False Hyperchloremia in Bromism

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Plasma chloride concentration measured by an ion-specific electrode can be interfered by other ions. The authors experienced a case of phantom limb pain with a marked hyperchloremia (251 mEq $\cdot l^{-1}$) which was measured by the ion-specific electrode method. The patient was diagnosed as bromide intoxication due to chronic ingestion of analgesic tablets which contain bromvalerylurea. A toxic level of plasma bromide concentration supported the diagnosis. Elevated plasma chloride and bromide concentrations were normalized in three weeks after discontinuation of the analgesic intake.

Laboratory study revealed that fluoride ion did not affect chloride concentration measured by an ion-specific electrode. Bromide and iodide ions, however, interfered with the electrode and produced a large overestimation of chloride concentration.

Hyperchloremia should be interpreted carefully when chloride was measured by an ion-specific electrode method. (Key words: bromism, hyperchloremia, ion-specific electrode)

(Yamamoto K, Kobayashi H, Kobayashi T, et al.: False hyperchloremia in bromism. J Anesth 5: 88–91, 1991)

Since ion-specific electrode method was introduced into clinical practice, chloride measurement has become easier and more reliable. This method, however, has a pitfall that some other ions could interfere with the electrode to produce a large error. We have experienced several cases of bromide intoxication in which extremely high plasma chloride concentrations were observed. This study was designed to investigate the effects of halogen ions on the chloride measurement by the ion-specific electrode method.

Report of a Case

A 56-year-old man visited the pain clinic of Kanazawa University Hospital for phantom limb pain in his left arm. His arm was crushed by an accident four years ago. One month after the accident, phantom limb pain developed and became worse gradually. Two years after the accident, he began to take an analgesic drug (SEDES-A®) which contains ethenzamid 200 mg, acetaminophen 80 mg, bromvalerylurea 100 mg, and caffeine 25 mg per tablet. Daily doses of the drug were gradually increased to relieve the pain. At his initial visit to our pain clinic, he had been taking 40–50 tablets of SEDES-A a day.

Physical examinations showed no abnormal findings other than acneiform eruptions on his chest. The phantom limb pain was exaggerated by applying slight pressure to the stump of his arm. Laboratory data revealed extreme hyperchloremia (251 mEq$\cdot l^{-1}$) without any other electrolyte abnormalities (Na^+ 138 mEq$\cdot l^{-1}$, K^+ 3.6 mEq$\cdot l^{-1}$, Ca^{2+} 4.7 mEq$\cdot l^{-1}$ Mg^{2+} 2.2 mEq$\cdot l^{-1}$, P^{2+} 2.7 mEq$\cdot l^{-1}$). Since a chloride measurement was carried out by an ion-specific electrode method in the biochemical

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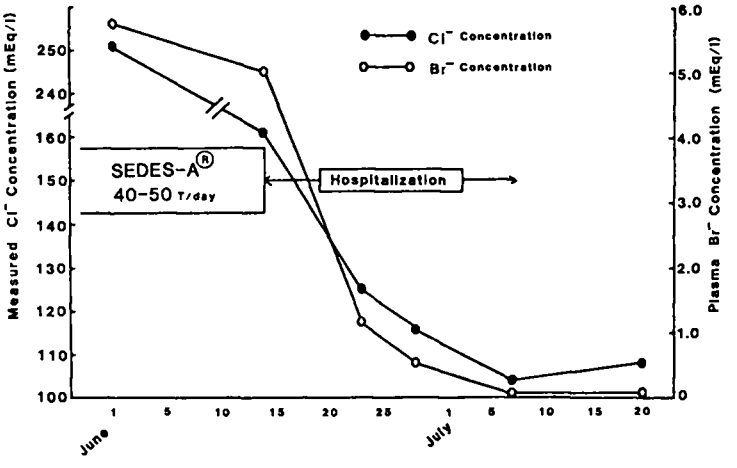

Fig. 1. Course of consecutive plasma bromide and electrode-measured chloride concentrations. T/day: tablets/day.

laboratory of our hospital, hyperchloremia observed in this patient was suspected to be caused by an interference to the electrode by other anions. Bromide was suspected as a possible causative ion because the patient had been taking a large amount of bromvalerylurea which is a component of the analgesic tablet. Plasma bromide concentration of the patient determined by a colorimetric measurement showed 5.75 mEq·l^{-1}, which was nearly at a toxic level. Although bromism was strongly suspected, he could not discontinue taking the analgesic tablets for further two weeks until admission to the hospital for the control of pain.

