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RAPID COMMUNICATION

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Clinical Outcomes Following Supply-Driven Transition From Intranasal to Oral Desmopressin in AVP-Deficiency—A Single Centre Experience Including The Pituitary Foundation Desmopressin Shortage Impact Report

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ABSTRACT

Introduction: Arginine vasopressin deficiency (AVP-D) requires lifelong desmopressin replacement. In March 2025, the national suspension of intranasal desmopressin necessitated urgent transition to oral alternatives. However, optimal conversion ratios and clinical response remain undefined. We evaluated clinical outcomes following this supply-driven transition.

Methods: A retrospective study at a tertiary UK centre (01/01/2025–01/07/2025) identified patients with confirmed AVP-D switched from intranasal to oral desmopressin. Demographic and clinical data were collected. Conversion ratios (intranasal: oral) were calculated before and after titration.

Results: Forty two patients were included (mean age 52.6 ± 2.3; 31% male). 15/42 (35.7%) isolated AVP-D; 11/42 (26.2%) partial hypopituitarism; 16/42 (38.1%) panhypopituitarism. Median intranasal desmopressin dose pre-switch was 10 mcg/day (IQR 10–20 mcg). Initial median oral dose before titration was 200 mcg/day (IQR 100–200 mcg); final median oral dose after titration was 200 mcg/day (IQR 162.5–300 mcg). 23/42 (54.8%) were switched initially using 1:10 ratio (10 mcg intranasal desmopressin to 100 mcg oral tablet). 13/23 (56.5%) reported symptomatic recurrence, warranting further titration. The remaining 19/42 (45.2%) were switched initially using a median ratio of 1:20 (IQR 1:11.8–1:20). 10/19 (52.6%) reported symptomatic recurrence. Overall, switching from intranasal to oral desmopressin resulted in 16 patient calls, 79 additional blood tests and one hospitalisation. Similarly, the findings of The Pituitary Foundation Impact Report demonstrated that the switch led to 121/161 (75.2%) of patients reporting poorer symptomatic control post-switch, and 76/161 (47.2%) requiring additional endocrine input.

Conclusion: 45.2% (19/42) of patients achieved adequate symptom control post-switch with varying conversion ratios, and over half (13/23, 56.5%) of patients switched with an initial 1:10 conversion ratio reported symptomatic recurrence. Although a higher initial conversion ratio closer to 1:15 may reduce symptomatic recurrence in some patients, initiating treatment at a 1:10 ratio with careful up-titration represents a safe and pragmatic approach that minimises the risk of over-replacement and hyponatraemia, although inter-patient variability necessitates tailored titration. In parallel, national patient-reported data from The Pituitary Foundation Impact Report demonstrate the substantial patient and clinical burden of this supply-driven switch, highlighting the need for standardised guidance and prospective studies.

1 | Introduction

Arginine vasopressin deficiency (AVP-D), formerly known as cranial diabetes insipidus, is a chronic condition resulting from impaired synthesis and/or secretion of the posterior pituitary hormone arginine vasopressin (AVP), resulting in uncontrolled diuresis [1, 2]. Desmopressin, a synthetic form of AVP, is used in the treatment of AVP-D, in the form of oral preparations, nasal or parenteral formulations [1, 3]. It is a life-sustaining medication and omission can lead to excessive polyuria and severe dehydration [4]. However, the availability of intranasal desmopressin (Desmopressin Spray 10 micrograms/dose Nasal Spray solution, Aspire Pharma Limited, Petersfield, United Kingdom) in the United Kingdom (UK) has been suspended since March 2025 [5], necessitating the transition to a suitable alternative. Oral desmopressin was the preferred alternative at the Norfolk and Norwich University Hospital. Monitoring sodium concentrations and evaluating symptoms after switching route of administration is essential, to ensure adequate desmopressin replacement and reduce the likelihood of symptomatic recurrence and possible hospital admissions.

Several studies have assessed the outcomes of switching from intranasal to oral desmopressin and have found better disease control and lower hyponatraemia rates with oral desmopressin [6–9]. Post-marketing analyses also suggest a reduced hyponatraemia risk with oral compared to intranasal formulations [10], and other recent AVP-D cohorts also found no increased hyponatraemia risk with oral compared to intranasal formulations [11, 12].

However, there is currently no standardised guidance regarding the optimal dosage and conversion ratio when switching from nasal to oral administration.

Expert recommendations emphasise early endocrine follow-up after changes in desmopressin therapy to review sodium, urine output and hydration status [13].

We present the clinical outcomes of patients who were switched from intranasal to oral desmopressin in a tertiary UK centre. In addition, we also present patient insights on the impact of the 2025 desmopressin nasal spray shortage by The Pituitary Foundation.

2 | Methods

A retrospective cohort study was conducted at a single UK centre, between 01/01/2025 and 01/07/2025. Our methods and results were reported according to the STROBE guidelines [14].

