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Horizon Scanning Technology

Prioritising Summary

HypoMon®: a non-invasive device for the detection of hypoglycaemia in Type I diabetics

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PRIORITISING SUMMARY

REGISTER ID: **000154**

NAME OF TECHNOLOGY: **HYPOMON®**

PURPOSE AND TARGET GROUP: **NON-INVASIVE DEVICE FOR THE DETECTION OF HYPOGLYCAEMIA IN TYPE I DIABETICS**

STAGE OF DEVELOPMENT (IN AUSTRALIA):

☐	Yet to emerge	☐	Established
☐	Experimental	☐	Established *but* changed indication or modification of technique
☒	Investigational	☐	Should be taken out of use
☐	Nearly established		

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

☐	Yes	ARTG number
☒	No	
☐	Not applicable	

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
Australia	✓		

IMPACT SUMMARY:

Aimedics Pty Ltd provides the HypoMon® with the aim of providing a non-invasive means of detecting hypoglycaemia. Aimedics Pty Ltd is currently applying for TGA approval and it is likely that if this device were made available that it would be provided on a prescription basis through general practitioners or diabetes clinics for individuals, particularly children, with type I diabetes.

BACKGROUND

Type I diabetes usually arises in children or young adults and is characterised by the inability to produce insulin. Although treatment regimens and types of insulin available have developed over time, individuals with type I diabetes are still required to self inject with insulin to control their blood sugar levels. Insulin doses must be adjusted according to carbohydrate intake and the degree of physical activity being undertaken. Hypoglycaemia, or low blood sugar levels, is one of the most common side effects among individuals with type I diabetes and is a barrier to achieving and maintaining tight glycaemic control. Tight glycaemic control (maintaining glycaemic

levels to a target HbA_{1c}[1] level of seven per cent has been demonstrated to lower the risk of developing retinopathy by 47 per cent, nephropathy by 54 per cent and neuropathy by 60 per cent (Nguyen, Ghevondian et al. 2008).

Individuals who experience frequent episodes of hypoglycaemia and those who have been on insulin therapy for a long period of time may develop impaired awareness of hypoglycaemia. Early warning symptoms such as tremor and sweating may no longer occur and symptoms including drowsiness and lack of concentration become more prominent. Impaired hypoglycaemic awareness occurs in approximately 25 per cent of individuals with type I diabetes. Severe hypoglycaemia may lead to coma or organ damage and may result in accidents especially road traffic accidents. The cumulative long-term effect of hypoglycaemia in an individual is unknown. Nocturnal episodes of hypoglycaemia are of concern as the sympatho-adrenal response is dulled and the usual warning symptoms are absent. Nocturnal hypoglycaemia is common but usually remains undetected however indications that an episode may have occurred include a morning headache, poor quality sleep, nightmares and profuse night sweats. Fatal nocturnal hypoglycaemic episodes may be a result of cardiac arrhythmias (Frier 2008). Approximately 50 per cent of severe hypoglycaemic episodes occur at night (Nguyen, Ghevondian et al. 2008).

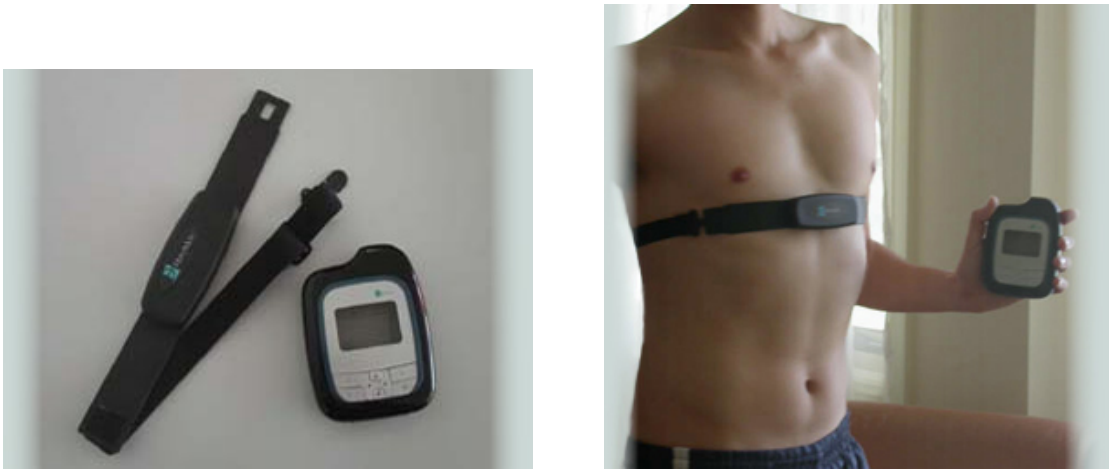

Figure 1 The HypoMon® device (Aimedics 2007)

