Features of Acid–Base Balance of Bone Marrow

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Abstract

Context: Bone marrow (BM) pH has rarely been measured, and the long BM has barely been studied at all because intravital obtaining of the long BM is impossible due to the extreme strength of the long bone tissue. **Aims:** The study aimed to investigate the acid–base balance of the BM and to compare the acid–base properties of long BM and flat BM. **Subjects and Methods:** Forty flat BM samples were extracted by sternal puncture. Forty long BM samples were extracted from the femora in patients who had to have a limb amputated. A blood gas and acid–base status analyzer were used to determine pH. **Results:** Flat BM pH is similar to blood pH; the long BM pH is acidic and ranges from 6.7 to 6.9. Hematopoietic stem cells occur in both acidic and slightly alkaline environments. The blood gas and acid–base status analyzer used in this study are suitable for determining the acid–base properties of BM. **Conclusions:** The acid–base status appears to be an important factor of stem cell differentiation. This paper can be of interest to biotechnologists and researchers who investigate possibilities to influence the differentiation and properties of the stem cells.

Keywords: Bone marrow, stem cells, sternal puncture, tubular bone marrow

Introduction

The acid–base balance, or blood pH, has an important function within the body.[1] An imbalance in acids or bases can have dangerous consequences for human health.[2] Normal blood pH varies depending on the blood vessel. Venous blood pH is usually 7.32–7.42, while arterial blood pH is 7.36–7.43. In medical practice, life is normally no possible if blood pH falls below 6.8 or rises above 7.8.

The acid–base status of the bone marrow (BM) has been little studied both in practical medicine and scientific research. However, such indicant may be critical for the assessment of the expected response to treatment and the functional state of the BM.[3,4] By changing the pH value, one can, probably, affect the activity and the differentiation of the stem cells.[5,6] Acidosis can be caused by alcoholism or complications associated with diabetes, such as inadequate delivery of oxygen to the organs and tissues.[7,8]

When studying BM pH, it is necessary to collect enough measurements to determine the standard balance and the normal values. This research uses the BM pH values obtained in case of certain diseases; however, it can be hypothesized that such pH values are normal for the BM.

When extracting the BM for the purposes of this research, some samples were contaminated with blood and the pH values were significantly different that is why only the "clean" samples were selected for analysis. The interior milieu can be seen as an integrated system of humoral transport that includes the general blood flow and circulation in the continuous chain: blood – interstitial fluid – tissue (cell) – interstitial fluid – lymph – blood. It seems reasonable to include the BM into this chain.

Most intracellular processes follow at neutral pH when their rate is maximal. In biological tissues and organs, constant pH is maintained by means of the efficient buffer systems, which by their chemical nature, prevent the pH changes that occur during the metabolic processes.[9-11] In some tissues and organs, a slight change in pH of the environment causes a manifestation of the biological activity. The acid–base balance of the long BM is considered in this paper. The stem cells of the BM determine the differentiation of cells into different types. Therefore, it is necessary to know to what extent the pH changes affect the physical properties and physiological activity of the BM.

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Objectives of this research are (1) to determine pH of the BM of the long and flat bones and to conduct a comparative analysis of the acid–base status of the BM depending on the site of sample aspiration and (2) to investigate the possibility to use a blood gas and acid–base status analyzer (Radiometer Medical ApS, Akandevej 21 DK-2700 Bronshoj, Denmark) to determine pH status of the BM.

Subjects and Methods

Forty long BM samples were obtained in patients who gave the informed consent. Patient's mean age was 63 ± 12 (mean ± standard deviation) years. Twenty-five (62.5%) participants were male and 15 (37.5%) participants were female. Most patients (96%) had diabetes mellitus type 2 complicated by neuroischemic diabetic foot syndrome. Due to sphacelation, each patient had a lower limb amputated. The BM was extracted from the femur (upper or lower third of the thigh bone) into a sterile test tube, and the samples were transported to the laboratory.

Forty flat BM samples were extracted by sternal puncture in hematological patients and undiagnosed patients for diagnostic purposes. For comparison, flat BM samples were also obtained in patients who did not have hematologic malignancies. The BM extraction by sternal puncture was carried out in a standard way: the sternum front was punctured with Kassirsky's needle at the level of III–IV ribs along the mammillary line or near manubrium of the sternum; the needle penetrated the compact substance of the frontal surface of the sternum and entered the medullary space, which feels like reaching a cavity. Next, the mandrel was removed from the sternal needle and a 20 ml syringe was attached to aspirate the bone contents, and 1–2 ml of blood was extracted by applying vacuum. The contents of the syringes were delivered to the laboratory.