2.1 | Setting

All patients with a confirmed diagnosis of permanent AVP-D, who were previously managed with intranasal desmopressin and required transition to oral desmopressin were identified after a search on our electronic outpatient letters database (Electronic Document Template).

2.2 | Outcomes

Clinical response was based on serum sodium concentrations (pre- and post-switch), documented symptoms of over- or under-replacement post-switch (e.g., polyuria, polydipsia), number of hospital admissions post-switch, and the number of dose titrations required during follow-up. Patients who were already established on oral desmopressin prior to the study period were excluded.

2.3 | Data Measurement

Data collection included the above, as well as the baseline intranasal desmopressin dose, dose of oral desmopressin post-switch, number of days elapsed between date of switch (as determined by date of outpatient electronic letter) and first blood test post-switch, including end date in calculation.

Demographic data such as patient age at diagnosis, gender, other hormonal replacement and pituitary function were also collected. All eligible patients were systematically included from the database search.

2.4 | Statistical Analysis

Statistics were performed using the IBM SPSS Statistics Software Version 29.0.2.0. A total of 46 patients were identified under the Endocrine Department from 01/01/2025 to 01/07/2025. Our study included 42 patients in total after applying exclusion criteria (one excluded due to already taking oral desmopressin, two excluded due to loss to follow-up, one excluded due to duplicate).

3 | Results

3.1 | Patient and Sample Characteristics

The 42 analysed patients had a mean age of 52.6 ± 2.3 years (27–82 years old). 13/42 (31%) were males. 20/42 (47.6%) were diagnosed post-surgically.

15/42 (35.7%) had isolated AVP-D. Adrenocorticotropic hormone (ACTH) deficiency was present in 24/42 (57.1%) patients, thyroid-stimulating hormone (TSH) deficiency in 24/42 (57.1%), growth hormone (GH) deficiency in 9/42 (21.4%), and gonadotrophin (FSH/LH) deficiency in 15/42 (35.7%) patients.

Table 1 summarises the baseline characteristics of the patient cohort.

3.2 | Intranasal Desmopressin and Oral Desmopressin Doses

The median daily dose of intranasal desmopressin pre-switch was 10 mcg/day (IQR 10–20 mcg). The median initial daily dose (before dose titration) was 200 mcg/day (IQR 100–200 mcg) (range 100–400 mcg). The median final daily dose of oral desmopressin (after dose titration) was 200 mcg/day (IQR 162.5–300 mcg) (range 100–550 mcg).

41/42 (97.6%) of patients were switched to Desmotabs® (Ferring Pharmaceuticals, Kiel, Germany), whilst the remaining one was switched to DesmoMelt® (Ferring Pharmaceuticals, Kiel, Germany).

TABLE 1 | Baseline characteristics of the patient cohort.

Patient ID	Sex	Age	Pituitary function	Total daily dose of Desmospray (mcg)	Bodyweight (on day of clinic right before transition date) (kg)	Initial daily ratio	Final daily ratio	First sodium concentration after switch (mmol/L) (reference range 133–146 mmol/L)	Symptom recurrence after switch	Hospital admission after switch
1	F	54	Partial hypopituitarism	20	78	1 to 10	1 to 10	139	No	No
2	F	68	Panhypopituitarism	40	71.3	1 to 7.5	1 to 7.5	143	No	No
3	F	27	Panhypopituitarism	40	58.9	1 to 10	1 to 12.5	141	Yes	Yes
4	F	52	Partial hypopituitarism	40	73	1 to 5	1 to 7.5	137	Yes	No
5	F	77	Partial hypopituitarism	10	59	1 to 40	1 to 20	126	Yes	No
6	F	81	Isolated AVP-D	10	57.5	1 to 10	1 to 10	128	No	No
7	F	33	Partial hypopituitarism	20	80.9	1 to 10	1 to 22.5	143	Yes	No
8	M	57	Partial hypopituitarism	20	108	1 to 10	1 to 10	141	No	No
9	M	56	Panhypopituitarism	10	55.6	1 to 10	1 to 10	126	No	No
10	M	52	Panhypopituitarism	10	97.9	1 to 30	1 to 30	144	No	No
11	M	54	Partial hypopituitarism	20	95.6	1 to 20	1 to 20	143	No	No
12	M	74	Panhypopituitarism	10	88.4	1 to 10	1 to 15	143	Yes	No
13	F	43	Panhypopituitarism	10	97.3	1 to 12	1 to 12	135	No	No
14	F	32	Partial hypopituitarism	10	78.7	1 to 10	1 to 10	143	No	No
15	M	58	Partial hypopituitarism	10	97	1 to 10	1 to 20	143	Yes	No
16	F	32	Panhypopituitarism	10	106.3	1 to 20	1 to 20	140	No	No
17	F	58	Isolated AVP-D	20	118.6	1 to 10	1 to 15	144	Yes	No
18	F	46	Isolated AVP-D	20	53.9	1 to 10	1 to 15	139	Yes	No
19	F	82	Isolated AVP-D	10	120.7	1 to 10	1 to 10	142	No	No
20	F	61	Isolated AVP-D	10	60	1 to 20	1 to 40	143	Yes	No
21	M	35	Partial hypopituitarism	20	105	1 to 10	1 to 25	140	Yes	No
22	M	74	Panhypopituitarism	20	93.7	1 to 5	1 to 10	142	Yes	No
23	F	63	Isolated AVP-D	30	114	1 to 10	1 to 15	145	Yes	No
24	M	56	Panhypopituitarism	10	132.8	1 to 20	1 to 30	143	Yes	No
25	F	60	Panhypopituitarism	10	82.5	1 to 10	1 to 20	145	Yes	No
26	M	27	Panhypopituitarism	10	90	1 to 20	1 to 30	141	Yes	No
27	M	44	Isolated AVP-D	10	91.4	1 to 20	1 to 20	140	No	No
28	M	64	Partial hypopituitarism	10	97	1 to 20	1 to 20	142	No	No
29	F	38	Isolated AVP-D	20	67.8	1 to 10	1 to 15	139	Yes	No

