochloremic at that time point, had significantly higher SCl levels at the end of surgery [111 (109–113) vs.108 (106–111) mEq/L, respectively, $P < 0.001$].

The age, weight, and type of scoliosis (idiopathic or non-idiopathic) did not differ between children with and without hyperchloremia at the end of surgery and 12 hours postoperatively (data not shown).

SECONDARY ENDPOINTS

- **Fluids**

Hyperchloremia at the end of surgery: Significantly more patients who were hyperchloremic at the end of surgery were transfused with 0.9% NaCl diluted cell-saver blood as compared to normochloremic patients. Also, larger intraoperative volumes of 10% HAES were administered to patients who were hyperchloremic at the end of surgery. The duration of surgery was also longer in these patients [Table 2].

Hyperchloremia 12 hours postoperatively: The volume of 10%HAES administered during surgery was significantly larger in patients with hyperchloremia 12 hours postoperatively [Table 2]. The amount of intraoperative PRBC and RL as well as the amount of PRBC, RL, 10% HAES and 0.9% NaCl administered in the PICU up to 12 hours postoperatively did not differ between patients with and without hyperchloremia at the end of surgery and 12 hours postoperatively.

- **Diuresis**

Intraoperative UO did not differ between patients with and without hyperchloremia at the end of surgery. UO during the first 12 hours after surgery was lower in patients who were hyperchloremic at the end of surgery when compared with patients who were normochloremic [median (IQR) 0.7 (0.5–1.1) ml/kg/hr vs. 1.0 (0.7–1.4) ml/kg/hr, respectively, $P = 0.05$]. The accumulated time of SBP ≤ 80 mmHg during surgery was similar among patients who developed hyperchloremia and those who did not [end of surgery: median (IQR) 41 (17–122) minutes vs. 24 (10–77) minutes, respectively, $P = 0.08$, 12 hours postoperatively: 40 (12–101) minutes vs. 32 (12–86) minutes, respectively, $P = 0.9$]. Postoperative oliguria was diagnosed in 7 children (9%) at 12 hours post-surgery, of whom 6 children (86%) were hyperchloremic at the end of surgery. The need

Table 2. Duration of surgery and administration of cell-saver blood and 10%HEAS in hyperchloremic vs. normochloremic patients at the end of surgery and 12 hours postoperatively

	End of surgery			12 hours postoperatively		
	Serum Cl < 110 mEq/L	Serum Cl ≥ 110 mEq/L	*P*	Serum Cl < 110 mEq/L	Serum Cl ≥ 110 mEq/L	*P*
n (%)	33 (44.6)	41 (55.4)		35 (47.3)	39 (52.7)	
Surgery duration (hrs)	5.0 (4.4–5.9 [3.5–8.2])	5.7 (4.8–7.2 [4–9.8])	0.019	5.4 (4.7–6.3 [3.5–9.8])	5.4 (4.6–6.6 [4–8.9])	0.76
Cell saver, n (%)	14 (42)	33 (80)	0.001	20 (58.8)	26 (68.4)	0.39
Cell saver (ml/kg)	0 (0–7.3 [0–15.7])	6.8 (2.5–11 [0–31])	0.003	4.1 (0–9.6 [0–31])	7.0 (0–9.7 [0–15.7])	0.26
Intraoperative 10% HAES, n (%)	19 (57.6)	28 (68.3)	0.34	19 (55.9)	27 (71.1)	0.18
Intraoperative 10% HAES (ml/kg)	4.4 (0–9.8 [0–22])	10.0 (0–12.8 [0–31.2])	0.02	6.0 (0–10.0 [0–31])	10.0 (0–12.5 [0–23.2])	0.04

Values are median (IQR [range]) unless stated otherwise

for vasopressors during surgery and 12 hours postoperatively did not differ between normochloremic and hyperchloremic patients (data not shown).

- **Other outcomes**

Preoperative serum creatinine, blood urea nitrogen, sodium and chloride levels did not differ between patients with and without hyperchloremia. The blood urea nitrogen at the end of surgery was significantly lower in patients who were hyperchloremic at the end of surgery [median (IQR) 9 (7–11) mg/dl vs. 12 (10–13) mg/dl, $P < 0.001$ respectively] and 12 hours postoperatively [median (IQR) 10 (8–11.5) mg/dl vs. 13 (9–13) mg/dl, $P = 0.004$ respectively]. The creatinine levels as measured at the end of surgery and 12 hours postoperatively did not differ between patients with and without hyperchloremia at both time points.

There was no difference in end-of-surgery sodium levels between patients with and without hyperchloremia at the end of surgery [median (IQR) 139 (136.5–141) mEq/L vs. 137 (136–139) mEq/L, $P = 0.08$ respectively]. However, patients who were hyperchloremic 12 hours after surgery had significantly higher serum sodium levels both at the end of surgery [median (IQR) 139 (137–141) mEq/L vs. 136.8 (135–139) mEq/L, $P = 0.001$] and 12 hours postoperatively [median (IQR) 136.4 (134.8–137.2) mEq/L vs. 134.1 (132.6–135.9) mEq/L, $P = 0.001$] as compared to normochloremic patients. Perioperative serum pH, base excess, and creatinine values did not differ between patients with and without hyperchloremia.