The HypoMon® is a non-invasive monitoring device capable of detecting hypoglycaemia in insulin dependent type I and II individuals. When the device detects blood glucose levels below 2.5mmol/L (45mg/dL)[2] an alarm sounds to alert the individual or carer. This may be especially useful in avoiding nocturnal episodes of hypoglycaemia. The HypoMon® may also assist in maintaining tight glycaemic control. The HypoMon® consists of a battery powered chest belt which houses a set of four skin surface bio-sensor electrodes (Figure 1). The chest belt digitises, encrypts

[1] HbA_{1c} = glycolsylated haemoglobin
[2] Hypoglycaemia < 3.5 mmol/L, normal glucose levels: 4-6 mmol/L before meals, 4-8 mmol/L after meals, high glucose levels: > 7 mmol/L before meals, > 11 mmol/L after meals (Diabetes Australia - Victoria 2004).

and transmits the measured physiological parameters (heart rate, corrected QT interval and skin impedance) to a receiver computer using a wireless communication link. The collected data are applied to an algorithm which determines the level of hypoglycaemia. There is an alarm system that can be activated in case of severe hypoglycaemia, to warn the patient or physician in critical situations (Aimedics 2007).

CLINICAL NEED AND BURDEN OF DISEASE

In New Zealand the incidence of type I diabetes appears to be increasing and in the year 2000 it was estimated that the prevalence of people with type I diabetes was 10,564[3] (Health Funding Authority 2000). The estimated incidence of type-1 juvenile diabetes was 25.8 cases per 100,000 persons aged up to 19 years in 2001.[4] In New Zealand individuals with type I diabetes represent approximately five per cent of all diabetic cases in Maori and Pacific Islanders, however 11 per cent of individuals of European decent with diabetes have type I.

In Australia during the period 2000-2006, the annual age-adjusted incidence rate of type I diabetes for children aged 0-14 years was 22.4 new cases per 100,000 population. There has been a slight increase in the incidence in this age group from 19.2 in 2000 to 22.6 in 2006, with the greatest increase occurring in 10-14 year olds (Catanzariti, Faulks et al. 2008). In comparison to other OECD countries, the incidence of type I diabetes in Australia is high, with only Norway, Sweden and Finland having a higher annual incidence. Amongst people aged 15 years and over at first insulin use, there were an average of 1,260 new cases per year. The rate of new cases amongst people aged over 15 years decreases dramatically with age and plateaus at aged 45 years. The peak incidence rate of type I diabetes occurs at age 15 years (Pieris-Caldwell, Templeton et al. 2008).

DIFFUSION

The HypoMon® device does not have TGA approval and therefore has not diffused into the Australian health care sector as yet. The company estimate that the product will be marketed in Australia within a 1-2 year time frame (personal communication Aimedics Pty Ltd).

COMPARATORS

The current gold standard for use by the patient in the home for self-monitoring of blood glucose (SMBG) is the blood glucose meter, which is a small, portable battery-operated device. There are currently more than 25 different brands of commercially available glucose meters. SMBG is recommended for all people with diabetes, but especially for those treated with insulin. It is recommended that patients with Type-1 diabetes test glucose levels three or more times per day. SMBG plans may

[3] Estimated population of New Zealand in 2000 was 3,857,800 (Statistics New Zealand 2008).
[4] Lipid and Diabetes Research Group, Christchurch Hospital, New Zealand.

recommend testing glucose levels before all meals, two hours after meals and before retiring for the night. All portable blood glucose meters measure the amount of glucose in whole blood. Glucose levels in plasma are generally 10-15 per cent higher than glucose measurements in whole blood. The results are displayed on a digital readout approximately 1-2 minutes after the test strip is placed into the meter. Glucose meters can detect glucose over the range 0-34 mmol/L. Many SMBG meters now give results as "plasma equivalent", using a built in algorithm, allowing comparison of home glucose measurements to those determined from plasma by HPLC (FDA 2005).

