Title: What's in a name? That which we call diabetes does not taste sweet!

Running head: Diabetes insipidus naming dilemma

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What's in a name?

Shakespeare famously raised that questioned in "Romeo and Juliet", where Juliet dismisses the importance of a name: "that which we call a rose by any other name would smell as sweet". And yet, the name (in their case the last names, which identified them as belonging to enemy families) mattered enormously and eventually contributed to their tragic deaths. In medicine, misunderstandings about names can have similarly fatal consequences.

When the name is a problem: "diabetes insipidus"

Anyone caring for patients with nephrogenic diabetes insipidus is probably familiar with this scenario: an affected subject is brought to hospital, for instance because of a gastrointestinal infection, and when they inform the staff of the underlying diagnosis, only one word is understood: "diabetes". Virtually every health care professional is familiar with "diabetes", a shortening of the name for the common disorder "diabetes mellitus". In contrast, "diabetes insipidus", is rare and many practitioners are unfamiliar with this diagnosis, let alone it's pathophysiology and management. Consequently, a blood sugar may be checked and the patient reassured and sent home. And even if a set of electrolytes is obtained and hypernatraemic dehydration revealed, erroneous treatment in the form of isotonic solutions may be administered, with potentially serious consequences [1]. Moreover, patients may suffer from iatrogenic hypernatraemia, if kept nil by mouth for prolonged periods prior to a planned procedure or given intravenous fluids with a tonicity that exceeds that of their urine [2]. Such inadvertent mismanagement is not only experienced by patients with nephrogenic, but also central diabetes insipidus, as recently reported by a group of endocrinologists [3]. They performed an online survey of patients with central diabetes insipidus on their experience with management and complications of their disease, awareness of the condition

by health care professionals and their opinion on renaming the condition. More than a thousand patients participated and the results are sobering. Central diabetes insipidus is typically treated with desmopressin, yet roughly a quarter of participants reported difficulties of accessing desmopressin when in hospital (e.g., for acute illness or elective surgery), typically because of non-availability or absence of a prescription. More than half reported being asked to abstain from drinking and eating for medical reasons during hospitalisations and 54% of those reported receiving no intravenous fluids during that time. Incredibly, only 3% of those kept nil by mouth and not receiving intravenous fluids reported being prescribed desmopressin! Another 72% reported using their own desmopressin and 25% stated they did not receive any desmopressin and experienced typical symptoms of dehydration [3]. A staggering 80% of participants indicated that health care professionals had confused their condition with diabetes mellitus on at least one occasion. And 86% felt that physicians' (not directly involved in the regular management of their diabetes insipidus) general knowledge of their condition was insufficient. When asked to rate this on a scale of 1-10, the average response was a sobering "2". Perhaps unsurprisingly, 85% of participants stated that they favoured a renaming of their condition with the most common suggestions being "vasopressin deficiency" or "arginine vasopressin deficiency" [3].

Should we rename the diabetes insipidus conditions?

The results of this patient survey are indeed alarming. While based on self-reporting by patients rather than review of documented hospital records, there is no reason to assume that patients would exaggerate or distort their experiences. It is, of course, possible that patients who have experienced mismanagement may be more likely to participate in such a survey as those who have not experienced any complications, leading to biased results. Yet,

our own experience with nephrogenic diabetes insipidus suggests that the proportion of patients reporting confusion of their condition with diabetes mellitus by health care professionals is probably realistic. Reluctance to publicly declare errors leads to an obvious publication bias so that reports of such confusion and the resulting mismanagement are rarely, if ever reported in the literature. Presumably, in most cases, the consequences are minor, such as repeated unnecessary blood sugar testing, as also reported by the patients with central diabetes insipidus in the survey. But in other cases, the consequences may be more severe, such as failure to obtain electrolytes to detect and manage hypernatraemic dehydration or treatment with inappropriate intravenous fluids.

