



LETTER TO THE EDITOR

Reply to “Letter to the Editor: Clinical implications for the effect of glucosamine sulfate iontophoresis on fasting plasma glucose levels”

Ayodele Teslim Onigbinde, BMR PT, PhD ^{a,*}, Adetayo Egun Talabi, PhD ^b,
Raheem Adaramaja Shehu, PhD ^b, Chidozie E. Mbada, MSc PT ^a

^a Medical Rehabilitation Department, College of Health Sciences, Obafemi Awolowo University, Ile-Ife, Osun State, Nigeria

^b Human Kinetics and Health Education Department, University of Ilorin, Ilorin, Kwara State, Nigeria

We appreciate the comments of Mohan and Joseph [1] on our research work entitled “Acute effects of combination of glucosamine sulfate iontophoresis with exercise on fasting plasma glucose of participants with knee osteoarthritis.” We wish to reply to their comments in order.

First and foremost, the research paper was a technical report on a *preliminary experimental study* in a verdant area in patient care, which may serve as a foundation for future studies.

In our opinion, this study has potential clinical applicability and usefulness in spite of its quasi-experimental design. A quasi-experimental design approximates to a true experimental design but with the limitation that it does not allow a complete control of extraneous variables. However, the quasi-experimental design is closer to reality in clinical practice, and has higher external validity than a classic randomized controlled design.

The electromotive drug administration (EMDA) process for iontophoresis seems to be gaining wider acceptance among physiotherapists, although it is still difficult, in most clinical settings and research studies, to establish the pharmacodynamic and pharmacokinetic properties of most drugs administered via EMDA. Glucosamine has been used clinically since 1960s, but its pharmacokinetics are not well

defined due, at least in part, to a lack of sensitive or easy assays. Consequently, more studies on the pharmacokinetics of glucosamine seem to be needed to help resolve the controversial data generated from various clinical trials [2]. In our study, the bioavailability of glucosamine could not be determined because of a non-availability of high-performance liquid chromatography assay and an inability in our laboratory to carry out radioisotope labelling to detect plasma glucosamine. Glucosamine is an amino sugar that lacks chromophores, hence it is undetectable in the ultraviolet–visible light range, and most radiolabelled compounds cannot differentiate between the parent compound and its biosynthetic or degraded products [3].

It was assumed that the dose of 300 mg glucosamine sulfate cream applied transdermally would be adequate based on reported efficacy in terms of pain relief in previous studies [4–6]. The trend of pain relief suggested that the drug is bioavailable to exert therapeutic effects. Lee et al strongly suggested that a high and sustainable level of glucosamine in the blood could be achieved via a topical application of Mediflex glucosamine cream and was able to provide enzymes with a sufficient amount of substrate for the processes of cartilage regeneration and rehabilitation [4]. The implication is that the concentration of glucosamine achieved via iontophoresis is likely to be physiologically active and affect the glucose concentration.

Like most clinical trials involving human subjects seen over a period of time, our study suffered from attrition, thereby affecting our sample size. However, the sample size used in this preliminary study was an improvement over

DOI of original article: 10.1016/j.hkpj.2011.11.001.

* Corresponding author. Medical Rehabilitation Department, Faculty of Basic Medical Sciences, College of Health Sciences, Obafemi Awolowo University, Ile-ife, Osun State, Nigeria.

E-mail address: ayotesonigbinde@yahoo.co.uk (A.T. Onigbinde).

those of previous studies. The aerobic exercise carried out on cycle ergometer in this study was unloaded considering the subjects' knee pathology, while maintaining uniformity in time for 15 minutes. In addition, we encouraged all participants, via a prerecorded audioverbal motivational message, to pedal as quickly as possible.

"Direct current" was a term formerly used for galvanic current and was intended to be used synonymously in this study. We believed that reverse iontophoresis has nothing to do with current mode but may have an effect on the charge of the drug or molecule when the skin is negatively charged at a buffered pH.

The lower plasma glucose levels among the participants in group 2 might be due to the effect of electrical muscle stimulation. During electrical muscle stimulation, electrical signals cause cross-bridge cycling between myosin and actin, which generates force. There is an excitation and reversing of contraction; and various activities that requires energy [7]. Muscles use energy in the form of Adenosine Tri-phosphate (ATP), and during aerobic respiration in muscles, glucose, glycogen, fats and amino acids are broken down in the presence of oxygen to produce more ATP [7]. The combination of voluntary and electrical muscle contractions have previously been observed to decrease fasting blood glucose, although this was after 12 weeks' training [8]. Muscle contraction compresses the blood vessels within the muscle, resulting in diminished blood flow, which will subsequently reduce the glucose level. Electrical muscle contraction alone and insulin alone increased glucose uptake significantly in a study by Brozinick et al [9], although this was on rat skeletal muscle. Our study showed that, despite the administration of the amino sugar glucosamine sulfate to participants in group 2, there was still a further depletion of plasma glucose concentration.

In conclusion, we appreciate the comments of Mohan and Joseph on our study. We have noted the limitations pointed out in the article, will definitely address these in

future studies, and look forward to collaborating with their institution.

References

- [1] Vikram M, Leonard J. Clinical implications for the effect of glucosamine sulfate iontophoresis on fasting plasma glucose levels. *Hong Kong Physiother J* 2012;30:2–3.
- [2] Vlad SC, LaValley MP, McAlindon TE, Felson DT. Glucosamine for pain in osteoarthritis: why do trial results differ? *Arthritis Rheum* 2007;56:2267–77.
- [3] Setnikar I, Giacchetti C, Zanolio G. Pharmacokinetics of glucosamine in the dog and in man. *Arzneimittelforschung* 1986;36:729–35.
- [4] Lee CW, Li Z, Patel K, Oloo J, Lee EJD, Gor LB. The transdermal profile of Mediflex glucosamine cream in mouse and man [Internet]. Indonesia: 4th National Congress of Indonesian Society of Rheumatology. Available from: <http://www.lynkbiotech.com/pdf/publications/tgl/A5RL.pdf>; 2005.
- [5] Onigbinde AT, Adedoyin RA, Olaogun MOB, Ojoawo OA, Akinpelu AO, Onibokun A. Efficacy of glucosamine iontophoresis in the management of knee osteoarthritis [abstract]. *Niger Med Pract*; 2008:54.
- [6] Onigbinde AT, Adetogun GE, Ojoawo AO, Omotuyi OC. Comparative efficacy of low metal glucosamine sulphate iontophoresis in the management of lumbar spondylosis. *Indian J Physiother Occup Ther* 2009;3(3):12–5.
- [7] Craig F. How muscles work [Internet; cited 2012 Jan 5]. Available from: <http://science.howstuffworks.com/environmental/life/human-biology/muscle2.htm>.
- [8] Takumi K, Naoto S, Yoshio T, Takashi M, Michio S. Hybrid training of voluntary and electrical muscle contractions decreased fasting blood glucose and serum interleukin-6 levels in elderly people: a pilot study. *Appl Phys Nutr Metab* 2011;36: 276–83.
- [9] Brozinick JT, Etgen GJ, Yaspelkis BB. The effects of muscle contraction and insulin on glucose-transporter translocation in rat skeletal muscle. *Biochem J* 1994;297(Pt 3): 539–45.