(Continues)

TABLE 1 | (Continued)

Patient ID	Sex	Age	Pituitary function	Total daily dose of Desmospray (mcg)	Bodyweight (on day of clinic right before transition date) (kg)	Initial daily ratio	Final daily ratio	First sodium concentration after switch (mmol/L) (reference range 133–146 mmol/L)	Symptom recurrence after switch	Hospital admission after switch
30	F	58	Isolated AVP-D	10	79.1	1 to 10	1 to 10	138	No	No
31	F	56	Isolated AVP-D	20	77	1 to 15	1 to 15	143	Yes	No
32	F	43	Panhypopituitarism	10	69.8	1 to 30	1 to 30	141	No	No
33	M	53	Isolated AVP-D	20	133.5	1 to 15	1 to 20	141	Yes	No
34	M	45	Panhypopituitarism	20	73.9	1 to 5	1 to 5	138	No	No
35	F	60	Partial hypopituitarism	10	86.6	1 to 10	1 to 10	134	No	No
36	F	54	Panhypopituitarism	20	76.4	1 to 10	1 to 20	141	Yes	No
37	F	56	Isolated AVP-D	10	93.4	1 to 10	1 to 15	145	Yes	No
38	F	33	Isolated AVP-D	30	83	1 to 11.67	1 to 18.33	138	Yes	No
39	F	76	Isolated AVP-D	10	81.1	1 to 10	1 to 10	139	No	No
40	F	33	Panhypopituitarism	10	69.8	1 to 10	1 to 30	137	Yes	No
41	F	37	Panhypopituitarism	20	92.6	1 to 10	1 to 10	141	No	No
42	F	46	Isolated AVP-D	20	82.5	1 to 15	1 to 20	139	Yes	No

3.3 | Symptomatic Recurrence

23/42 (54.8%) reported symptomatic recurrence (polyuria, polydipsia) post-switch, and among these, 1/42 (2.4%) had one episode of hospital admission due to AVP-D post-switch.

Among the 9/24 patients previously receiving intranasal desmopressin 10 mcg daily, 55.6% (5/9) were switched to Desmotabs® 100 mcg daily, 33.3% (3/9) to Desmotabs® 200 mcg daily, and 11.1% (1/9) to Desmotabs® 400 mcg daily.

Out of the 10/24 patients on intranasal desmopressin 20 mcg daily, 10% (1/10) were switched to Desmotabs® 100 mcg daily, 60% (6/10) were switched to Desmotabs® 200 mcg daily and 30% (3/10) to Desmotabs® 300 mcg daily.

Out of the 2/24 patients on intranasal desmopressin 30 mcg daily, one was switched to 200 mcg and one to 350 mcg daily.

Out of the remaining 2/24 patients on intranasal desmopressin 40 mcg daily, one was switched to 200 mcg and one to 400 mcg daily.

The one patient switched to DesmoMelt® did not experience any symptomatic recurrence post-switch.

3.4 | Dose Titrations

19/42 (45.2%) did not require any dose titrations post-switch. Out of the 23 that required dose titration, 19/23 (82.6%) required one dose titration post-switch, three (13%) required two dose titrations post-switch and one (4.3%) required three dose titrations post-switch.

Table 2 summarises the dose titrations of all the patients post-switch, if it was required.

3.5 | Conversion Ratios Before and After Dose Titrations

Of the 42 patients, 23 were switched initially using 1:10 ratio (10 mcg intranasal desmopressin to 100 mcg oral tablet). Out of these 23, 56.5% ($n = 13$) reported inadequate symptom control, warranting further titration.

The remaining 19 patients who were switched initially using a median ratio of 1:20 (IQR 1:11.8–1:20, range 1:5–1:40). 10/19 (52.6%) reported inadequate symptom control, warranting further titration.

3.6 | Overall

The median initial conversion ratio of intranasal desmopressin to oral desmopressin (based on the initial daily dose of oral desmopressin, before dose titrations) was 1:10 (IQR 1:10–1:15) (range 1:5–1:40).