Hyperchloremia and elevated plasma bromide concentration were still observed at the time of admission. During his hospitalization, the analgesic tablet was discontinued because nerve blocks and transcutaneous electric nerve stimulation greatly relieved his pain. Plasma chloride concentration measured by the ion-specific electrode method was markedly reduced as well as plasma bromide concentration in three weeks (fig. 1). This case prompted us to perform following study.

Methods

Sodium chloride solutions (100 mEq·l^{-1}) containing sodium fluoride, or sodium bromide, or sodium iodide with various concentrations (0, 2, 4, 6, 8 and 10 mEq·l^{-1}) were prepared. All reagents were of analytical grade (Wako Pure Chemical Industries, Osaka, Japan). Chloride concentrations in these sample solutions were measured by three different chloride ion-specific electrodes. The electrodes examined were; (A) Selectrode® F3100, Radiometer, (B) PVA-4M®, Photovolt, and (C) Stat/Ion® System, Technicon. Each sample was measured two times at ambient temperature.

Results

Fluoride did not interfere with the ion-specific chloride electrodes at concentrations as high as 10 mEq·l^{-1}. On the other hand, chloride concentrations measured were increased as the bromide and iodide concentrations increased (fig. 2). The degree of interference by bromide and iodide was variable in these three electrodes.

Discussion

Present study demonstrated that both bromide and iodide ions interfere with the chloride measurement by the ion-specific electrode.

Normal ranges of plasma bromide and iodide concentrations are 28–94 μEq·l^{-1} and 0.006–0.047 μEq·l^{-1}, respectively[1,2]. The biological half-life of bromide ion is about two weeks[3]. The bromide ion can be accumulated in any case of the long term administration of bromide compounds, such

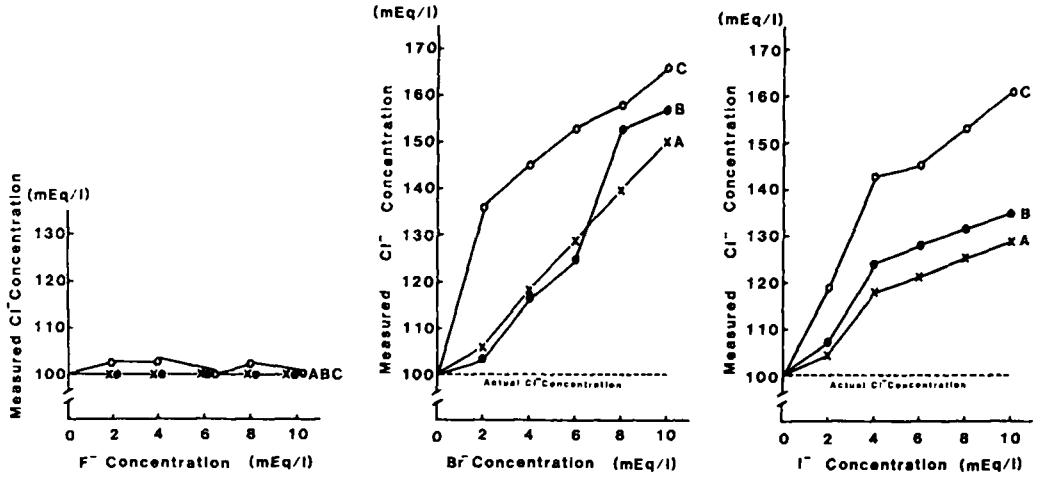

Fig. 2. Effects of fluoride, bromide and iodide on the readings of chloride concentration by three different chloride ion-specific electrodes. Points represent mean values (n = 2).
(A, Selectrode® F3100, Radiometer; B, PVA-4M®, Photovolt; C, Stat/Ion® System, Technicon)

