NOVEL PROTEOMIC BIOMARKERS IN DIABETIC RETINOPATHY

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Rationale

Diabetic retinopathy (DR), a major complication of diabetes is one of the leading causes of blindness worldwide. Blindness is preventable if DR is detected and treated early. Regular ophthalmic screening of at risk patients is a major burden on finite clinical resources. The identification of circulating biomarkers that help appropriate risk stratification of DR will allow for early diagnosis and rationalise screening programmes.

Aim

In this study we aimed to identify novel proteomic signatures for proliferative (PDR) and non-proliferative DR (NPDR).

Methods

Plasma samples from a total of 60 patients with active PDR or severe NPDR, 60 patients with minimal or moderate NPDR and 60 patients without DR were obtained. Following albumin depletion, plasma protein levels in each subgroup were analysed using isobaric tags for relative and absolute quantitation (iTRAQ) conducted using mass spectrometry on precisely constructed equi-volume plasma pools from type 2 diabetics.

Results

We identified a panel of 42 proteins significantly altered in the plasma of diabetic patients with PDR/NPDR when compared to diabetic controls without DR. The most significant PDR biomarker candidates ($p=1.0 \times 10^{-6}$) were selected as diagnostic screening candidates; apolipoprotein B-100 (APOB100) ($p<1.0 \times 10^{-27}$), Fibronectin ($p<1.0 \times 10^{-6}$), Ceruloplasmin (CP) ($p=5.34 \times 10^{-12}$), Gelsolin ($p=9.51 \times 10^{-12}$), Complement comonent 5 (C5) ($p=4.71 \times 10^{-8}$), zinc-alpha (2)–glycoprotein (ZAG) ($p=5.35 \times 10^{-7}$), CD5 antigen-like protein (CD5L) ($p=6.57 \times 10^{-6}$), and alpha-1microglobulin/bikunin precurcor (AMBP) ($p=2.04 \times 10^{-6}$).

Discussion

Of these four are novel to our study; CP, C5, AMBP and CD5L. Four have been previously identified in association with DR: APOB100 has been implicated as a candidate PDR; a study of vitreous samples revealed levels of the ZAG and Gelsolin significantly increased in PDR compared to non-diabetic controls; Fibronectin has been shown to increase in the retina, vitreous and newly formed capillaries of patients with DR.

Conclusion

Our study has shortlisted candidates of potential DR biomarkers and confirmed some previously identified markers. Replication and further confirmation to refine these candidates is required. Once confirmed, these biomarkers could be used to improve DR risk stratification and eventually incorporated into current clinical diabetes eye care management.