Dried Blood Spot in Toxicology

Subjects: Toxicology

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Dried Blood Spot (DBS) is becoming very popular in various medical fields, especially in toxicology. Nowadays, it is commonly used in newborn screening for inherited or congenital diseases. DBS does not require trained medical staff to collect the samples and can be effortlessly transported to the laboratory, which makes it an easy and quick procedure. A venous blood spot, collected from a finger or a heel, is put on the special paper card, which can result in a different distribution of blood and concentration of detecting substances. DBS enables drugs analysis, detecting substances of abuse as well as trace elements. It also serves its purpose in newborn screening and testing in SARS-CoV-2 serology. DBS is certain to develop rapidly and become even more worldwide used.

Keywords: dried blood spot ; dried blood spots ; dried blood filter ; dry blood spot ; toxicology ; forensic

1. Introduction

Dried Blood Spot (DBS) is a technique that involves collecting small samples of venous blood (plasma or serum are applicable as well), usually from a finger, toe, or heel, onto an absorbent filter paper. Whatman® 903 paper is frequently used since it is made from pure cotton fibers [1][2]. Exceptionally, at the crime scene, other materials than paper are used. After the drop of blood is air-dried, it can be transported to a laboratory and analyzed.

2. History

DBS was discovered in 1913 by Ivar Bang, who used it for glucose concentration monitoring in rabbits. Half a century later, in 1963, Guthrie and Susi managed to prove blood sampling useful in screening for phenylketonuria. In the 1970s, DBS was implemented in serological surveillance and used to diagnose syphilis and detect antibodies for mumps and measles. Due to the increase in HIV morbidity, DBS has attracted attention at the beginning of the year 2000 and successfully helped to monitor HIV infection. Nowadays it is used commonly in various fields such as medicine, pharmacy, and new technologies [3][4].

3. Drugs Analysis

DBS may be significant for detecting drugs and help pharmaceutical concerns in conducting research. Multiple substances can be measured in DBS: benzodiazepines, Z-drugs (zolpidem, zopiclone), opiates (6-monoacetylmorphine, morphine, codeine, hydromorphone, hydrocodone, oxycodone, noroxycodone), tramadol, methadone, buprenorphine, fentanyl, ketamine, and their respective metabolites [5] (and references therein). Moreover, there are reports that it is possible to mark the level of ethyl glucuronide that serves as an alcohol abuse marker [5] (and references therein). Analyzing drugs with DBS serves two main purposes. Firstly, it can detect drug abuse in adults or measure the level of medication (TDM—Therapeutic Drug Monitoring) and improve a follow-up. Secondly, it can evaluate the exposure to the drugs before birth in newborns. Both therapeutic and illegal ones. The aforementioned TDM used with DBS has proven to be highly effective in monitoring busulfan in children, who had to undergo a hematopoietic stem cell transplantation [6]. In addition, a study by Hahn et al. showed that topiramate TDM is also possible and highly beneficial [7]. Finally, a study by Duthaler et al. contains good results of therapeutic drug monitoring of antiretroviral drugs in resource-poor regions using the DBS technique [8].

4. Advantages of DBS

DBS has several advantages. Firstly, it can be easily collected. It is simple and there is no need for trained medical staff to perform sampling. The extraction procedure is simplified, economical, and cost-effective. There is a possibility for automatization, which would increase the speed of this already rapid process. Secondly, there is a low biohazard risk during transportation. There is no leakage because paper cards with blood are dry so it is safe for the personnel. Safety is

also maintained due to the loss of infectivity of some viruses during the drying process. That applies to the HIV-1 and -2 viruses, the human T-cell leukemia/lymphoma virus-I and -II, and the hepatitis C virus [9]. Thirdly, DBS has a stabilizing effect on drugs and it inhibits degradation of the substance [10]. The other advantage of DBS that is worth mentioning is the ability to assess the acute state of the patient. This technique is quick and can provide crucial information about a patient's health, to treat him as fast as possible [9]. Another important advantage is gender neutrality and lack of adulteration issues [11]. The other asset to be enumerated is the ability to keep DBS paper cards as evidence, even when the case is closed and other evidence is discarded. Their storage is uncomplicated and they do not require a lot of space. The downside of this idea is that paper cards cannot be stored forever due to their limited preservation time [5] (and references therein). Therapeutic drug monitoring is a perfect place for DBS. Due to easy sampling and speed, DBS can be performed before the doctor's arrival and show the concentration of certain substances (such as antibiotics, antidepressants, immunosuppressants, and antiretrovirals) in the patient's blood [12]. Liquid extraction or solid-phase extraction requires more blood (around 100–2000 µL) than DBS (10–100 µL), which makes DBS more convenient [10]. Finally, there is an opportunity to perform roadside testing for impaired driving. Collecting blood on the crime scene is reliable and practical [10].

5. Disadvantages of DBS

DBS may seem flawless, but it has some downsides as well. The drying time is quite long and lasts around 2 h, depending on the conditions such as the type of card and blood volume. Also, the blood can coagulate or lyze, which makes the distribution on the paper card differ [13]. The viscosity of the blood has a similar impact on blood distribution [2]. Then, the results may be disturbed and not reliable [10]. Moreover, detecting some substances may be difficult. Few substances have been measured with the DBS technique. Further research is needed. Due to the small volume of blood collected, it may be impossible to detect multiple drug groups at once. It would require a few DBS samples, so the whole process would be elongated and more complicated [1].

6. Future Perspectives

DBS has enormous potential for massive development. It is constantly being automatized and new robots are being designed to make DBS less dependent on human beings. Direct analysis technologies are evolving and filter paper is being brought to perfection. Probably, it will be good enough to provide the same blood distribution within the spot and preserve the substances for a longer period. Standardization of the whole process may contribute to the increase of results reliability. Hopefully, in the future, there will be extensive research of postmortem samples, that are hemolyzed and putrefied [14]. Furthermore, there are derivatives of the DBS technique such as perforated DBS (PDBS), bilayer DPS card, and Hemaspot technology [15]. They may replace usual DBS and create new possibilities for substances detection. Especially, the pharmaceutical sector is bound to use DBS even more and it may improve their clinical studies [16]. Also, worldwide preparing DBS kits divided into panels for metabolic, hormonal, and cardiovascular disorders can speed along the diagnostics.

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