as bromvalerylurea, sodium bromide, potassium bromide and ammonium bromide, and also repeated and prolonged halothane anesthesia, which liberate bromide ion as a degradation product[4]. Clinical manifestations of bromism, such as tremor, ataxia, headache, emotional instability, hallucination, skin eruption, and speech disturbance can occur when plasma bromide concentration exceeds 5–6 $mEq \cdot l^{-1}$ [5]. In the present case, observed hyperchloremia must be attributed to the interference of bromide to the electrode, rather than increased plasma chloride concentration per se. Conversely, when patients who are taking bromide compounds reveal hyperchloremia, elevated plasma bromide concentration should be suspected.

Iodide also significantly affected the result of chloride determination by the ion-specific electrode. Iodide agents such as expectorant, x-ray contrast medium, ointment containing molecular iodide are widely used. Iodism such as skin eruption and parotitis develops in more than 0.87 $mEq \cdot l^{-1}$ of plasma iodide concentration[2]. The false hyperchloremia, therefore, may be observed also in the iodism patients. In fact, Fishman reported a hyperchloremic case in which potassium iodide was abused[6].

Normal plasma fluoride concentration is 1–2 $\mu Eq \cdot l^{-1}$ [7]. Characteristic renal dysfunction due to fluoride has been well described. Clinical manifestations become evident in more than 200 $\mu Eq \cdot l^{-1}$ of plasma fluoride concentrations[8]. In this study, fluoride did not exert appreciable, observable effect on the electrode in a range of 0–10 $mEq \cdot l^{-1}$. Plasma fluoride concentrations higher than 10 $mEq \cdot l^{-1}$ would be seldom in clinical practice, therefore, fluoride intoxication might not be necessary to take into account as a possible cause of the false hyperchloremia.

Though hyperchloremia is observed in many pathological conditions associated with metabolic acidosis[9], it should be suspected that extreme hyperchloremia without metabolic acidosis could result from a technical error due to an interference with the ion-specific electrode by some unknown ions.

We investigated the effects of fluoride, bromide and iodide ions on the measurement of chloride by an ion-specific electrode. Fluoride did not interfere with the electrode, however, bromide and iodide did significantly with the electrode and produced a large error in the measurement of chloride concentration. Hyperchloremia, therefore, should be interpreted carefully when chloride is mea-

sured by an ion-specific electrode.

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References

1. Sada T: Colorimetric measurement of plasma bromide concentration. Jpn J Anesthesiol 30:351–355, 1981
2. Harden R McG: Submandibular adenitis due to iodide administration. Brit Med J 1:160–161, 1968
3. Söremark R: The biological half-life of bromide ions in human blood. Acta Physiol Scand 50:119–123, 1960
4. Kobayashi H, Sada T, Lin SY: Bromide accumulation following repeated halothane anesthesia. Hiroshima J Anesth 20:1–4, 1984
5. Trump DL, Hochberg MC: Bromide intoxication. Johns Hopkins Med J 138:119–123, 1976
6. Fishman RA, Fairclough GF, Cheigh JS: Iodide and negative anion gap. N Engl J Med 298:1035–1036, 1978
7. Sada T, Tohyama Y, Murakami S: Plasma fluoride concentration and urinary fluoride excretion following Fluosol-DA administration in man, Oxygen carrying colloidal blood substitutes. Edited by Frey R. München, W. Zuckschwerdt Verlag, 1982, pp. 225–229
8. Mazz IR, Trudell JR, Cousins MI: Methoxyflurane metabolism and renal dysfunction; clinical correlation in man. Anesthesiology 35:247–252, 1971
9. Morris RC, Sebastian A: Disorders of renal tubule that cause disorders of fluid, acid-base and electrolyte metabolism, Clinical disorders of fluid and electrolyte metabolism. Edited by Maxwell MH, Keeman CR. 3rd ed., New York, McGraw-Hill, 1980