The use of hospital's analyzer constituted a risk because of the possibility to put it into inoperable condition.[12-14] The cell pellets and adipose tissue were removed by 10-min settling of the samples, at that the BM fat rises to the upper layer. Without disturbing the upper layer, the lower phase containing the nuclear cells of the BM was withdrawn into a clean tube. In addition, the obtained BM was twice filtered through four layers of gauze fabric to exclude damage to the analyzer. Acid–base properties were determined on a blood gas and acid–base status analyzer (Radiometer Medical ApS, Akandevej 21 DK-2700 Bronshoj, Denmark). This paper focuses on the acid–base balance; however, the data on the BM gas composition can also be of interest.[15]

Results

For the BM samples obtained by sternal puncture from flat bones, the values ranged within blood pH: 7.35–7.45 to 7.8. The study included data of patients whose diagnosis was not confirmed. The pH values and gas composition of the BM samples obtained by sternal puncture were identical to those of blood.[16-18]

The studied properties of the BM obtained from the long bones were different. The acid–base balance remained in a tight range from 6.7 to 6.9. If BM pH happened to be beyond these limits, it appeared that such samples were contaminated with blood, but only uncontaminated samples were selected for the purpose of this study. Most patients in this study had type 2 diabetes, which as the reason for lower limb amputation. However, the patients who were not diagnosed with diabetes have also had pH within the range from 6.7 to 6.9. Hence, type 2 diabetes could not have affected pH. Sites of hematopoiesis were sometimes observed in the long BM; these tissue sites were not removed. Blood pH of 7.4 is considered healthy and indicates that the blood chemistry is slightly alkaline. The values below this norm are described as acidic and indicate the increased acidity in the blood. Such state is called acidosis.

The comparison of the pH values of the flat BM obtained by sternal puncture and the long BM revealed a remarkable difference between the two series of samples. The flat BM (sternal puncture) has slightly alkaline properties, similar to blood,[19-21] while the long BM has an acidic status of 6.7–6.9. Differing acid–base balance argues for the differences in the functional activity.[22-24] Primarily, the BM in these samples can be distinguished by the cellular composition.

Further, the presence of stem cells was studied. In the flat BM, obtained by sternal puncture, only hematopoietic stem cells were found, while in the long BM, there were both hematopoietic and mesenchymal cells. It should be noted that hematopoietic cells in the long bones exist in the acidic environment, while the environment in the flat bones is slightly alkaline, similar to blood pH.[25-27] It can be assumed that hematopoietic cells originate in the long BM, and their further differentiation or maturation occurs in the flat bones, where they become functionally active.

Discussion

By controlling or changing the pH values, it can be possible to alter the BM cellular composition in the desired direction and to affect the differentiation of cells and their functional state.[28] The obtained results are subject to further analysis, and collection of data on the acid–base balance of the BM is to be continued.

This research revealed the following:

1. The BM (of both long and flat bones) has a permanent pH value
2. BM pH depends on the type of bone: flat BM pH is similar to blood pH; the long BM pH is acidic and ranges from 6.7 to 6.9
3. Hematopoietic stem cells occur in both acidic and slightly alkaline environments
4. Mesenchymal stem cells are, presumably, the source of hematopoietic stem cells and occur in the long bones in the acidic environment with pH of 6.7–6.9
5. The acid–base status appears to be an important factor of stem cell differentiation

6. A blood gas and acid–base status analyzer (Radiometer Medical ApS, Akandevej 21 DK-2700 Bronshoj, Denmark) is suitable for determining the acid–base properties of BM.

The study of the acid–base properties of BM is to be continued.[29] Given the development of stem cell technologies, the ability to control the stem cell differentiation and direct it as required using the environment pH is an urgent and relevant issue.

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Conflicts of interest

There are no conflicts of interest.