The median final conversion ratio of intranasal desmopressin to oral desmopressin (based on the final daily dose of oral desmopressin, after dose titrations) was 1:15 (IQR 1:10–1:20) (range 1:5–1:40).

In the 23 patients who reported symptomatic recurrence post-switch, the median initial conversion ratio before dose titration was 1:10 (IQR 1:10–1:15) (range 1:5–1:40). All patients required dose titrations. The median final conversion ratio after dose titration was 1:20 (IQR 1:15–1:21.3) (range 1:7.5–1:40).

In the 19 patients who did not report symptomatic recurrence post-switch, the median conversion ratio was 1:10 (IQR 1:10–1:20) (range 1:5–1:30).

There was found to be no statistically significant difference between the final conversion ratios of the patients who did not report symptomatic recurrence post-switch, and the initial conversion ratios after dose titration, of the patients who did report symptomatic recurrence post-switch ($p = 0.582$, $U = 245.5$, Mann-Whitney U test).

There was found to be a statistically significant difference between the final conversion ratios of the patients who did not report symptomatic recurrence post-switch, and the final conversion ratios after dose titration, of the patients who did report symptomatic recurrence post-switch ($p = 0.0077$, $U = 322.5$, Mann-Whitney U test).

Figure 1 illustrates paired patient changes in oral desmopressin dose following switch. Each line represents an individual patient, connecting the initial dose to the final dose after titration.

3.7 | Sodium Concentrations

The median time to the first follow-up blood test post-switch (calculated from date of outpatient letter indicating switch, to date of follow-up blood test, including end date in calculation) was 18.5 days (IQR 13–40 days, range 4–106 days).

Overall, the median sodium concentration of the 42 patients (taken at the first follow-up blood test post-switch) was 141 mmol/L (reference range 133–146 mmol/L) (IQR 139–143, range 126–145).

3/42 (7.1%) patients developed hyponatraemia post-switch, at the first follow-up blood test. Two patients did not report symptomatic recurrence (128 mmol/L, 126 mmol/L) and did not require dose titration. Sodium concentrations normalised without intervention by the next blood test (10 days and 7 days after respectively). The remaining one patient reported symptomatic recurrence (urinary frequency, 126 mmol/L), and subsequently required one dose titration (400 to 200 mcg). This patient had an intact feeling of thirst and sodium concentration normalised by the next blood test (7 days after). Advice regarding desmopressin escape was given.

There was no statistically significant difference ($p > 0.05$) between the median sodium concentrations of the 23 patients who experienced symptomatic recurrence post-switch (141 mmol/L, IQR 139–143, range 126–145) and the 19 patients who remained stable post-switch (140 mmol/L, IQR 138–142, range 126–144).

3.8 | Hospital Admission

One patient required hospitalisation due to symptomatic recurrence post-switch (polyuria and polydipsia), with a sodium concentration of 143 mmol/L, and subsequently required dose titration (from 400 to 500 mcg), which resolved the symptoms.

TABLE 2 | Dose titrations of all the patients post-switch, if it was required.

Total daily intranasal desmopressin spray dose pre-switch (mcg)	Total daily Desmotabs® dose post-switch, before dose-titrations (mcg)	Number of patients	Number of patients who stayed on initial dose (did not report symptomatic recurrence therefore did not require dose titration)	Number of patients who reported symptomatic recurrence therefore required dose titration	Total daily Desmotabs® dose post-switch, after dose-titrations (mcg)
10	100	12 (28.6%)	7 (16.7%)	5 (11.9%)	150 ($n = 2$); 200 ($n = 2$); 300 ($n = 1$)
	120 (DesmoMelt®)	1 (2.4%)	1 (2.4%)	0	—
	200	6 (14.3%)	3 (7.1%)	3 (7.1%)	300 ($n = 2$); 400 ($n = 1$)
	300	2 (4.8%)	2 (4.8%)	0	—
	400	1 (2.4%)	0	1 (2.4%)	200 ($n = 1$)
20	100	2 (4.8%)	1 (2.4%)	1 (2.4%)	200 ($n = 1$)
	200	10 (23.8%)	4 (9.5%)	6 (14.3%)	300 ($n = 3$); 400 ($n = 1$); 450 ($n = 1$); 500 ($n = 1$)
	300	3 (7.1%)	0	3 (7.1%)	300 ($n = 1$); 400 ($n = 2$)
30	200	1 (2.4%)	0	1 (2.4%)	300 ($n = 1$)
	350	1 (2.4%)	0	1 (2.4%)	550 ($n = 1$)
40	200	1 (2.4%)	0	1 (2.4%)	300 ($n = 1$)
	300	1 (2.4%)	1 (2.4%)	0	—
	400	1 (2.4%)	0	1 (2.4%)	500 ($n = 1$)