Length of stay in the PICU and in hospital did not differ between patients with and without hyperchloremia, or between patients with and without postoperative oliguria (data not shown).

DISCUSSION

The incidence of hyperchloremia has previously been reported for pediatric critically ill patients [6-9,11,12]. This study assessed the incidence of hyperchloremia in major non-cardiac surgical pediatric patients. Additionally, the present study evaluated the association of postoperative hyperchloremia, intraoperative fluid management, and early postoperative diuresis.

The principal findings of this retrospective cohort study of children undergoing spinal corrective surgery for idiopathic and non-idiopathic scoliosis were as follows: hyperchloremia is common at the end of surgery and 12 hours postoperatively; hyperchloremia at the end of surgery was associated with the administration of larger volumes of NaCl-diluted cell-saver blood and 10% HAES; patients who developed hyperchloremia at the end of surgery had decreased UO during the first 12 hours postoperatively; and postoperative oliguria is not uncommon in the early postoperative period.

A prospective study in adults undergoing major spine surgery compared the intraoperative effects of large-volume infusion of 0.9% NaCl vs. RL on serum electrolytes [14]. Patients who received 0.9% NaCl had significantly higher SCl levels as compared to patients who received RL from the second hour of surgery (119 ± 4 vs. 114 ± 5 mEq/L, $P < 0.01$ respectively), persisting up to 12 hours postoperatively (115 ± 5 vs. 109 ± 7 mEq/L, $P < 0.05$ respectively) [14]. A recent Cochrane review concluded that the use of buffered fluids is associated with less metabolic derangement, in particular hyperchloremia [15]. Current guidelines for perioperative intravenous fluid therapy in children recommend a physiologically composed balanced isotonic electrolyte solution for the intraoperative background infusion to avoid hyperchloremia [16].

In the present study in surgical pediatric patients undergoing scoliosis surgery, acute hyperchloremia (SCl ≥ 110 mEq/L) was present in 55% and 52% of the patients at the end of surgery and 12 hours postoperatively, respectively. In our cohort, during surgery, all patients received RL as the crystalloid fluid. The amount of intraoperative cell-saver blood and 10% HAES was significantly larger in patients who were hyperchloremic at the end of surgery. We routinely transfuse cell-saver blood after dilution with 0.9% NaCl, in addition, the concentration of sodium chloride in the 10% HAES solution is identical to 0.9% NaCl. Hence, we suggest that the hyperchloremia observed in our study at the end of surgery and 12 hours after surgery may, in part, be attributed to the excess chloride in cell-saver blood and 10% HAES.

Interestingly, the serum sodium levels at the end of surgery did not differ between patients with and without hyperchloremia at that time. This might be explained by the hyponatremic effect of intraoperative RL administration as the crystalloid fluid [14] that counteracted the sodium influx from 10% HAES solution and 0.9% NaCl diluted cell-saver blood. Patients who were hyperchloremic 12 hours after surgery had significantly higher serum sodium levels both at the end of surgery and 12 hours post-surgery. Administration of 0.9% NaCl during the PICU stay may result in the increased sodium levels 12 hours post-surgery accompanying hyperchloremia, and we speculate that higher sodium levels at the end of surgery in these patients may be an early indication of persistent hyperchloremia.

Hyperchloremia may not be benign. A meta-analysis of high- versus low-chloride content in perioperative and critical care fluid management demonstrated that high-chloride fluids were associated with a significantly higher risk of AKI, hyperchloremic metabolic acidosis, and higher serum chloride level [5]. In surgical adult patients the administration of 0.9% NaCl was also found to increase the rate of postoperative infection, renal failure requiring dialysis, electrolyte disturbance, and mortality [17]. On the other hand, a recent prospective study concluded that among patients receiving crystalloid fluid therapy in the intensive care unit, use of a buffered crystalloid compared with saline did not reduce the risk of acute kidney injury [18].

In the present study, UO during the first 12 hours after surgery was lower in children who were hyperchloremic at the end of surgery. Intraoperative hypotension might result in oliguria; however, the duration of intraoperative hypotension (SBP ≤ 80) was similar in patients with and without hyperchloremia. These data suggest that it was not the hypotension, but rather the hyperchloremia that might have contributed to the decreased UO during the first 12 hours after surgery in hyperchloremic children. These results are in agreement with recent findings in healthy volunteers in whom infusion of 0.9% NaCl was associated with hyperchloremia, longer time to first micturition, and smaller post-infusion urinary volume as compared to Plasma-Lyte infusion [1]. Moreover, a recent study reported that fluid resuscitation with NaCl may increase the severity of AKI [19]. The current study also found postoperative oliguria (UO < 0.5 ml/kg/hr for 12 hours) in 7 children (9%), of whom 6 (86%) were hyperchloremic at the end of surgery.