Renaming of diabetes insipidus should be carefully considered, as it is a well-established medical term. The first description dates back to 1794, when Johann Peter Frank of the University of Pavia described patients characterized by "long continued abnormally increased secretion of nonsaccharine urine which is not caused by a diseased condition of the kidneys" and introduced the term "diabetes insipidus" [5]. This term was picked up in 1892 by McIlraith and has been in clinical use, textbooks and publications ever since, with "diabetes" referring to polyuria and "insipidus" to the tasteless nature of the urine that distinguished it from the sweet tasting polyuria of "diabetes mellitus" [4]. Yet, with increasing longevity and affluence, the prevalence of diabetes mellitus has skyrocketed and consequently has become synonymous with just "diabetes". Given this synonymity, misunderstandings with regards to "diabetes insipidus" are probably inevitable with a high risk of patient harm.

What would be a better name?

The "Working Group for Renaming Diabetes Insipidus" has suggested the terms "vasopressin deficiency" for cranial and "vasopressin resistance" for nephrogenic diabetes insipidus, which

make sense, as they do reflect the pathophysiology [5]. But, of course, the issue is complicated by the fact that the involved hormone has at least three different names: “vasopressin”, “arginine vasopressin” and “antidiuretic hormone”. Personally, we would prefer “antidiuretic hormone deficiency/resistance”, as the pathophysiology primarily concerns the antidiuretic effects of the hormone, mediated by the type 2 receptor AVPR2 in the kidney collecting duct cells, rather than the vasopressor effects, mediated by AVPR1.

The critical and obvious questions are: would renaming the condition really decrease the frequency of mismanagement? Would a health care professional be more aware of the diagnosis and its implications, if a patient told them that they have a diagnosis of antidiuretic hormone resistance? The knowledge and understanding of health care practitioners of such a rare condition will probably be just as limited, even if the name clearly reflects the pathophysiology. But the risk of confusion with “diabetes” is abolished and, when faced with an unknown rare diagnosis, the health care professional may be more inclined to look this up or consult a specialist.

Conclusion

We therefore propose that like our endocrinology colleagues, we should survey our patients with nephrogenic diabetes insipidus, patient advocacy organisations (such as the NDI foundation, https://ndif.org/), as well as our nephrology colleagues through our national and international professional societies, with respect to experiences of diagnostic confusion with the term “diabetes” and their thoughts and ideas about renaming the condition. We believe that if supported by those surveyed, and a consensus is built, replacement of "DI" by the terms "ADH Deficiency" and "ADH Resistance" will benefit patients, their families and health care providers. For our dilemma is unlike that of Shakespeare’s Juliet: she dismissed the

importance of different names for the same thing, as it was the characteristics that mattered ("that which we call a rose by any other name would smell as sweet"). In contrast, we have the problem of having the same name for two different conditions, with clearly different characteristics: that which we call diabetes (insipidus) does not taste sweet!

Conflict of Interest.

The authors declare no conflicts of interest.

References

1. Bockenhauer D, Bichet DG (2017) Nephrogenic diabetes insipidus. Curr Opin Pediatr, 29: 199-205 https://doi.org/10.1097/MOP.0000000000000473
2. Bockenhauer D, Bichet DG (2015) Pathophysiology, diagnosis and management of nephrogenic diabetes insipidus. Nat Rev Nephrol, 11: 576-588 https://doi.org/10.1038/nrneph.2015.89
3. Atila C, Loughrey PB, Garrahy A, Winzeler B, Refardt J, Gildroy P, Hamza M, Pal A, Verbalis JG, Thompson CJ, Hemkens LG, Hunter SJ, Sherlock M, Levy MJ, Karavitaki N, Newell-Price J, Wass JAH, Christ-Crain M (2022) Central diabetes insipidus from a patient's perspective: management, psychological co-morbidities, and renaming of the condition: results from an international web-based survey. Lancet Diabetes Endocrinol: https://doi.org/10.1016/S2213-8587(22)00219-4
4. McIlraith CH (1892) Notes on some cases of diabetes insipidus with marked family and hereditary tendencies. Lancet, 2: 767
5. Working Group for Renaming Diabetes I, Arima H, Cheetham T, Christ-Crain M, Cooper D, Gurnell M, Drummond JB, Levy M, McCormack AI, Verbalis J, Newell-Price J, Wass JAH (2022) Changing the name of diabetes insipidus: a position statement of The Working Group for Renaming Diabetes Insipidus. Endocr J: https://doi.org/10.1507/endocrj.EJ20220831