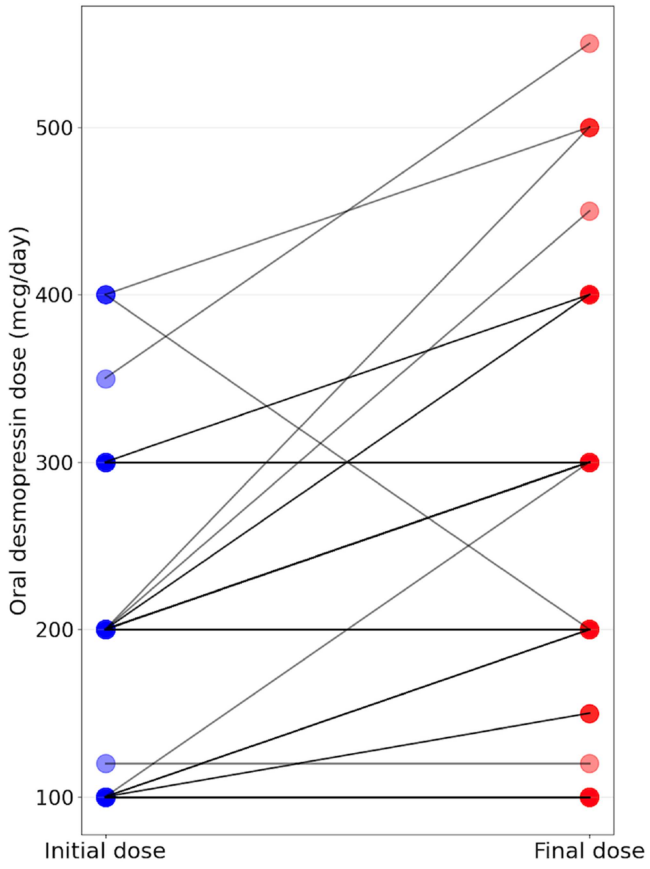

FIGURE 1 | Paired patient changes in oral desmopressin dose following switch. Each line represents an individual patient, connecting the initial dose to the final dose after titration. Point shading reflects overlap density, with darker circles indicating a larger number of patients at the same dose.

3.9 | Predictors of Conversion Ratio and Initial Conversion Ratio, Final Conversion Ratio and Requirement for Dose Titration

3.9.1 | *Age*

Exploratory analyses did not identify age as a predictor of initial conversion ratio ($\rho = -0.156$, $p = 0.323$, Spearman's rank correlation), final conversion ratio ($\rho = -0.277$, $p = 0.075$, Spearman's rank correlation), or requirement for dose titration ($U = 229.0$, $p = 0.586$, Mann-Whitney U test) (median age with no titration 56 (IQR 46–64), median age with titration 57.5 (IQR 46–64)).

3.9.2 | *Sex*

Exploratory analyses also did not identify sex as a predictor of initial conversion ratio ($U = 230.5$, $\rho = 0.320$, Mann-Whitney U test), final conversion ratio ($U = 243.5$, $p = 0.201$, Mann-Whitney U test), or requirement for dose titration (OR 0.75, $p = 0.748$, Fisher's exact test).

3.9.3 | *Bodyweight*

Exploratory analyses also did not identify bodyweight as a predictor of initial conversion ratio ($\rho = 0.20$, $p = 0.21$, Spearman's rank correlation), final conversion ratio ($\rho = 0.18$, $p = 0.26$, Spearman's rank correlation), or requirement for dose titration ($U = 207.0$, $p = 0.78$, Mann-Whitney U test) (median bodyweight with no titration 86.6 kg (IQR 76–97.2 kg), median bodyweight with titration 82.5 kg (IQR 71.4–95.3 kg).

3.9.4 | *Disease Duration*

Exploratory analyses did not identify disease duration (deemed from date of diagnosis to date of switch, rounded to years) as a predictor of initial conversion ratio ($\rho = -0.12$, $p = 0.440$, Spearman's rank correlation) and final conversion ratio ($\rho = -0.29$, $p = 0.063$, Spearman's rank correlation), or requirement for dose titration ($U = 234.0$, $p = 0.88$, Mann-Whitney U test) (median duration with no titration 23 years (IQR 7–36), median duration with titration 21 years (IQR 5–38)).

Patients with both recent diagnosis and long-standing AVP-D exhibited wide variability in final conversion ratios, regardless of whether dose titration was required.

3.9.5 | *Co-Existent Pituitary Hormone Insufficiency*

When stratified according to the presence of whether there were additional co-existent pituitary hormone deficiencies, no significant relationship was observed between additional hormonal insufficiency and the need for dose titration ($\chi^2 = 1.39$, $p = 0.50$, chi-square test).

Likewise, there was no statistically significant difference in initial conversion ratios ($H = 2.75$, $p = 0.253$, Kruskal-Wallis test) and final conversion ratios ($H = 0.31$, $p = 0.86$, Kruskal-Wallis test) (Figure 2) between patients with isolated AVP-D, partial hypopituitarism, or panhypopituitarism.