Due to the limited number of study patients and of those who developed postoperative oliguria, further studies in a larger patient population are needed to clarify the association between postoperative oliguria and postoperative hyperchloremia in pediatric surgical patients. Lastly, 10% HAES by itself was found to have adverse effects on renal function [20]; therefore, it might also contribute to the reduced UO in hyperchloremic patients.

Several possible mechanisms for the effects of hyperchloremia on diuresis and renal function have been proposed. Early experimental studies suggested that chloride might have direct effects on renal blood flow [2,3]. The capacity of the proximal tubule to reabsorb chloride might be overwhelmed by infusion of a large volume of chloride-rich solutions, thereby leading to greater chloride delivery to the thick ascending limb and activation of tubule-glomerular feedback by the macula densa, resulting in a reduction in the glomerular filtration rate [21-23]. The ability of chloride to modify renal responsiveness to vasoconstrictor agents may contribute to the increase in renal vascular resistance and decrease in the glomerular filtration rate [24]. Additionally, chloride directly induces prostaglandin release, such as thromboxane, resulting in vasoconstriction [25].

LIMITATIONS

This was a single-center study performed in a relatively limited group of patients, so no definite conclusions can be made regarding the effect of hyperchloremia on postoperative oliguria. Second, since the study is retrospective, and during the relevant time period there were no data regarding urine osmolality, electrolytes and creatinine levels at all-time points, we were unable to analyze the possibility of the syndrome of inappropriate antidiuretic hormone secretion in depth. Third, we lacked the data regarding accurate blood loss during surgery that might have affected the transfusion of fluids and blood products. However, as stated in the Methods section, fluid and blood administration were managed according to a strict protocol. Also, we found no difference in the amount of time spent with SBP ≤ 80 mmHg during surgery, or the need for vasopressors during surgery between hyperchloremic and normochloremic patients.

CONCLUSIONS

Hyperchloremia is common in pediatric patients undergoing scoliosis surgery and may be attributed to the administration of 10% HAES and cell-saver blood diluted in 0.9% NaCl. Reduced postoperative diuresis was found in hyperchloremic patients, the significance of which needs further evaluation. Most patients who developed postoperative oliguria were hyperchloremic. These data suggest that fluid management during scoliosis surgery in children should be based on balanced intravenous solutions, with special care taken regarding chloride serum levels.

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Capsule

Exercise-linked FNDC5/irisin rescues synaptic plasticity and memory defects in Alzheimer's models

Defective brain hormonal signaling has been associated with Alzheimer's disease (AD), a disorder characterized by synapse and memory failure. Irisin is an exercise-induced myokine released on cleavage of the membrane-bound precursor protein fibronectin type III domain-containing protein 5 (FNDC5), also expressed in the hippocampus. **Lourenco** and colleagues showed that FNDC5/irisin levels are reduced in AD hippocampi and cerebrospinal fluid, as well as in experimental AD models. Knockdown of brain FNDC5/irisin impairs long-term potentiation and novel object recognition memory in mice. Conversely, boosting brain levels of FNDC5/irisin rescues synaptic plasticity and memory in AD mouse models. Peripheral overexpression of FNDC5/irisin rescues memory impairment, whereas blockade of either peripheral or brain FNDC5/irisin attenuates the neuroprotective actions of physical exercise on synaptic plasticity and memory in AD mice. By showing that FNDC5/irisin is an important mediator of the beneficial effects of exercise in AD models, these findings place FNDC5/irisin as a novel agent capable of opposing synapse failure and memory impairment in AD.

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Capsule

m6A modification controls the innate immune response to infection by targeting type I interferons

N6-methyladenosine (m6A) is the most common mRNA modification. Recent studies have revealed that depletion of m6A machinery leads to alterations in the propagation of diverse viruses. These effects were proposed to be mediated through dysregulated methylation of viral RNA. **Winkler** et al. showed that following viral infection or stimulation of cells with an inactivated virus, deletion of the m6A 'writer' METTL3 or 'reader' YTHDF2 led to an increase in the induction of interferon-stimulated genes. Consequently, propagation of different viruses was suppressed in an interferon signaling-dependent manner. Significantly, the mRNA of *IFNB*, the gene encoding the main cytokine that drives the type I interferon response, was m6A modified and was stabilized following repression of METTL3 or YTHDF2. Furthermore, the authors showed that m6A-mediated regulation of interferon genes was conserved in mice. Together, these findings uncover the role that m6A serves as a negative regulator of interferon response by dictating the fast turnover of interferon mRNAs and consequently facilitating viral propagation.

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"If you wish to forget anything on the spot, make a note that this thing is to be remembered"

Edgar Allan Poe (1809–1849), American writer, editor, and literary critic