References

1. Nikolaeva LP, Cherdantsev DV, Stepanenko AV, Dyatlov VY. Change in antioxidant system state in patients with diabetic foot. Fund Res 2010;11:95-7.
2. Paltsev MA. Medicine of the 21 century in the light of cellular biology. Vestn Ross Akad Med Nauk 2004;9:3-11.
3. Veldhoen ES, de Vooght KM, Slieker MG, Versluys AB, Turner NM. Analysis of bloodgas, electrolytes and glucose from intraosseous samples using an i-STAT(®) point-of-care analyser. Resuscitation 2014;85:359-63.
4. Ummenhofer W, Frei FJ, Urwyler A, Drewe J. Are laboratory values in bone marrow aspirate predictable for venous blood in paediatric patients? Resuscitation 1994;27:123-8.
5. Miller LJ, Philbeck TE, Montez D, Spadaccini CJ. A new study of intraosseous blood for laboratory analysis. Arch Pathol Lab Med 2010;134:1253-60.
6. Orlowski JP, Porembka DT, Gallagher JM, Van Lente F. The bone marrow as a source of laboratory studies. Ann Emerg Med 1989;18:1348-51.
7. Paladino L, Sinert R, Wallace D, Anderson T, Yadav K, Zehtabchi S, *et al.* The utility of base deficit and arterial lactate in differentiating major from minor injury in trauma patients with normal vital signs. Resuscitation 2008;77:363-8.
8. Shirakabe A, Hata N, Kobayashi N, Shinada T, Tomita K, Tsurumi M, *et al.* Clinical significance of acid-base balance in an emergency setting in patients with acute heart failure. J Cardiol 2012;60:288-94.
9. Rudkin SE, Kahn CA, Oman JA, Dolich MO, Lotfipour S, Lush S, *et al.* Prospective correlation of arterial vs venous blood gas measurements in trauma patients. Am J Emerg Med 2012;30:1371-7.
10. Strandberg G, Eriksson M, Gustafsson MG, Lipcsey M, Larsson A. Analysis of intraosseous samples using point of care technology-an experimental study in the anae 2008 etherized pig. Resuscitation 2012;83:1381-5.
11. Nicoll SJ, Rochester SJ. Blood sampling through intraosseous needles: Time to stop? Resuscitation 2008;79:168.
12. Vos G, Engel M, Ramsay G, van Waardenburg D. Point-of-care blood analyzer during the interhospital transport of critically ill children. Eur J Emerg Med 2006;13:304-7.
13. Sediame S, Zerah-Lancner F, d’Ortho MP, Adnot S, Harf A. Accuracy of the i-STAT bedside blood gas analyser. Eur Respir J 1999;14:214-7.
14. Papadea C, Foster J, Grant S, Ballard SA, Cate JC 4th, Southgate WM, *et al.* Evaluation of the i-STAT portable clinical analyzer for point-of-care blood testing in the intensive care units of a university children’s hospital. Ann Clin Lab Sci 2002;32:231-43.
15. Nolan JP, Soar J, Zideman DA, Biarent D, Bossaert LL, Deakin C, *et al.* European resuscitation council guidelines for resuscitation 2010 section 1. Executive summary. Resuscitation 2010;81:1219-76.
16. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;1:307-10.
17. Franssen MA, Kleinveld HA, Bussmann-Willems D, Raijmakers MT. Kan beenmerg afgenomen met een intraossale canule voor laboratoriumonderzoek gebruikt worden. Ned Tijdschr Klin Chem 2013;38:130-1.
18. Hurren JS. Can blood taken from intraosseous cannulations be used for blood analysis? Burns 2000;26:727-30.
19. Grisham J, Hastings C. Bone marrow aspirate as an accessible and reliable source for critical laboratory studies. Ann Emerg Med 1991;20:1121-4.
20. Bland JM, Altman DG. Measuring agreement in method comparison studies. Stat Methods Med Res 1999;8:135-60.
21. Kelly AM. Review article: Can venous blood gas analysis replace arterial in emergency medical care. Emerg Med Australas 2010;22:493-8.
22. Abdelmoneim T, Kissoon N, Johnson L, Fiallos M, Murphy S. Acid-base status of blood from intraosseous and mixed venous sites during prolonged cardiopulmonary resuscitation and drug infusions. Crit Care Med 1999;27:1923-8.
23. Kissoon N, Rosenberg H, Gloor J, Vidal R. Comparison of the acid-base status of blood obtained from intraosseous and central venous sites during steady- and low-flow states. Crit Care Med 1993;21:1765-9.
24. Kissoon N, Peterson R, Murphy S, Gayle M, Ceithaml E, Harwood-Nuss A, *et al.* Comparison of pH and carbon dioxide tension values of central venous and intraosseous blood during changes in cardiac output. Crit Care Med 1994;22:1010-5.
25. Schuster HP. Prognostic value of blood lactate in critically ill patients. Resuscitation 1984;11:141-6.
26. Müllner M, Sterz F, Domanovits H, Behringer W, Binder M, Laggner AN, *et al.* The association between blood lactate concentration on admission, duration of cardiac arrest, and functional neurological recovery in patients resuscitated from ventricular fibrillation. Intensive Care Med 1997;23:1138-43.
27. Shinozaki K, Oda S, Sadahiro T, Nakamura M, Hirayama Y, Watanabe E, *et al.* Blood ammonia and lactate levels on hospital arrival as a predictive biomarker in patients with out-of-hospital cardiac arrest. Resuscitation 2011;82:404-9.
28. Seeger FH, Toenne M, Lehmann R, Ehrlich JR. Simplistic approach to prognosis after cardiopulmonary resuscitation-value of pH and lactate. J Crit Care 2013;28:317.e13-20.
29. Ciesla B. Hematology in Practice. Moscow: Prakticheskaya Meditsina; 2011.