3.9.6 | *Relationship of Split Dosing and Symptomatic Recurrence*

Out of 42 patients, 28 (66.7%) were on once-daily (OD) regimen with the intranasal desmopressin of whom 12/28 (42.9%) had recurrence of symptoms and therefore required dose-titration post-switch.

The remaining 14 patients (33.3%) were on twice-daily (BD) regimen with the intranasal desmopressin of whom 11/14 (78.6%) required dose-titration post-switch.

Patients on a BD regimen pre-switch were statistically significantly more likely to require dose titration post-switch ($p = 0.048$, Fisher's exact test).

3.9.7 | *Service Impact*

Patients who are established and stable on intranasal desmopressin are usually reviewed annually along with annual blood tests. Switching from intranasal desmopressin to oral tablets resulted in an additional 16 patient calls to the endocrine nurses, 79 additional blood tests, and one hospitalisation.

3.9.8 | *The Pituitary Foundation's Desmopressin Shortage Impact Report*

In parallel to our clinical findings, recent national data reinforced the wide-ranging impact of the intranasal

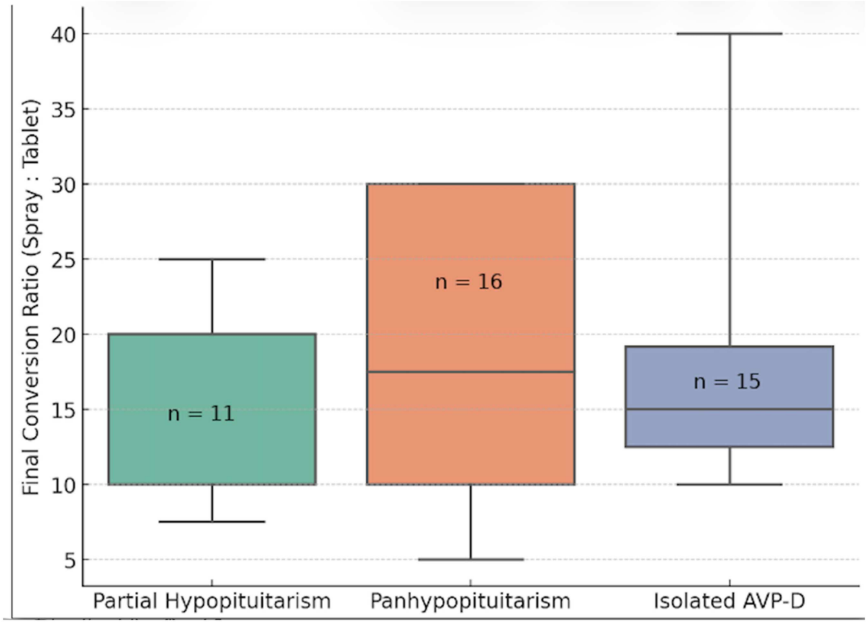

FIGURE 2 | Relationship of co-existent pituitary hormone insufficiency and final conversion ratio ($n = 11$ partial hypopituitarism; $n = 16$ panhypopituitarism; $n = 15$ isolated AVP-D).