SAFETY AND EFFECTIVENESS ISSUES

The HypoMon® was used to measure the physiological parameters of 16 children during a 10-hour overnight stay in a children's hospital (mean age 14.6 ± 1.5 years). Data were continuously collected via the HypoMon® device and compared to blood glucose levels. They then were used to determine the effect of natural nocturnal hypoglycaemia on physiological responses (level III-2 diagnostic evidence). Data were normalised to reduce patient to patient variability. During hypoglycaemic episodes, compared to non-hypoglycaemia, the heart rate increased slightly (1.082 ± 0.298 vs 1.033 ± 0.242, $p<0.06$) and the corrected QT interval increased significantly (1.06 ± 0.084 vs 1.031 ± 0.086, $p< 0.001$). There was no difference in skin impedances (1.111 ± 1.460 vs 1.108 ± 1.277, $p<0.984$). Data were divided into training and testing sets, each with eight patients randomly selected. Using an optimal Bayesian neural network and an algorithm developed from the training data, a sensitivity of 89.2 per cent was obtained for the detection of hypoglycaemia in the test data set. During natural nocturnal hypoglycaemia, the measured physiological parameters did not correlate as well to the actual blood glucose levels as those observed during induced hypoglycaemia during glucose clamp studies (described below) (Nguyen, Ghevondian et al. 2008).

Similar results were reported by the same author in two earlier studies. In the 2006 study, 21 children (mean age 14.4 ± 1.6 years) volunteered to undergo a 4-hour glucose clamp study[5]. The HypoMon® device continuously collected data during the clamp study and blood glucose levels were obtained simultaneously (level III-2 diagnostic evidence). The clamp study consisted of five phases: baseline (30 mins) euglycaemia[6] (60 mins), ramp phase (30 min), hypoglycaemia (40 min) and euglycaemia (30 min). During hypoglycaemic episodes all three physiological parameters increased significantly: heart rate (1.16 ± 0.16 vs 1.03 ± 0.112, $p<0.0001$), corrected QT interval (1.09 ± 0.09 vs 1.02 ± 0.07, $p< 0.0001$) and skin impedances (0.66 ± 0.19 vs 0.82 ± 0.21, $p< 0.0001$). Data were divided into training and testing sets, each with seven patients randomly selected. Using an optimal Bayesian neural network and an algorithm developed from the training data (as with the 2008 study), a

[5] Glucose clamp studies are used to quantify beta cell sensitivity to glucose or tissue sensitivity to insulin by varying the concentration of either glucose or insulin, as described in the protocol.
[6] Normal blood glucose

sensitivity and specificity of 95 and 41 per cent, respectively, was obtained for the detection of hypoglycaemia in the test data set (Nguyen, Ghevondian et al. 2006). The 2007 study was slightly larger (n=25, mean age 14.4 ± 1.6 years) and may include results from the 2006 study. Using the same Bayesian inference, the ROC[7] plot for the training data was 0.9135 with 95% CI [0.8748, 0.9521]. Applying the selected neural network algorithm applied to the test data, a sensitivity and specificity of 83 and 64 per cent were obtained, respectively (Nguyen, Ghevondian et al. 2007).

COST IMPACT

Although the device is currently not available in Australia, the company estimates that the price of the device would be A$500 (personal communication Aimedics Pty Ltd).

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No issues were identified/raised in the sources examined.

OTHER ISSUES

The HypoMon® is a device that has been developed in conjunction with the University of Technology, Sydney, Australia. One of the authors on all three papers, N. Ghevondian, is employed by AIMedics Pty Ltd.

SUMMARY OF FINDINGS

Only three small studies all emanating from the same research group were available for assessment. These studies correlated the values obtained for physiological parameters with the HypoMon® with blood glucose levels. Only one study described results obtained under true conditions of nocturnal hypoglycaemia, whereas the remaining two studies described those obtained under the induced hypoglycaemic conditions of a glucose clamp study. The sensitivities obtained for the detection of a true hypoglycaemic episode were good, ranging from 83-95 per cent. However the conditions of a glucose clamp study are different from those experienced under true nocturnal conditions, therefore further large scale studies would need to be conducted before this device could be used in the home.

HEALTHPACT ACTION:

Although readings obtained with the HypoMon® device had a high sensitivity, the specificity obtained with the device was low. Individuals may decide to purchase this device to assist with the monitoring of hypoglycaemic episodes, therefore it is likely that this device will diffuse into the health care system of its own accord. Therefore HealthPACT has recommended that further assessment of this technology is no longer warranted.

[7] ROC = receiver operator characteristic

NUMBER OF INCLUDED STUDIES

Total number of studies	
Level III-2 diagnostic evidence	3

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SEARCH CRITERIA TO BE USED:

Algorithms
Bayes Theorem
Diabetes Mellitus, Type 1/complications/*diagnosis
Diagnosis, Computer-Assisted
Hypoglycemia/*diagnosis/etiology

Neural Networks (Computer)
Blood Glucose/metabolism
Glucose/metabolism