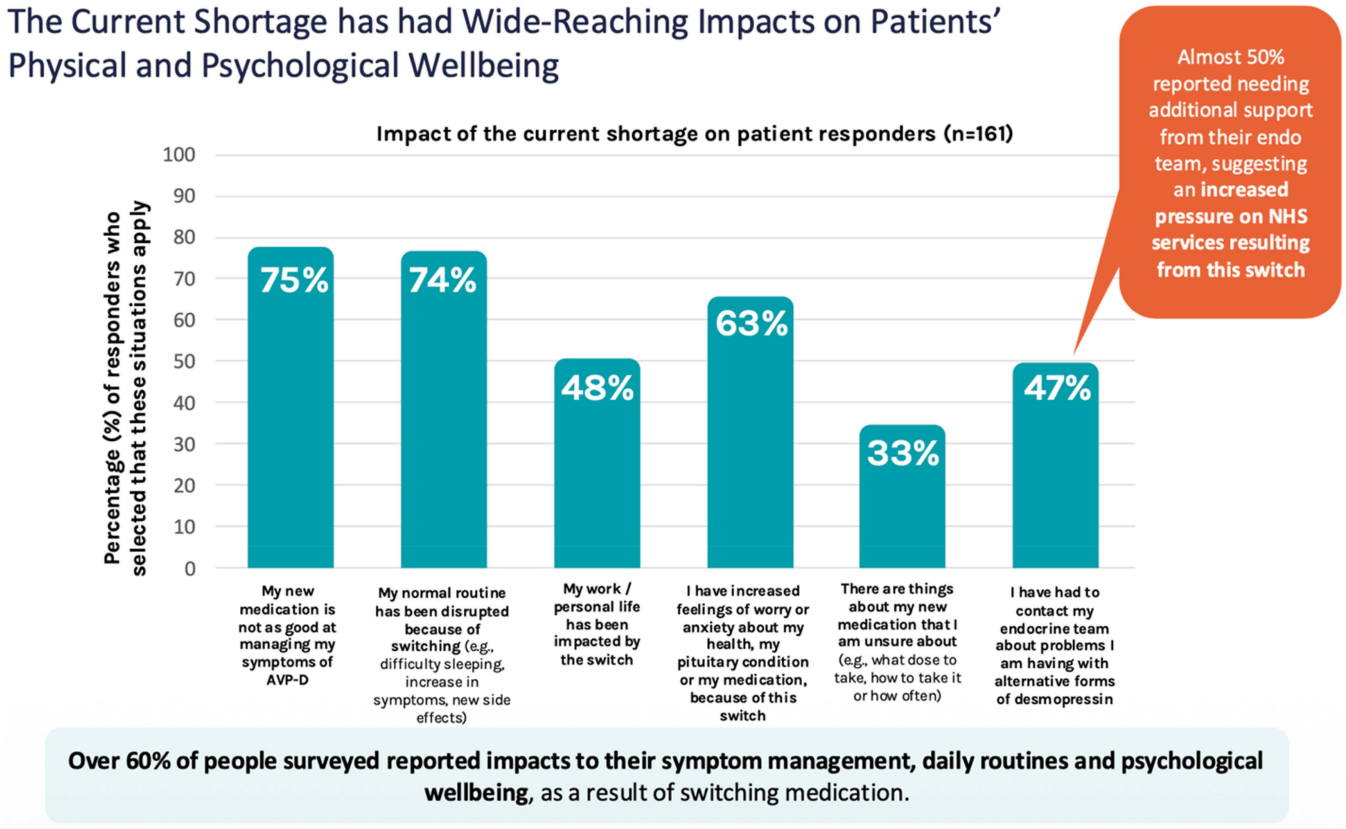

FIGURE 3 | Survey from The Pituitary Foundation showing the wide-ranging impact of the intranasal desmopressin shortage.

desmopressin shortage. The Pituitary Foundation conducted a national survey on 224 patients in June 2025, which found that 176/224 (78.6%) of respondents had previously relied on intranasal desmopressin, with the majority now transitioned to Desmotabs® (147/192; 76.6%) or DesmoMelts® (45/192; 23.4%). 121/161 (75.2%) reported poorer symptomatic control post-switch, causing disruption to daily routines, along with negative psychological effects (Figure 3).

Almost half (76/161; 47.2%) required additional input from their local endocrine teams, reflecting increased pressure on NHS services (Figure 3). Patients cited many difficulties resulting

from the switch. Themes included poor absorption and delayed action of oral alternatives, sleep disturbance, urinary incontinence, social withdrawal, and heightened anxiety regarding sodium fluctuations and long-term stability. These patient experiences highlight the profound human and healthcare system burden of this supply-driven switch, complementing our centre's clinical data and underscoring the urgent need for clear conversion protocols and sustainable access to desmopressin therapies (Supporting Information S1).

4 | Discussion

4.1 | Principal Findings

The results of our study highlight that over half of patients with AVP-D who were switched from intranasal to oral desmopressin experienced inadequate symptom control, requiring dose titration. While higher initial conversion ratios (e.g., closer to 1:15) may reduce symptomatic recurrence in some patients, the use of a 1:10 conversion ratio remains a reasonable and safe initial strategy, with careful up-titration based on clinical response, to minimise the risk of over-treatment and hyponatraemia.

4.2 | Comparison With Related Literature

The commonly used initial conversion ratio when switching from intranasal desmopressin to oral desmopressin is 10:100 mcg (1:10); however, pharmacokinetic and regulatory data suggest higher conversion ratios. For instance, the bioavailability of Stimate® Nasal Spray when administered by the intranasal route is between 3.3% and 4.1% [15], whilst desmopressin bioavailability via the oral route has been reported to be around 0.08%–0.16% [16], implying a conversion ratio favouring higher ranges. Other studies have also found on average a 10–20 times higher bioavailability with the nasal compared to oral form [17–20], suggesting a dosing ratio of 1:10–1:20, whilst higher conversion ratios according to bioequivalence data have also been shown to be at 1:24 [21, 22].

Similar to our findings, prior studies have shown that dosage requirements varied widely between patients, with mean daily dose ratios ranging from 1:12 to 1:96 observed (mean ratio 1:24) [8], whilst earlier switch data likewise suggested a similar mean dosage ratio of 1:20 [23]. Previous regulatory pharmacodynamic data by the US FDA also indicated 0.2–0.4 mg oral doses were similar to the 0.01 mg intranasal dose, corresponding to a ratio of 1:20–1:40, but due to the highly variable pharmacodynamic data between subjects, individual dosing titration is recommended [24]. Inter-patient variability was also found in another cohort where the mean ratio was 17 ± 7.6:1 [25], similar to another proposed ratio of 1:18 on a cohort of 14 patients [26].

Several studies have demonstrated that the incidence of hyponatraemia is significantly reduced in patients who were on oral desmopressin compared to intranasal formulations [5–8]. Kataoka et al. proposed the reason for this phenomenon was that the concentration of desmopressin peaked sooner with intranasal desmopressin and remained higher for longer, leading to increased risk of excess water consumption and hyponatraemia [7]. However, the risk of hyponatraemia becomes more likely with all formulations [27]. Previously, a cohort study involving 144 patients showed that 77 (53.5%) developed hyponatraemia within the first 30 days of desmopressin (regardless of route of administration) [22], with another suggesting a small dose of desmopressin should be started initially and increased as necessary [28].

Advantages of oral desmopressin over the intranasal formulations have also been shown as the effect of food ingestion was not found to affect the pharmacodynamics of oral desmopressin [29], whereas with intranasal desmopressin, changes in the nasal mucosa as a result of rhinitis, scarring or oedema can cause erratic, unreliable absorption [30–32]. The effectiveness and ease of administration of oral desmopressin make it preferable to most patients, compared to nasal spray. This is supported by an observational study of almost 200 patients, 100% of whom chose oral over nasal DDAVP [33].

The survey by The Pituitary Foundation highlights the significant impact the transition has had on patients with AVP-D, particularly on their quality of life, with the majority (74%) finding the switch has disrupted normal routine and 63% experiencing increased feelings of worry or anxiety about their condition. Given that this group of patients are more likely to experience psychological comorbidities including depression and anxiety, despite adequate symptom control [32], the long-term effects on their mental health because of this transition is concerning and clear guidance to support patients through this period is needed.

4.3 | Strengths and Limitations

Our study presents some strengths and limitations. One major strength of this study is that it is the first to demonstrate the impact that the national shortage of intranasal desmopressin has had on patients with AVP-D, and also, to our knowledge, the largest reported UK cohort examining real-world outcomes following this supply-driven switch. As there is no standardised guidance for this nor any established literature, we hope this data can guide clinicians on making appropriate changes from intranasal to oral desmopressin. Due to this time-critical clinical context, our study is highly relevant to clinicians dealing with this problem in real time.

Another important strength is the practical applicability of our findings. By reporting real-world dosing strategies, symptomatic recurrence, biochemical safety outcomes, and the need for dose titration following conversion, our study reflects everyday clinical management. Our study also stratified patients by whether there was any co-existent pituitary hormone deficiency (isolated AVP-D, partial hypopituitarism, panhypopituitarism) and by dosing regimen (OD vs. BD), ensuring the results are generalisable across multiple clinical sub-groups.

We also evaluated the impact of this switch on our service, which strengthens the paper by showing the wider healthcare consequences and not just clinical outcomes, and can inform service planning and resource allocation in future shortages.

However, there are limitations. Firstly, our retrospective design limits generalisability. The relatively small cohort size also reduces statistical power, particularly for sub-group analyses. As follow-up was relatively short, we were also unable to

evaluate the longer-term safety and stability of patients maintained on oral desmopressin post-switch, including risks such as hyponatraemia. The enforced nature of the switch also introduces potential confounding. Clinicians may have been more cautious with dosing and monitoring during the shortage, potentially affecting outcomes compared with a planned, elective transition. The lack of a control group of patients maintained on intranasal desmopressin during the period also limits interpretation.

5 | Conclusion

Our study, investigating the switch from intranasal to oral desmopressin, demonstrated that over half of patients had symptomatic recurrence and therefore required dose titration to ensure adequate replacement. Although over half of patients switched with an initial 1:10 conversion ratio (13/23, 56.5%) reported symptomatic recurrence; overall, a substantial proportion (19/42, 45.2%) of patients achieved adequate symptom control post-switch with varying conversion ratios, without further need for titration.

While higher initial conversion ratios (e.g., closer to 1:15) may reduce symptomatic recurrence in some patients, the use of a 1:10 conversion ratio remains a reasonable and safe initial strategy, with careful up-titration based on clinical response, to minimise the risk of over-treatment and hyponatraemia. Importantly, national patient-reported data from The Pituitary Foundation support these findings, demonstrating significant symptomatic, psychological and clinical burden associated with the intranasal desmopressin shortage.

Given the significant inter-patient variability in dosing and conversion ratios, tailored titration remains essential. Further studies to investigate the long-term clinical outcomes of patients on oral desmopressin following switch from intranasal formulation are needed to facilitate the management of patients with AVP-D.

6 | Proposed Question

With the return of intranasal desmopressin in December 2025, clinicians are now faced with a critical question: should patients be switched back to their original therapy, or remain on oral desmopressin if stable?

Author Contributions

Conceptualisation, R.A; Data curation, T.T and A.M and A.W; Formal analysis, T.T, Investigation, T.T, A.M, A.W; Methodology, R.A.; Supervision, R.A; Validation, R.A, Visualisation, T.T; Writing- original draft, T.T and A.M; Writing- review and editing, F.S, K.D and R.A; Survey curation and distribution, A.S and P.M. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The authors confirm that the data supporting the findings of this study are available within the article.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.
TPF_Desmopressin Shortage Impact Report_Final.pdf.